CHILD PSYCHOPATHOLOGY

THIRD EDITION

edited by

ERIC J. MASH

RUSSELL A. BARKLEY

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Preface

Research in child, adolescent, and developmental psychopathology continues to flourish, even more so than when the first edition of this text was published. Previously recognized disorders are even better delineated than they were only a few years ago, and a few new ones seem to have been discovered along the way. The publication rate in this field is extraordinary, with many journals now focusing exclusively on childhood mental illness and health, and numerous articles on children appearing each month in journals that were once the exclusive domains of adult psychopathology. To those of us who take a developmental view of psychopathology, this is a most gratifying state of affairs as we come to recognize the roots of many adult disorders in childhood and adolescence. The down side, of course, is that even the expert researchers in the various disorders that constitute this field find it harder than ever to keep abreast of research findings appearing at such a rapid clip. And woe to the clinical professionals who must deal with these childhood disorders: They may find themselves quickly and hopelessly behind in the advancements occurring in the understanding of these clinical conditions. Hence the need for a volume such as this, and especially for its third edition, to assist the clinical professional, student, and even expert in remaining current on child and adolescent psychopathological disorders.

Now more than ever, the field of child psychopathology epitomizes the dynamic, accumulative, and self-correcting nature of the scientific enterprise, as new findings expand upon and are assimilated with the established facts in any given disorder. Often these new findings challenge older theoretical or conceptual assumptions or more explicit models of these disorders, at times even leading to small-scale paradigm shifts in perspective. In short, the literature on child and adolescent psychopathology is alive, well, prosperous, and rapidly advancing. Old questions undoubtedly get answered, but along the way those answers raise new questions for researchers to pursue in ever more complex programs of research on each of the childhood disorders covered here. Although the pace and excitement levels vary considerably across different areas of child psychopathology, within each area the eager anticipation of new knowledge remains palpable as new lines of research and methodologies—such as neuroimaging, behavioral and molecular genetics, structural equation modeling, and longitudinal designs—come to overlap old ones and so provide greater opportunities to better understand these disorders.

The challenge remains for this third edition as it was for the first: How are we to capture the current status of this rapidly evolving field? Our answer was again to identify those experts who

have dedicated their professional careers to these disorders, and let them—unfettered by fashion or the editors' pet perspectives—tell us what they have learned. In other words, we tried to find the most knowledgeable professionals on particular disorders and asked them to provide up-to-date and comprehensive summaries of the nature of the disorders in which they have specialized. We asked only that their discussions be grounded in their respective bodies of scientific literature, eschewing clinical lore, dogmatic wisdom, the sayings of the guru *du jour*, or political agendas. We also asked that they set aside the concerns of assessment and treatment of their respective disorders, so as to have ample room for the burgeoning findings on the disorders themselves. These other topics are the focus of related books (Mash & Barkley, 2006, 2007).

In essence, each author or group of authors was once more challenged to answer these basic questions: "What do we know about this disorder?", "What are the implications for future research into further understanding the disorder?", and, just as important, "Where are the current limitations or gaps in our knowledge that deserve future attention?" If sound, scientifically grounded theoretical or conceptual models of the disorder exist, then these were also to be reviewed. In addressing these questions, the experts assembled here were directed to cover (1) the nature of the behavior, symptoms, and/or cognitive and emotional deficits that typify the core of each disorder; (2) the historical perspective; (3) any criteria that exist to establish its presence (diagnosis) and a candid appraisal of those criteria; (4) epidemiological knowledge pertaining to the prevalence, gender distribution, and ethnic and cultural factors associated with the disorder; (5) the developmental course and varied pathways shown to be associated with the disorder; (6) the psychiatric, psychological, and social disorders or difficulties that most often coexist with the disorder (comorbidity); and (7) a survey of those things believed to give rise to the disorder (etiology). Once more, we believe that the many authors assembled here have done a marvelous job accomplishing their charge. We trust the reader will concur.

As before, we are indebted to the professionals who agreed to write for this edition on their respective disorders. We genuinely appreciate the substantial time commitment they have made to writing their chapters, many of which are major updates of their previous work. Many others deserve our gratitude as well, including Kitty Moore, Sawitree Somburanakul, Marie Sprayberry, and Laura Specht Patchkofsky, for shepherding the manuscript through the production process. Special thanks are also owed to our long-time friends, the founders of The Guilford Press, Seymour Weingarten (Editor-in-Chief) and Bob Matloff (President), for more than 30 years of support for our various books, including this one. Last, but hardly least, we thank our families—Heather Mash, and Pat, Ken, and Steve Barkley—for relinquishing the family time such a project requires, and for their support, patience, and encouragement of our careers in this field.

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PART I

INTRODUCTION TO CHILD PSYCHOPATHOLOGY

CHAPTER 1

Child Psychopathology

A Developmental–Systems Perspective

ELIZABETH P. HAYDEN
ERIC J. MASH

This volume provides a comprehensive account of the diagnosis, phenomenology, developmental pathways, correlates, causes, and outcomes of psychopathology in children.[1] Our understanding of developmental psychopathology has grown exponentially over the past several decades (Beauchaine & Hinshaw, 2013; Cicchetti, 2006; Cicchetti & Toth, 2009; Mash & Wolfe, 2013; Rutter, 2005). New conceptual frameworks and findings, as well as advances in knowledge and methods, continue to further our understanding of childhood disorders (Granic, 2005; Iacono & Malone, 2011; Moffitt, 2005; Roth & Sweatt, 2011; Rutter & Sroufe, 2000; Sameroff & Mackenzie, 2003), as well as our ability to assess and treat children with problems (Gunnar, Fisher, & The Early Experience, Stress, and Prevention Network, 2006; Kraemer et al., 2003; March, 2009; Mash & Barkley, 2006; Weisz, Sandler, Durlak, & Anton, 2005). However, this understanding is tempered by the often unsystematic and fragmented fashion in which research findings in child psychopathology have accrued, and by the conceptual and research complexities inherent in the study of such a rapidly changing and socially embedded organism as the child (Hinshaw, 2001; Sameroff & Mackenzie, 2003). In this introductory chapter, we address several central themes and issues related to conceptualizing childhood dysfunction and its many determinants. In doing so, we provide a developmental–systems framework for understanding child psychopathology—one that emphasizes the role of developmental processes, the importance of context, and the influence of multiple and interacting events and processes in shaping adaptive and maladaptive development.

FACTORS THAT COMPLICATE THE STUDY OF CHILD PSYCHOPATHOLOGY

Since modern views of mental illness began to emerge in the late 18th and early 19th centuries, the study of psychopathology in children has lagged behind that of adults (Silk, Nath, Siegel, & Kendall, 2000). For example, in 1812, Benjamin Rush, the first American psychiatrist, suggested that children were less likely to suffer from mental illness than adults because the immaturity of their developing brains would prevent them from retaining the mental events that caused insanity (Silk et al., 2000). However, it is now well established that many childhood disorders are common, early-occurring, and chronic, and that they exact a high toll from children, their families, and society (Costello, Egger, & Angold, 2006; Costello, Foley, & Angold, 2006). Furthermore, disorders of childhood often show significant homo- and heterotypic continuity with later

child and adult psychopathology (Bufferd, Dougherty, Carlson, Rose, & Klein, 2012; Copeland, Shanahan, Costello, & Angold, 2009; Reef, Diamantopoulou, van Meurs, Verhulst, & van der Ende, 2009), further supporting the relevance of childhood psychopathology for long-term adjustment. Looking backward from adulthood, epidemiological researchers have found that many adults with a mental disorder first developed psychopathology as children (Kessler et al., 2005). Thus interest in the study of child psychopathology has rightly increased dramatically.

However, an array of unresolved issues hampers progress in the investigation of psychopathology in children. Critically, issues concerning the conceptualization and definition of psychopathology in children continue to be vigorously debated (Rutter & Uher, 2012). Until fairly recently, much of the field's accumulated knowledge about the phenomenology of disorders of childhood was extrapolated from work with adults. For example, only in recent decades have child-focused models of depressive disorders emerged (e.g., Abela & Hankin, 2008). While it is well established that children can and do meet criteria for depression derived largely from research with adults, it is also clear that there are key differences in the presentation of the disorder across development (Rohde, Lewinsohn, Klein, Seeley, & Gau, 2013; Weiss & Garber, 2003). Furthermore, in contrast to adult forms of the disorder, evidence for the genetic basis of childhood depression is decidedly mixed (Rice, 2010), suggesting that aspects of models of adult depression may not extrapolate well to earlier manifestations of the disorder. This is but one example of the complexities regarding continuities and discontinuities of disorders across development.

Even in studies conducted with children, much of our knowledge is based on findings obtained at a single point in a child's development and in a single context. Although useful, such findings provide still photographs of moving targets and fail to capture the dynamic changes over time that characterize most forms of child psychopathology (Achenbach & Dumenci, 2001; Lewis & Granic, 2000). Although contextual models (e.g., Bronfenbrenner, 1977) and longitudinal approaches (e.g., Robins, 1966) have been applied to the field of child study for decades, researchers have only fairly recently begun to use developmentally sensitive systems-oriented models to account for the emergence of psychopathology in children (Granic, 2005; Sameroff, 2000). While longitudinal studies have become much more common, such studies are complicated by multiple issues including the question of how to best implement developmentally sensitive measures that can differentiate between true change and stability across a broad span of development from change in measurement strategy (Singer & Willett, 2003, pp. 13–14). In addition, many prior studies have not consistently attended to the broader familial, social, and cultural contexts in which atypical child development occurs (Davies & Cummings, 2006; Marks, Patton, & García Coll, 2011; Serafica & Vargas, 2006), often focusing solely on intrinsic characteristics of the child to the neglect of the broader context in which development unfolds.

The study of child psychopathology is further complicated by the fact that many childhood problems are not narrow in scope or expression, and that most forms of psychopathology in children are known to overlap and/or coexist with other disorders (Angold, Costello, & Erkanli, 1999; Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Drabick & Kendall, 2010; Lilienfeld, 2003). For example, it has been established for some time that there is pervasive overlap among such problems as child maltreatment, violence, emotional and behavioral disorders, substance abuse, delinquency, and learning difficulties, between childhood anxiety and depression and between reading disabilities and anxiety and depression (e.g., Garber & Weersing, 2010; Oshri, Rogosch, & Cicchetti, 2013; Seligman & Ollendick, 1998; Willcutt & Pennington, 2000b). Many behavioral and emotional disturbances in youth are also associated with specific physical symptoms and/or medical conditions and poor health outcomes (Costello, Egger, & Angold, 2006; Nigg, 2013; Pinquart & Shen, 2010; Reynolds & Helgeson, 2011; Spady, Schopflocher, Svenson, & Thompson, 2005).

It is also the case that distinct boundaries between many commonly occurring childhood behaviors (e.g., noncompliance, defiance) and those problems that come to be labeled as "disorders" (e.g., oppositional defiant disorder) are not easily drawn (e.g., Loeber, Burke, Lahey, Winters, & Zera, 2000). There is mounting evidence that most forms of psychopathology differ *in degree* from normative behavior, rather than *in kind* (i.e., distinctions between normal and abnormal behavior are typically quantitative, rather than qualitative; see Coghill & Sonuga-Barke, 2012, for a review of this issue in child psychopathology). Furthermore, judgments of deviancy often depend as much on other child characteristics (e.g., age, sex, intelligence), the situational appropriateness of a child's behavior, the social and cultural context in which judgments are made,

and the characteristics and decision rules of adults who make these judgments as they do on any specific behaviors displayed by the child (Achenbach, 2000; De Los Reyes & Kazdin, 2005; Mash & Barkley, 2007).

It has become increasingly evident that most forms of child psychopathology are etiologically heterogeneous and cannot be attributed to a single unitary cause. Although a handful of rare disorders (e.g., phenylketonuria, fragile-X intellectual disability, Rett's disorder) may be caused by single genes, behavioral and molecular genetics research indicate that more common and complex disorders are likely the result of multiple genes (Goldsmith, Gottesman, & Lemery, 1997; McGuffin, Riley, & Plomin, 2001; O'Conner & Plomin, 2000), and that most forms of child psychopathology are likely to have an oligo- or polygenic basis, involving susceptibility genes that interact with one another and with environmental influences to result in observed levels of impairment (Dodge & Rutter, 2011; Dodge & Sherrill, 2007; Moffitt, Caspi, & Rutter, 2006; State, Lombroso, Pauls, & Leckman, 2000). Child and family disturbances are likely to result from multiple, frequently co-occurring, reciprocal, and interacting risk factors, causal events, and processes (e.g., El-Sheikh, Keiley, Erath, & Dyer, 2013; Jaffee & Price, 2007; Rutter, 2007a). Contextual events exert considerable influence in producing child and adolescent disorders—an influence that is almost always equivalent to, or greater than, those factors usually thought of as residing "within" the child (Davies & Cummings, 2006; Reiss & Neiderhiser, 2000; Rutter, 2000). Furthermore, it has become increasingly clear that genetic influences on disorder risk can no longer be assumed to be static in their effects, as the functional impact of polymorphisms is further moderated by an array of regulatory processes known as "epigenetic effects" (Mill, 2011; Zhang & Meaney, 2010), some of which unfold in response to environment conditions. For example, animal models indicate that epigenetic effects may account for the influence of early caregiver behavior on offspring outcomes via its impact on the expression of specific genes (Weaver, Meaney, & Szyf, 2006). Life experiences that alter gene expression may also account for monozygotic twin discordance on highly heritable psychiatric phenotypes (e.g., Petronis et al., 2003). The best way to capture this dynamic interplay between genetic and environmental risks with respect to psychopathology processes has yet to be determined.

Numerous risk markers for child psychopathology have been identified, including genetic influences (e.g., Goodyer, Bacon, Ban, Croudace, & Herbert, 2009; Gotlib, Joormann, Minor, & Hallmayer, 2008; Sheikh et al., 2013); temperament (e.g., Hayden, Klein, Durbin, & Olino, 2006; Olino, Klein, Dyson, Rose, & Durbin, 2010); insecure child–parent attachments (e.g., Lee & Hankin, 2009; Priddis & Howieson, 2012); social-cognitive deficits (e.g., Luebbe, Bell, Allwood, Swenson, & Early, 2010; Zadeh, Im-Bolter, & Cohen, 2007); deficits in social learning (e.g., Arsenio & Lemerise, 2010; Lansford, Malone, Dodge, Pettit, & Bates, 2010); emotion regulation and dysregulation (e.g., Feng et al., 2009; Tortella-Feliu, Balle, & Sesé, 2010); effortful control and related constructs (Eisenberg et al., 2005; Gusdorf, Karreman, van Aken, Dekovic, & van Tuijl, 2011); neuropsychological and/or neurobiological dysfunction (e.g., Cicchetti & Cannon, 1999; Lopez-Duran, Kovacs, & George, 2009); maladaptive patterns of parenting and maltreatment (e.g., Beauchaine, Neuhaus, Zalewski, Crowell, & Potapova, 2011; Cicchetti & Toth, 2005; Harkness, Stewart, & Wynne-Edwards, 2011; Lovejoy, Graczyk, O'Hare, & Neuman, 2000); parental psychopathology (e.g., Goodman & Gotlib, 1999; Pettit, Olino, Roberts, Seeley, & Lewinsohn, 2008); parental discord (e.g., Fear et al., 2009; Pagani, Japel, Vaillancourt, Côté, & Tremblay, 2008; Shelton & Harold, 2008); limited family resources and other poverty-related life stressors (e.g., Dupéré, Leventhal, & Lacourse, 2009; Najman et al., 2010; Schreier & Chen, 2013; Tracy, Zimmerman, Galea, McCauley, & Vander Stoep, 2008); institutional deprivation (e.g., Ellis, Fisher, & Zaharie, 2004); and a host of other factors. However, these factors cannot be understood in isolation, and for most disorders, research does not support granting central etiological status to any single risk or causal factor (e.g., Sameroff, 2010).

Since the many causes and outcomes of child psychopathology are often interrelated and operate in dynamic and interactive ways over time, they are not easy to disentangle. The designation of a specific factor as a cause or an outcome of child psychopathology usually reflects (1) the point in an ongoing developmental process at which the child is observed, and (2) the perspective of the observer. For example, a language deficit may be viewed as a disorder in its own right (e.g., language disorder), the cause of other difficulties (e.g., impulsivity), or the outcome of some other condition or disorder (e.g., autism spectrum disorder). In addition, biological and environmental determinants interact at all periods of development. For example, Belsky and de Haan (2011) recently noted that the characteristic

styles parents use influence critical patterns of cortical and subcortical development across childhood and well into adolescence. Consistent with this, Dougherty, Klein, Rose, and Laptook (2011) reported that familial depression and parental hostility interacted to predict heightened cortisol reactivity to stress in a sample of community-dwelling preschoolers—a finding that suggests altered activity of the stress-regulating hypothalamic–pituitary–adrenocortical (HPA) system among children with multiple facets of risk for psychopathology. The majority of this work has focused on the impact of severe early adversity (e.g., maltreatment), so that far less is known about the impact of more normative experiences on children's brain development. Still, these and many other findings indicate that early experiences may shape neural structure and function, which may then create dispositions that direct and shape a child's later experiences and behavior (Cicchetti & Walker, 2001; Fox, Zeanah, & Nelson, 2012; Glaser, 2000; Kaufman & Charney, 2001).

In a volume covering child psychopathology, it is also worth noting that there may be issues related to the stigma of mental illness with particular relevance to children. Although definitions of stigma have varied across studies, it appears to be a multidimensional construct that is not well characterized with respect to disorders of childhood, relative to adulthood. Stigma can be experienced across different contexts and targets (Mukolo, Heflinger, & Wallston, 2010), and appears to play a role in decreasing the likelihood that services are sought for children with a mental disorder, particularly in minority groups and cultures (e.g., Yeh, McCabe, Hough, Dupuis, & Hazen, 2003). Differentiating the consequences of mental health stigma from those related to the symptoms of disorder can be difficult and has not always been closely attended to in research designs (e.g., caregiver strain could stem from both children's symptoms of disorder and parents' own symptoms, as well as perceived negative responses to the children's status as patients; Brannan & Heflinger, 2006). Additional work on the origins and role of stigma, especially as it pertains to the willingness of families to seek care or to participate in basic science on the etiology of disorder, is therefore critical.

As will be discussed throughout this volume, current models of child psychopathology seek to incorporate the roles of evolved mechanisms; neurobiological factors; early parent–child relationships; attachment processes; a long-term memory store that develops with age and experience; micro- and macrosocial influences; cultural factors; age and gender; and reactions from the social environment as variables and processes that interact and transform one another over time. In short, then, current approaches view the roots of developmental and psychological disturbances in children as the result of complex interactions over the course of development between the biology of brain maturation and the multidimensional nature of experience (Belsky & de Haan, 2011; D'Onofrio, Rathouz, & Lahey, 2011; Reiss & Neiderhiser, 2000; Rutter et al., 1997).

The experience and the expression of psychopathology in children have cognitive, affective, physiological, and behavioral components; in light of this, many differing descriptions and definitions of dysfunctionality in children have been proposed. As we discuss in a later section, a common theme in defining child psychopathology has been "adaptational failure" in one or more of these components or in the ways in which these components are organized and integrated (Rutter & Sroufe, 2000; Sameroff, 2000). Adaptational failure may involve deviation from age-appropriate norms (Achenbach, 2001); exaggeration or diminishment of normal developmental expressions; interference in normal developmental progress; failure to master developmental tasks; failure to develop a specific function or regulatory mechanism; and/or the use of non-normative skills (e.g., rituals, dissociation) as a way of adapting to regulatory problems or traumatic experiences (Sroufe, 1997).

A multitude of etiological models and treatment approaches have been proposed to explain and remediate psychopathology in children. Unfortunately, most of these have yet to be substantiated or even adequately tested (Kazdin, 2000, 2001). These models and approaches have differed in their relative emphasis on certain causal mechanisms and constructs, often using very different terminology and concepts to describe seemingly similar child characteristics and behaviors. Although useful, many of these models have been based on what seem to be faulty premises concerning singular pathways of causal influence that do not capture the complexities of child psychopathology (Kazdin & Kagan, 1994).

In this regard, evolutionary models have emphasized the role of selection pressures operating on the human species over millions of years; biological paradigms have emphasized genetic mutations, neuroanatomy, and neurobiological mechanisms as factors contributing to psychopathology; psychodynamic models have focused on intrapsychic mechanisms, conflicts, and defenses;

attachment models have emphasized the importance of early relationships and the ways in which internal representations of these relationships provide the foundation for constructing working models of self, others, and relationships more generally; behavioral/reinforcement models have emphasized excessive, inadequate, or maladaptive reinforcement and/or learning histories; social learning models have emphasized the importance of observational learning, vicarious experience, and reciprocal social interactions; cognitive models generally focus on the child's distorted or deficient cognitive structures and processes; affective models have emphasized dysfunctional emotion-regulating mechanisms; and family systems models have conceptualized child psychopathology within a framework of intra- and intergenerational family systems and subsystems and have emphasized the structural and/or functional elements surrounding family relational difficulties.

The distinctiveness of each model mentioned above is in the relative importance it attaches to certain events and processes. However, it should be emphasized that despite these variations in the relative emphasis given to certain causes versus others, most models recognize the role of multiple interacting influences. For example, although they differ in emphasis, social learning and affective models both place importance on the role of symbolic representational processes in explaining childhood dysfunction.

There is a growing recognition of the need to integrate currently available models through intra- and interdisciplinary research efforts. Such integration generally requires looking beyond the emphasis of each single-cause theory to see what can be learned from other approaches, as well as a general openness to relating concepts and findings from diverse theories (cf. Arkowitz, 1992). Studies suggest that theoretical integration is becoming more common in psychopathology research (e.g., Beauchaine, 2001). Attachment theory has, for instance, been increasingly integrated with cognitive models (e.g., Ingram & Ritter, 2000). Theoretical integration is also apparent in studies combining proximal cognitive and interpersonal factors with distal variables, such as genetic markers of risk, the early home environment, and patterns of attachment (e.g., Caspi et al., 2003; Gibb, Beevers, & McGeary, 2013; Hayden, Klein, et al., 2010; Lara, Klein, & Kasch, 2000). The link between cognitive and neuropsychological functioning is likewise being tested more frequently (e.g., Nigg, Blaskey, Huang-Pollack, & Rappley, 2002). Thus researchers increasingly recognize the importance of combining theoretical approaches, and are accepting the monumental task of incorporating increased complexity into their research designs. The need for such integrative research approaches has important implications for training future developmental psychopathologists to be conversant in a broad array of research approaches and theories.

On a related note, interdisciplinary perspectives on child psychopathology mirror the considerable investment in children on the part of many different disciplines and professions. The study of the etiology and maintenance of psychopathology in children has been and continues to be the subject matter of psychology, medicine, psychiatry, education, and numerous other disciplines. Clearly, no one discipline has proprietary rights to the study of childhood disturbances, and each has tended to formulate child psychopathology in terms of its own unique perspective. Particularly relevant, in the context of this chapter, is that child psychopathology and normality in medicine and psychiatry have traditionally been conceptualized and defined categorically in terms of the presence or absence of a particular disorder or syndrome that is believed to exist "within the child." In contrast, psychology has more often conceptualized psychopathology–normality as representing extremes on a continuum or dimension of characteristics, and has also focused on the role of environmental influences that operate "outside the child." However, the boundaries between categories and dimensions, or between inner and outer conditions and causes, are arbitrarily drawn, and there is a continuing need to find workable ways of integrating the two different world views of psychiatry/medicine and psychology (Pickles & Angold, 2003; Richters & Cicchetti, 1993; Scotti & Morris, 2000; Shaffer, Lucas, & Richters, 1999).

Despite these ongoing issues in the field, the subsequent chapters in this volume attest to the substantial and rapid accrual of research on child psychopathology. This in turn has resulted in a rapidly expanding and changing knowledge base. Each chapter in this volume provides a comprehensive review of current research and theory for a specific form of child psychopathology, and a discussion of new developments and directions related to this disorder. In the remainder of this introductory chapter, we provide a discussion of the following: an overview of the significance and implications of child psychopathology; epidemiological considerations; key concepts in the field; approaches to the definition and conceptualization of childhood disorders; an overview of the developmental psycho-

pathology framework; predominant theories regarding etiology; and prevalent and recurrent conceptual and methodological issues that cut across the wide spectrum of disorders represented in this volume. Particular emphasis is given to concepts, methods, and strategies capturing the complexities, reciprocal influences, and divergent pathways that current models and research have identified as crucial for understanding child psychopathology.

SIGNIFICANCE OF CHILD PSYCHOPATHOLOGY

There has been and continues to be a great deal of misinformation and folklore concerning disorders of childhood. Many unsubstantiated theories have emerged in both the popular and scientific literatures. These have ranged from mid-19th-century views that overstimulation in the classroom causes insanity (see Makari, 1993), to mid-20th-century views that inadequate parenting causes autism (Bettelheim, 1967) or that chemical food additives are the primary cause of hyperactivity (Feingold, 1975). In addition, many of the constructs used to describe the characteristics and conditions of psychopathology in children have been globally and/or poorly defined (e.g., "adjustment problem," "emotional disturbance"). Despite the limitations, uncertainties, and definitional ambiguities that exist in the field, it is also evident that psychopathology during childhood represents a frequently occurring and significant societal concern that is gradually coming to the forefront of the political agenda.

Increasingly, researchers in the fields of child development, developmental psychopathology, child psychiatry, and clinical child psychology are considering the social policy implications of their work and striving to effect improvements in the identification of and services for youth with mental health needs (Cicchetti & Toth, 2000; Kazdin & Blase, 2011; Shonkoff, 2010; Shonkoff & Bales, 2011). For example, such work contributed to a recent report of the Surgeon General's office on suicide prevention, part of which focused on prevention of suicide in youth (U.S. Public Health Service, 2012). Such efforts are critical, given that public policies that promote early socioemotional well-being and reduce the conditions that lead to early child maltreatment may provide the foundation needed for later school success and positive peer and teacher relationships. Policy makers are generally not well acquainted with children's mental health concerns, or with the serious ramifications of early maladjustment (Nelson & Mann, 2011). Furthermore, public policy has not kept pace with advances in the field of child psychopathology (Zero to Three, 2012), especially with regard to recognizing how common and pervasive disorders of childhood are, or having an awareness of the benefits of early screening and intervention (Sices, 2007). Strategies to promote positive early development, as well as to prevent and treat early mental health problems, will require not only significant investment on the part of federal and local governments but an increased recognition that public policy should be shaped by empirical research. The need for policy to (1) support the training of individuals with the necessary expertise in children's mental health, and to (2) address the significant, ongoing obstacle faced by many parents of how to afford such expertise, has also been noted (Zero to Three, 2012).

The growing attention to children's mental health problems and competencies arises from a number of sources. First, many young people experience significant mental health problems that interfere with normal development and functioning. As many as one-third of children in the United States experience some type of difficulty (Costello, Mustillo, et al., 2003); this longitudinal study indicated that the risk of experiencing a psychiatric disorder by age 16 was much higher than previous estimates, derived from cross-sectional data, had indicated. Furthermore, this estimate probably underestimates the impact of psychopathology in youth, since it does not capture subclinical or undiagnosed disturbances that nevertheless place children at high risk for the later development of more severe clinical problems (e.g., Keenan et al., 2008). In addition, although not meeting formal diagnostic criteria, many subclinical conditions (e.g., depressed mood, eating problems) are associated with significant impairment in functioning (e.g., Angold, Costello, Farmer, Burns, & Erkanli, 1999; Lewinsohn, Striegel-Moore, & Seeley, 2000). Evidence gathered by the World Health Organization (WHO) suggests that by the year 2020, childhood neuropsychiatric disorders will rise by over 50% internationally to become one of the five most common causes of morbidity, mortality, and disability among children (U.S. Public Health Service, 2001b).

Second, a significant proportion of children do not grow out of their childhood difficulties, although the ways in which these difficulties are expressed change in dynamic ways over time (Masten & Cicchetti, 2010). Even when diagnosable psychopathology is not

evident at later ages, a child's failure to adjust during earlier developmental periods may still have a lasting negative impact on later family, occupational, and social adjustment. Furthermore, some forms of child psychopathology—for example, an early onset of antisocial patterns of behavior—are highly predictive of a host of negative outcomes later in life (e.g., Kim-Cohen et al., 2005).

Third, recent social changes and conditions may place children at increasing risk for the development of disorders, and also for the development of more severe problems at younger ages (Dupéré et al., 2009; Masten & Narayan, 2012). These social changes and conditions include multigenerational adversity in inner cities; chronic poverty in women and children; pressures of family breakup, single parenting, and homelessness; problems of the rural poor; direct and indirect exposure to traumatic events (e.g., terrorist attacks or school shootings); adjustment problems of children in immigrant families; difficulties of Native American children; and conditions associated with the impact of prematurity, HIV, cocaine, and alcohol on children's growth and development (McCall & Groark, 2000; Shonkoff & Phillips, 2000). In addition to sociocultural changes, medical advances associated with higher rates of fetal survival may also contribute to a greater number of children's showing serious behavior problems and learning disorders at a younger age.

Fourth, for a majority of children who experience mental health problems, these problems go untreated: Kataoka, Zhang, and Wells (2002) reported that of children identified as needing mental health services, only about 20% received such assistance. Rates of unmet need were even higher in ethnic minority groups and in children without insurance. Even when children are identified and receive help for their problems, this help may be less than optimal. For example, only about half of children with identified attention-deficit/hyperactivity disorder (ADHD) seen in real-world practice settings receive care that conforms to recommended treatment guidelines (Hoagwood, Kelleher, Feil, & Comer, 2000). The fact that so few children with mental health problems receive appropriate help is probably related to such factors as a lack of screening, inaccessibility, cost, a lack of perceived need on the part of parents, parental dissatisfaction with services, and the stigmatization and exclusion often experienced by these children and their families (Hinshaw, 2007; Hinshaw & Cicchetti, 2000). These and other factors have stimulated recent initiatives to identify children with unmet mental health needs (e.g., Jensen et al., 2011). Although empirically supported prevention and treatment programs for many childhood disorders have become increasing established in recent decades (Chorpita et al., 2011; Kazak et al., 2010), a pressing need remains for additional research on normative child development, developmental psychopathology, and the continued development and evaluation of prevention and intervention programs that are grounded in empirical evidence (Greenberg, Domitrovich, & Bumbarger, 2001; Kazdin, 2001; Rapport, 2001; Silverman & Hinshaw, 2008).[2]

Fifth, a majority of children with mental health problems who go unidentified and unassisted often end up in the criminal justice or mental health systems as young adults (Loeber & Farrington, 2000). They are at much greater risk for dropping out of school and of not being fully functional members of society in adulthood; this adds further to the costs of childhood disorders in terms of human suffering and financial burdens. For example, average costs of medical care for youngsters with ADHD are estimated to be double those for youngsters without ADHD (Leibson, Katusic, Barbaresi, Ransom, & O'Brien, 2001). Moreover, allowing just *one* youth to leave high school for a life of crime and drug abuse is estimated to cost society from $1.7 to $2.3 million or more (Cohen, 1998; Cohen & Piquero, 2009).

Finally, a significant number of children in North America experience maltreatment, and chronic maltreatment during childhood is associated with psychopathology in children and later in adults (Fergusson, Borden, & Horwood, 2008; Gunnar et al., 2006). Based on a review of the evidence, De Bellis (2001) has proposed that the psychobiological outcomes of abuse be viewed as "an environmentally induced complex developmental disorder" (p. 539). Although precise estimates of the rates of occurrence of maltreatment are difficult to obtain, due to the covert nature of the problem and other sampling and reporting biases (Cicchetti & Manly, 2001; Wekerle, Wolfe, Dunston, & Alldred, Chapter 16, this volume), the numbers appear to be large. Over 3.5 million suspected cases of child abuse and neglect are investigated each year by child protective service agencies, and about 1 million children in the United States were confirmed as victims of child maltreatment in 2010 (U.S. Department of Health and Human Services [USDHHS], 2011). It has been estimated that each year over 2,000 infants and young children die from abuse or neglect at the hands of their par-

ents or caregivers (USDHHS, 2011). Moreover, many reports of "accidental" injuries in children may be the result of unreported mistreatment by parents or siblings (Peterson & Brown, 1994). It would appear, then, that the total number of children who show adverse psychological and physical effects of maltreatment in North American society is staggering.

EPIDEMIOLOGICAL CONSIDERATIONS

Prevalence

Epidemiological studies seek to determine the prevalence and distribution of disorders and their correlates in particular populations of children who vary in age, sex, socioeconomic status (SES), ethnicity, or other characteristics (Costello & Angold, 2000). Although epidemiological studies of child psychopathology of the same scope as those of adult psychopathology (e.g., Kessler et al., 2005) have not been conducted, disorders of childhood appear to be common. Although reported rates vary widely from study to study, current best estimates are that 20–40% of all children worldwide have a clinically diagnosable disorder, and that many more children exhibit specific symptoms or subclinical problems (Belfer, 2008; Kessler et al., 2012; Merikangas, He, Brody, et al., 2010). Overall lifetime prevalence rates for childhood problems are on the order of 36% of all children (Costello, Mustillo, et al., 2003). Earlier studies also reported high rates of disorder; for example, Rutter, Tizard, and Whitmore (1970), in the classic Isle of Wight Study, found the overall rate of child psychiatric disorders to be 6–8% in 9- to 11-year-old children. Richman, Stevenson, and Graham (1975), in the London Epidemiological Study, found moderate to severe behavior problems for 7% of the population, with an additional 15% of children having mild problems. Boyle and colleagues (1987) and Offord and colleagues (1987), in the Ontario Child Health Study, reported that 19% of boys and 17% of girls had one or more disorders. Many other epidemiological studies have reported similar rates of prevalence (e.g., Brandenburg, Friedman, & Silver, 1990; Costello, Farmer, Angold, Burns, & Erkanli, 1997; Earls, 1980; Hewitt et al., 1997; Lapouse & Monk, 1958; MacFarlane, Allen, & Honzik, 1954; Shaffer et al., 1996; Verhulst & Koot, 1992; Werner, Bierman, & French, 1971). Perhaps the most consistent general conclusions to be drawn from these studies are that prevalence rates for childhood disorders are generally high, but that rates may vary with the nature of the disorder; the age, sex, SES, and ethnicity of the children; the criteria used to define the problem both concurrently and over time, the method used to gather information (e.g., interview, questionnaire); the informants (e.g., children, parents, teachers); sampling methods; and a host of other factors.

Age Differences

Bird, Gould, Yager, Staghezza, and Camino (1989) reported no significant age differences for children ages 4–16 years in the total number of *Diagnostic and Statistical Manual of Mental Disorders*, third edition (DSM-III) disorders diagnosed at each age. However, some studies have reported interactions among child age, number or type of problems, child sex, clinical status, and source of information (e.g., Simonoff et al., 1997). For example, Achenbach, Howell, Quay, and Conners (1991) found that externalizing problems showed a decline with age relative to internalizing problems, but only for those children who had been referred for treatment. More recently, using structured clinical interview data in a large sample of youth, Costello, Mustillo, and colleagues (2003) reported that the highest prevalence of disorder was found in children ages 9–10, with levels gradually falling through age 12 and then rising again throughout the adolescent years. The authors noted that this was likely due to the fact that the prevalence of many disorders of childhood (e.g., ADHD, separation anxiety disorder) decreases by age 12, while disorders of adolescence and adulthood (e.g., major depression) have not yet emerged. Merikangas, He, Burstein, and colleagues (2010) recently reported that 22% of adolescents had a disorder associated with severe impairment and/or distress in a nationally representative survey of adolescents ages 13–18.

These and other findings raise numerous questions concerning age differences in children's problem behaviors. Answers to even a seemingly simple question such as "Do problem behaviors decrease (or increase) with age?" are complicated by (1) a lack of uniform measures of behavior that can be used across a wide range of ages; (2) qualitative changes in the expression of behavior with development; (3) interactions between child age and sex; (4) the use of different informants across development; (5) the specific problem behavior(s) of interest; (6) the clinical status of the children being assessed; and (7) the use of different diagnostic criteria for children of different ages. Notwith-

standing these difficulties, both longitudinal and cross-sectional general population surveys are informative in depicting changes in the proportions of specific parent-, teacher-, or child-reported problem behaviors with age (e.g., "hyperactive," "argues," "cries"), as well as the manner in which the age changes vary as a function of problem type, child sex, and child clinical status. However, it should be emphasized that general age trends are based on group statistics, which may obscure the nonlinear and non-normative changes that often occur for individual children. In addition, general surveys do not provide information concerning the processes underlying age changes. Studies of change in individual children over time, and of the context in which this change occurs, are needed if such processes are to be understood.

Socioeconomic Status

Although most children treated for mental health problems are from the middle class, mental health problems are overrepresented among the very poor. It is estimated that 20% or more of children in North America are poor, and that as many children growing up in poverty are impaired to some degree in their social, behavioral, and academic functioning (McLeod & Nonnemaker, 2000). Lower-SES children have been reported to display more psychopathology and other problems than upper-SES children (e.g., McMahon & Luthar, 2007; Samaan, 2000). However, although the reported relationships between SES and child psychopathology are statistically significant, the effects are small and should be interpreted cautiously (Achenbach et al., 1991), as global estimates of SES tell us little about the multifarious processes through which SES and children's adaptive and maladaptive development are related (Schreier & Chen, 2013). Knowledge of such processes is needed to inform our understanding of disorders and to develop preventative efforts that target the appropriate mechanisms. For example, the effects of SES on aggression can be explained partly by stressful life events and by beliefs that reflect a tolerance or acceptance of aggression (Guerra, Tolan, Huesmann, Van Acker, & Eron, 1995). Other work suggests that the impact of SES on broader externalizing problems may be related to the reduced ability of impoverished parents to monitor their children (Costello, Compton, Keeler, & Angold, 2003). Further illustrating the complex interplay between risks, the environment that parents provide is also related to parental psychopathology, as in the case of adult ADHD, which is associated with low SES (Mannuzza, Klein, Bessler, Malloy, & LaPadula, 1998); in such a case, parents confer both genetic and contextual risk on offspring, and this contextual risk emerges at least in part through gene–environment correlation (with the potential for "downward drift," such that disorder reduces economic opportunity, in the present case).

Thus associations between socioeconomic disadvantage and children's mental health derive from the fact that SES is a marker of many potential sources of negative influence (Bradley, Corwyn, McAdoo, & García Coll, 2001). Low SES is often characterized by low maternal education, a low level of employment, single-parent status, parental psychopathology, limited resources, and both chronic and acute negative life events (e.g., poor nutrition, exposure to violence), in addition to low income. Since overall indices of SES may include one or more of these variables in any given study, the relationship that is reported between SES and child psychopathology may vary as a function of the particular index used, as well as ethnic factors (McLeod & Nonnemaker, 2000). In short, SES is a marker of many factors that influence risk for child psychopathology, and the way in which this indicator is operationalized has an impact on its associations with childhood disorder.

Some research findings in child psychopathology are confounded by a failure to include SES in models. For example, although physically abused children show higher levels of externalizing problems than nonabused children (Mash, Johnston, & Kovitz, 1983), it is not clear that physical abuse and externalizing problems are associated when the effects of SES are controlled for (Cummings, Hennessy, Rabideau, & Cicchetti, 1994; Fergusson et al., 2008). The relationships among SES, maltreatment, and behavior disorders are further complicated by other findings that the effects of physical abuse on internalizing disorders may be independent of SES, whereas the effects of abuse on externalizing disorders may be dependent on SES-related conditions (Okun, Parker, & Levendosky, 1994).

Sex Differences

Although sex differences in the expression of psychopathology have been formally recognized since Freud's writings at the beginning of the 20th century, psychopathology in girls has historically received far less research attention than psychopathology in boys (Bell-

Dolan, Foster, & Mash, 2005; Rose & Rudolph, 2006). Until recently, many studies either have excluded girls from their samples entirely or have failed to examine whether relevant effects differed across the two sexes. For example, until fairly recently, there were relatively few studies of disruptive behavior disorders in girls (e.g., Moffitt, Caspi, Rutter & Silva, 2001; Silverthorn & Frick, 1999), probably because such disorders are more common in boys than in girls during childhood. Also contributing to this may be sampling biases (in which boys, who are more severely disruptive, are more likely to be referred and studied), as well as the fact that the inclusionary diagnostic criteria most commonly used are derived and validated largely from studies with boys (Frick & Nigg, 2012; Spitzer, Davies, & Barkley, 1990).

Research has confirmed that there are important differences in the prevalence, expression, accompanying disorders, underlying processes, outcomes, and developmental course of psychopathology in boys versus girls (Willcutt & Pennington, 2000a; Zahn-Waxler, Shirtcliff, & Marceau, 2008). ADHD, autism spectrum disorder, childhood conduct and oppositional disorders, and learning and communication disorders are all more common in boys than girls, whereas the opposite is true for most anxiety disorders, adolescent depression, and eating disorders (Copeland et al., 2011; Rutter et al., 2004). Relatedly, boys exhibit higher levels of externalizing symptoms than girls do throughout childhood and early adolescence, whereas girls and boys are comparable in terms of internalizing symptoms in early childhood, with girls' levels of these symptoms increasing more rapidly than boys during adolescence (e.g., Bongers, Koot, van der Ende, & Verhulst, 2003). Although these sex differences are well established, their meaning is poorly understood (Martel, 2013). For example, it is difficult to determine whether observed sex differences are functions of referral or reporting biases, the way in which disorders are currently defined, differences in the expression of a disorder (e.g., direct vs. indirect aggressive behavior), sex differences in the genetic penetrance of disorders, sexual selection effects/evolutionary processes, or sex differences in biological characteristics and environmental susceptibilities. All are possible, and there is a need for research into the processes underlying observed differences. Clearly the mechanisms and causes of sex differences may vary for different disorders (e.g., ADHD vs. depression), or for the same disorder at different ages (e.g., child vs. adolescent obsessive–compulsive disorder or early- vs. late-onset conduct disorder). For example, Moffitt and Caspi (2001) found that sex differences in life-course-persistent antisocial behavior were attributable to differences in rates of risk factors for early-onset, persistent forms of such behaviors, such as hyperactivity, poor parenting, and neuropsychological dysfunction, which may disproportionately affect boys compared to girls.

Early research into sex differences focused mainly on descriptive comparisons of the frequencies of different problems for boys versus girls at different ages. In general, differences in problem behaviors between the sexes are small in children of preschool age or younger (e.g., Briggs-Gowan, Carter, Skuban, & Horwitz, 2001; Gadow, Sprafkin, & Nolan, 2001), but become increasingly common with age. For example, Weisz and Suwanlert (1989) studied children in the United States and Thailand, and found that boys were rated higher than girls on every problem for which there was a significant sex difference—including total problems, undercontrolled problems, overcontrolled problems, and culture-specific problems. Across cultures, boys have been found to display more fighting, impulsivity, and other uncontrolled behaviors than girls (Olweus, 1979). It has been found that boys show greater difficulties than girls during early and middle childhood, particularly with respect to ADHD and disruptive behavior disorders (Costello, Mustillo, et al., 2003). Girls' problems may increase during adolescence, with higher prevalence rates for depression and dysphoric mood from midadolescence through adulthood. For example, conduct disorder and ADHD have been found to be more frequent in 12- to 16-year-old boys than girls, whereas emotional problems have been found to be more frequent for girls than boys in this age group (Boyle et al., 1987; Offord et al., 1987).

However, not all studies have reported significant sex differences in overall rates of problem behavior (e.g., Achenbach & Edelbrock, 1981; Velez, Johnson, & Cohen, 1989), and even when significant overall sex differences have been found, they tend to be small and to account for only a small proportion of the variance. It has also been found that although there is a much larger predominance of externalizing problems in boys and of internalizing problems in adolescent girls in samples of children who are referred for treatment, sex differences in externalizing versus internalizing problems are minimal in nonreferred samples of children (Achenbach et al., 1991). Furthermore, there may be cohort effects on sex differences in some forms of psychopathology.

For example, the sex difference in substance use disorders, which historically consisted of higher rates of these disorders in boys compared to girls, appears to be disappearing in more recent cohorts due to increased substance use by girls (Johnston, O'Malley, Bachman, & Schulenberg, 2011).

Comparisons of the behavioral and emotional problems in boys versus girls over time can provide useful information about sex-related characteristics. However, taken in isolation, such global comparisons do not address possible qualitative differences in (1) expressions of psychopathology in boys versus girls; (2) the processes underlying these expressions; (3) the long-term consequences of certain behaviors for boys versus girls; and/or (4) the impact of certain environmental events on boys versus girls (Zahn-Waxler et al., 2008). As noted by Hops (1995), it seems likely that "the pathways from childhood to adolescence and adult pathology are age and gender specific and that these differences may be the result of different social contexts that nurture the development of health or pathology for female and male individuals" (p. 428). In addition to differential socialization practices, there are likely to be differences in the expression and outcome of psychopathology in boys versus girls as a function of biologically based differences. For example, in a study of the psychophysiology of disruptive behavior in boys versus girls, Zahn-Waxler, Cole, Welsh, and Fox (1995) found that disruptive girls showed high electrodermal responding relative to disruptive boys and were also highly activated by a sadness mood induction. These investigators suggested that girls' disruptive behavior may be more closely connected than boys' disruptive behavior to experiences of anxiety. Other research has found that increases in depression in females during adolescence are related mostly to accompanying changes in levels of estrogen and testosterone (Angold, Costello, Erkanli, & Worthman, 1999). It is also possible that for some disorders (e.g., ADHD), girls may require a higher genetic loading for the disorders than boys before the disorders are likely to express themselves (Rhee, Waldman, Hay, & Levy, 1999).

There may also be differences in the processes underlying the expression of psychopathology and distress in boys versus girls (Chaplin & Aldao, 2013; Kistner, 2009; Rutter, Caspi, & Moffitt, 2003). For example, a slower rate of biological maturation (Zahn-Waxler, Crick, Shirtcliff, & Woods, 2006; Zahn-Waxler et al., 2008), as well as sex differences in temperamental variables (Else-Quest, Hyde, & Goldsmith, 2006; Frick & Morris, 2004; Olino, Durbin, Klein, Hayden, & Dyson, 2013) may provide explanatory mechanisms for the higher rates of conduct problems in boys versus girls. In addition, depression in adolescent females has been found to be strongly associated with maternal depression, whereas a lack of supportive early care appears to be more strongly associated with depression in adolescent males (Duggal, Carlson, Sroufe, & Egeland, 2001). It has also been found that the types of child-rearing environments predicting resilience to adversity may differ for boys and girls. Resilience in boys is associated with households in which there is a male model (e.g., father, grandfather, older sibling), structure, rules, and some encouragement of emotional expressiveness. In contrast, resilient girls come from households that combine risk taking and independence with support from a female caregiver (e.g., mother, grandmother, older sister) (Werner, 1995). With respect to future goals for this specific aspect of research, the role of paternal psychopathology in offspring psychopathology risk, and whether its impact differs for boys versus girls, has not been explored to the extent it should (Connell & Goodman, 2002), given its known impact on other factors that shape child outcomes (e.g., paternal caregiving; Wilson & Durbin, 2010).

Zahn-Waxler and colleagues (2008) refer to the "gender paradox of comorbidities," which is that although the prevalence of disruptive behavior is lower in females than in males, the risk of comorbid conditions such as anxiety is higher in female samples. In explaining this paradox, these authors suggest that girls' heightened level of interpersonal sensitivity, caring, and empathy may be a protective factor with respect to the development of antisocial behavior. At the same time, girls' heightened sensitivity to the plight of others, and their reluctance to assert their own needs in situations involving conflict and distress, may elevate their risk for the development of internalizing problems. However, the relations between gender and comorbidity are likely to vary with the disorders under consideration, the age of a child, the source of referral, and other factors. For example, in contrast to Zahn-Waxler and colleagues (1995), Biederman and colleagues (2002) found that girls with ADHD had a significantly *lower* rate of comorbid major depression than did boys with ADHD. Martel (2013) has posited that sex differences such as these may have emerged via sexual selection processes related to the enhanced survival value or impact on mating opportunities linked to the biological substrates of these conditions.

Although findings relating to sex differences and child psychopathology are complex, inconsistent, and frequently difficult to interpret, the cumulative findings from research strongly indicate that the effects of gender are critical to understanding the expression and course of most childhood disorders (Bell-Dolan et al., 2005; Zahn-Waxler et al., 2008). It is particularly important to understand the processes and mechanisms underlying these gender effects, and to recognize that biological influences and differential socialization practices are likely to interact throughout development in accounting for any differences between the sexes that are found.

Rural versus Urban Differences

Although there is a general belief that rates of child behavior disorders are higher in urban than in rural areas, research findings in support of this view are weak and/or inconsistent. Findings from older studies of the Isle of Wight, Inner London Borough, and Ontario Child Health Studies reveal prevalence rates of problem behavior that were higher for urban than rural children (Offord et al., 1987; Rutter, 1981). On the other hand, in a cross-cultural investigation, Weisz and Suwanlert (1991) found few differences in parent or teacher ratings of child problems as a function of rural versus urban status in either of the cultures that were studied (United States and Thailand). In a detailed analysis that controlled for the effects of SES and ethnicity and also looked at gradations of urbanization, Achenbach and colleagues (1991) found few differences in children's behavior problems or competencies as a function of rural-versus-urban status, although there was a significant but very small effect indicating higher delinquency scores for children in urban environments. These investigators concluded that earlier findings of higher rates of problem behavior in urban than in rural areas "may have reflected the tendency to combine areas of intermediate urbanization with large urban areas for comparison with rural areas as well as a possible lack of control for demographic differences" (p. 86). Even in studies in which rural versus urban differences have been found, for the most part these differences were associated with economic and cultural differences between sites, and not with urbanization per se (Zahner, Jacobs, Freeman, & Trainor, 1993). Further complicating this issue is the possibility that the effects of urbanicity on psychopathology likely vary depending on disorder. For example, van Son, van Hoeken, Bartelds, van Furth, and Hoek (2006) found that rates of bulimia nervosa were higher in urban areas, whereas rates of anorexia nervosa did not differ depending on urbanization. Intriguingly, some of the effects of urbanicity on psychopathology may operate via gene–environment interaction; for example, environmental conditions appear to moderate the relative contribution of genetic effects on externalizing forms of psychopathology (Legrand, Keys, McGue, Iacono, & Krueger, 2008).

Ethnicity and Culture

Ethnicity

Numerous terms have been used to describe ethnic influences. These include "ethnicity," "race," "ethnic identity," "ethnic orientation," "acculturation," "bicultural orientation," and "culture." As Foster and Martinez (1995) have pointed out, there is a need to recognize the diversity of terminology that has been used in describing ethnicity, and the fact that these terms refer to related but different things. Despite the growing ethnic diversity of the North American population, ethnic representation in research studies and the study of ethnicity-related issues more generally have received less attention in studies of child psychopathology (García Coll, Akerman, & Cicchetti, 2000; U.S. Public Health Service, 2001a). Until recently, research into child psychopathology has generally been insensitive to possible differences in prevalence, age of onset, developmental course, and risk factors related to ethnicity (Yasui & Dishion, 2007), as well as to the considerable heterogeneity within specific ethnic groups (Murry, Bynum, Brody, Willert, & Stephens, 2001; Serafica & Vargas, 2006). In addition, few studies have compared ethnic groups while controlling for other important variables, such as SES, sex, age, and geographic region. Some recent studies suggest that children from minority groups are overrepresented in certain disorders, such as substance use disorders (Nguyen, Huang, Arganza, & Liao, 2007). Overall, studies with much larger national samples that included European American, African American, and Hispanic American children have reported either no or very small differences related to race or ethnicity when SES, sex, age, and referral status were controlled for (Achenbach & Edelbrock, 1981; Achenbach et al., 1991; Lahey et al., 1995). Thus, although externalizing problems have been reported more frequently among African American children (McLaughlin, Hilt, & Nolen-Hoeksema,

2007), this finding is probably an artifact related to SES. Unfortunately, African American and Hispanic American children are much less likely to receive specialty mental health services or psychotropic medications (García Coll & Garrido, 2000). Native American youth appear to have elevated rates of problem behaviors, including substance abuse and suicide (Whitbeck, Yu, Johnson, Hoyt, & Walls, 2008). Ethnicity has not been found to be strongly associated with risk for eating disorders (Leon, Fulkerson, Perry, & Early-Zald, 1995), although differences between European Americans and other groups have been reported for such subclinical eating disturbances as dietary restraint, ideal body shape, and body dissatisfaction (Wildes & Emery, 2001). More research is needed in which potentially important third variables (e.g., SES) are adequately addressed, but these and other findings suggest that the effects of ethnicity are likely to vary with the problem under consideration and its severity.

As is the case for SES and sex differences, global comparisons of the prevalence of different types of problems for different ethnic groups are not likely to be very revealing. On the other hand, studies into the processes affecting the form, associated factors, and outcomes of different disorders for various ethnic groups hold promise for increasing our understanding of the relationship between ethnicity and child psychopathology (e.g., Bird et al., 2001; Bradley, Corwyn, Burchinal, McAdoo, & García Coll, 2001).

Culture

The values, beliefs, and practices that characterize a particular ethnocultural group contribute to the development and expression of childhood distress and dysfunction, which in turn are organized into categories through cultural processes that further influence their development and expression (Achenbach & Rescorla, 2007; Harkness & Super, 2000; Wong & Ollendick, 2001). Through shared views about causality and intervention, culture also structures the way in which people and institutions react to a child's problems. Since the meaning of children's social behavior is influenced by cultural beliefs and values, it is not surprising that the form, frequency, and predictive significance of different forms of child psychopathology vary across cultures, or that cultural attitudes influence diagnostic and referral practices (Lambert et al., 1992). For example, shyness and oversensitivity in children have been found to be associated with peer rejection and social maladjustment in Western cultures, but with leadership, school competence, and academic achievement in Chinese children in Shanghai (Chen, Rubin, & Li, 1995). Similarly, Lambert, Weisz, and Knight (1989) found that overcontrolled problems were reported significantly more often for Jamaican than for American youngsters—a finding consistent with Afro-British Jamaican cultural attitudes and practices that discourage child aggression and other undercontrolled behavior, and that foster inhibition and other overcontrolled behavior.

Weisz and Sigman (1993), using parent reports of behavioral and emotional problems in 11- to 15-year-old children from Kenya, Thailand, and the United States, found that Kenyan children were rated particularly high on overcontrolled problems (e.g., fears, feelings of guilt, somatic concerns), due primarily to numerous reports of somatic problems. In this mixed-race sample, whites were rated particularly high on undercontrolled problems (e.g., "arguing," "disobedient at home," "cruel to others"). Weisz and Suwanlert (1987) compared 6- to 11-year-old children in the Buddhist-oriented, emotionally controlled culture of Thailand with American 6- to 11-year-olds. Parent reports revealed Thai–U.S. differences in 54 problem behaviors, most of which were modest in magnitude. Thai children were rated higher than American children on problems involving overcontrolled behaviors such as anxiety and depression, whereas American children were rated higher than Thai children on undercontrolled behaviors such as disobedience and fighting.

Weisz and Suwanlert (1991) compared ratings of behavior and emotional problems of 2- to 9-year-old children in Thailand and the United States. Parents and teachers in Thailand rated both overcontrolled and undercontrolled problems as less serious, less worrisome, less likely to reflect personality traits, and more likely to improve with time. These findings suggest that there may be cultural differences in the meanings ascribed to problem behaviors across cultures.

Findings from these and other studies suggest that the expression of, and tolerance for, many child behavioral and emotional disturbances are related to social and cultural values. The processes that mediate this relationship are in need of further investigation. In this regard, it is important that the results of research on child psychopathology not be generalized from one culture to another, unless there is support for doing so. There is some support for the notion that some processes—for example, those involved in emotion regulation and its

relation to social competence—may be similar across diverse cultures (Eisenberg, Pidada, & Liew, 2001). The rates of expression of some disorders, particularly those with a strong neurobiological basis (e.g., ADHD, autism spectrum disorder), may be less susceptible to cultural influences than others. However, even so, social and cultural beliefs and values are likely to influence the meaning given to these behaviors, the ways in which they are responded to, their forms of expression, their outcomes, and responses to intervention (Castro, Barrera, & Holleran-Steiker, 2010).

An important distinction to be made with respect to cross-cultural comparisons is whether there are substantive differences in the rates of a disorder, or differences in the raters' perceptions of these problems. For example, Weisz and Suwanlert (1989) compared the teacher-reported behavioral/emotional problems of Thai and U.S. children (ages 6–11 years). It was found that Thai teachers were confronted with students who were more prone to behavioral and emotional problems at school than were teachers in the United States, but that they applied different judgments to the behaviors they observed. Similarly, cultural factors are known to influence not only informal labeling processes but formal diagnostic practices as well. For example, reported prevalence rates of ADHD in Great Britain are much lower than in the United States because of differences in the way in which diagnostic criteria for ADHD are applied in the two countries. Such differences in diagnostic practices may lead to spurious differences in reported prevalence rates for different forms of child psychopathology across cultures.

Cross-cultural research on child psychopathology would suggest that the expression and experience of mental disorders in children is not universal (Fisman & Fisman, 1999). Patterns of onset and duration of illness and the nature and relationship among specific symptoms vary from culture to culture, and across ethnic groups within cultures (Achenbach, 2001; Hoagwood & Jensen, 1997; Yasui & Dishion, 2007). However, few studies have compared the attitudes, behaviors, and biological and psychological processes of children with mental disorders across different cultures. Such information is needed to understand how varying social experiences and contexts influence the expression, course, and outcome of different disorders across cultures. Greater social connectedness and support in more traditional cultures and greater access to resources and opportunities in industrialized societies are examples of mechanisms that may alter outcomes across cultures. Sensitivity to the role of cultural influences in child psychopathology has increased (Evans & Lee, 1998; Lopez & Guarnaccia, 2000), and is likely to continue to do so as globalization and rapid cultural change become increasingly more common (García Coll et al., 2000).

KEY CONCEPTS IN CHILD PSYCHOPATHOLOGY

Several recurrent and overlapping issues have characterized the study of psychopathology in children (Cicchetti & Toth, 2009; Rutter & Sroufe, 2000). A number of these are highlighted in this section, including (1) difficulties in conceptualizing psychopathology and normality; (2) the need to consider healthy functioning and adjustment; (3) questions concerning developmental continuities and discontinuities; (4) the concept of developmental pathways; (5) the notions of risk and resilience; (6) the identification of protective and vulnerability factors; and (7) the role of contextual influences.

Psychopathology versus Normality

The attempt to establish boundaries between what constitutes abnormal and normal functioning is an arbitrary process at best (see Achenbach, 1997), although this does not necessarily imply that such boundaries are meaningless, if they are informative with respect to impairment and other clinically significant factors. Traditional approaches to mental disorders in children have emphasized concepts such as symptoms, diagnosis, illness, and treatment; by doing so, they have strongly influenced the way we think about child psychopathology and related questions (Richters & Cicchetti, 1993). Childhood disorders have most commonly been conceptualized in terms of deviancies involving breakdowns in adaptive functioning, statistical deviation, unexpected distress or disability, and/or biological impairment.

Wakefield (1992, 1997, 1999b, 2010) has proposed an overarching concept of mental disorder as "harmful dysfunction." This concept encompasses a child's physical and mental functioning, and includes both value- and science-based criteria. In the context of child psychopathology, a child's condition is viewed as a disorder only if (1) it causes harm or deprivation of benefit to the child, as judged by social norms; and (2) it results from the failure of some internal mechanism to perform its natural function (e.g., "an effect

that is part of the evolutionary explanation of the existence and structure of the mechanism"; Wakefield, 1992, p. 384). This view of mental disorder focuses attention on evolved adaptations or internal functional mechanisms—for example, executive functions in the context of self-regulation (Barkley, 2001). Nevertheless, as Richters and Cicchetti (1993) have pointed out, this view only identifies the decisions that need to be made in defining mental disorders; it does not specify *how* such decisions are to be made.

As is the case for most definitions of mental disorder that have been proposed, questions related to defining the boundaries between normal and abnormal, understanding the differences between normal variability and dysfunction, defining what constitute "harmful conditions," linking dysfunctions causally with these conditions, and circumscribing the domain of "natural" or of other proposed mechanisms are matters of considerable controversy (Hudziak, Achenbach, Althoff, & Pine, 2007; Lilienfeld & Marino, 1995).[3] Categories of mental disorder stem from human-made linguistic distinctions and abstractions, and boundaries between what constitutes normal and abnormal conditions, or between different abnormal conditions, are not easily drawn. Although it may sometimes appear that efforts to categorize mental disorders are "carving nature at its joints," whether or not such "joints" actually exist is open to debate (e.g., Angold & Costello, 2009; Cantor, Smith, French, & Mezzich, 1980; Lilienfeld & Marino, 1995). However, clear distinctions do not necessarily need to exist for categorical distinctions to have utility. For instance, there is no joint at which one can carve day from night, although distinguishing the two has proven incredibly useful to humans in going about their social discourse and engagements. Likewise, although the threshold for determining disorder from high levels of symptoms may be fuzzy, it could be stipulated as being at that point along a dimension where impairment in a major, culturally universal life activity befalls the majority of people at or exceeding that point. Thus, despite the lack of clear boundaries between what is normal and abnormal, categorical distinctions are still useful as long as they adequately predict which children will be most likely to benefit from access to special education, treatment, or disability status.

Healthy Functioning

The study of psychopathology in children requires concomitant attention to adaptive developmental processes for several reasons. First, judgments of deviancy require knowledge of normative developmental functioning, both with respect to a child's performance relative to same-age peers and with respect to the child's own baseline of development. Second, maladaptation and adaptation often represent two sides of the same coin, in that dysfunction in a particular domain of development (e.g., the occurrence of inappropriate behaviors) is usually accompanied by a failure to meet developmental tasks and expectations in the same domain (e.g., the nonoccurrence of appropriate behaviors). It is important to point out, however, that adaptation should not be equated with the mere absence of psychopathology, nor should the converse be assumed (i.e., that symptoms can be equated with maladaptation). With respect to the former, Kendall and colleagues (Kendall, Marrs-Garcia, Nath, & Sheldrick, 1999; Kendall & Sheldrick, 2000), contend that it is important to use normative comparisons to evaluate treatment outcome; they suggest that improvement involves falling within a certain range of healthy functioning, in addition to decreased symptoms. Moreover, adaptation involves the presence and development of psychological, physical, interpersonal, and intellectual resources (see Fredrickson, 2001). With respect to the latter point, symptoms and impairment tend to be only moderately correlated, suggesting that for some children, symptoms do not have a pervasive negative impact on important life domains (Barkley, 2012a; Gordon et al., 2006).

Third, in addition to the specific problems that lead to referral and diagnosis, disturbed children are likely to show impairments in other areas of adaptive functioning. For example, in addition to their core symptoms of hyperactivity/impulsivity and inattention, children with ADHD typically show lower-than-average levels of functioning in their socialization, communication, and activities of daily living (e.g., Stein, Szumowski, Blondis, & Roizen, 1995). Fourth, most children with specific disorders are known to cope effectively in some areas of their lives. Understanding a child's strengths informs our knowledge of the child's disorder and provides a basis for the development of effective treatment strategies. Fifth, children move between pathological and nonpathological forms of functioning over the course of their development. Individual children may have their "ups and downs" in problem type and frequency over time. Sixth, many child behaviors that are not classifiable as deviant at a particular point in time may nevertheless represent less extreme expressions or compensations of an already existing disorder

or early expressions of a later progression to deviant extremes as development continues (Adelman, 1995). Finally, no theory of a childhood disorder is complete if it cannot be linked with a theory of how the underlying normal abilities develop and what factors go awry to produce the disordered state. Therefore, understanding child psychopathology requires that we also attend to these less extreme forms of difficulty and develop more complete models of the normal developmental processes underlying the psychopathology.

For these and other reasons to be discussed, the study of child psychopathology requires an understanding of both abnormal and healthy functioning (Cicchetti, 2006). As noted by Cicchetti and Richters (1993), "it is only through the joint consideration of adaptive and maladaptive processes within the individual that it becomes possible to speak in meaningful terms about the existence, nature, and boundaries of the underlying psychopathology" (p. 335). To date, far greater attention has been devoted to the description and classification of psychopathology in children than to healthy child functioning; to nonpathological psychosocial problems related to emotional upset, misbehavior, and learning; or to factors that promote the successful resolution of developmental tasks (Adelman, 1995; Sonuga-Barke, 1998). In light of this imbalance, there is a need for studies of normal developmental processes (Lewis, 2000), for investigations of normative and representative community samples of children (Ialongo, Kellam, & Poduska, 2000; Kazdin, 1989), and for studies of "resilient" children who show normal development in the face of adversity (Masten & Cicchetti, 2010).

Developmental Continuities and Discontinuities

A central issue for theory and research in child psychopathology concerns the continuity of disorders identified from one time to another and the relationship between child, adolescent, and adult disorders (Caspi, 2000; Rutter, Kim-Cohen, & Maughan, 2006; Schulenberg, Sameroff, & Cicchetti, 2004). Some childhood disorders, such as intellectual disability and autism spectrum disorder, are typically chronic conditions that will persist throughout childhood and into adulthood. Other disorders, such as functional enuresis and encopresis, occur during childhood and only rarely manifest themselves in adults (Walker, 2003). However, most disorders (e.g., mood disorders, schizophrenia, generalized anxiety disorder) are expressed, albeit in modified forms, in both childhood and adulthood and exhibit varying degrees of continuity over time. Evidence in support of the continuity between child and adult disorders is equivocal and depends on a number of methodological factors related to research design, assessment instruments, the nature of the study sample, and the type and severity of the disorder (Garber, 1984). In general, the literature suggests that child psychopathology is continuous with adult disorders for some, but not all, problems. As we discuss below, there is evidence that appears to favor the stability of externalizing problems over internalizing problems. However, previous findings may reflect the severity and pervasiveness of the disorders assessed, referral biases, and the fact that longitudinal investigations of children with internalizing and other disorders are just beginning to emerge. For example, recent longitudinal studies have found that anxiety disorders in childhood predict a range of psychiatric disorders in adolescence (e.g., Bittner et al., 2007). In another report, early-onset bulimia nervosa was associated with a 9-fold increase in risk for late-adolescent bulimia nervosa and a 20-fold increase in risk for adult bulimia nervosa (Kotler, Cohen, Davies, Pine, & Walsh, 2001).

The possible mechanisms underlying the relationships between early maladaptation and later disordered behavior are numerous and can operate in both direct and indirect ways (Garber, 1984; Rutter, 1994a; Sroufe & Rutter, 1984). Some examples of *direct* relationships between early and later difficulties include (1) the development of a disorder during infancy or childhood, which then persists over time; (2) experiences that alter an infant's or child's physical status (e.g., neural plasticity), which in turn influences later functioning (Courchesne, Chisum, & Townsend, 1994; Johnson, 1999; Nelson, 2000); and (3) the acquisition of early patterns of responding (e.g., compulsive compliance, dissociation) that may be adaptive in light of a child's current developmental level and circumstances, but may result in later psychopathology when circumstances change and new developmental challenges arise.

Some examples of *indirect* associations between child and adult psychopathology may involve early predispositions that eventually interact with environmental experiences (e.g., stressors), the combination of which leads to dysfunction. For example, Egeland and Hiester (1995) found that the impact of day care on disadvantaged high-risk children at 42 months of age was related to the children's attachment quality at 12 months of age, with securely attached children more likely to be negatively affected by early out-of-home

care. Other examples of indirect links between child and adult disturbance include (1) experiences (e.g., peer rejection) that contribute to an altered sense of self-esteem (DuBois & Tevendale, 1999), or that create a negative cognitive set, which then leads to later difficulties; and (2) experiences providing various opportunities or obstacles that then lead to the selection of particular environmental conditions, and by doing so guide a child's course of development (Rutter, 1987; Sroufe & Rutter, 1984).

Research efforts have focused not only on the continuities and discontinuities in childhood disorders, but also on the identification of factors that predict them. One factor that has been studied in the context of conduct disorder is age of onset, with early onset usually viewed as the occurrence of conduct disorder symptoms prior to age 10 years (American Psychiatric Association [APA], 2013b). It has been found that early onset of conduct disorder symptoms is associated with higher rates and more serious antisocial acts over a longer period of time for both boys and girls (Lavigne et al., 2001). However, there may be different subgroups of children with an early onset, and dispositional and psychosocial variables that are present prior to and following onset may influence the seriousness and chronicity more than age of onset per se does (Frick & Viding, 2009; Tolan & Thomas, 1995). A question that needs to be addressed is this: Does early age of onset operate in a causal fashion for later problems, and if so, how? Another issue is whether the causal processes that are associated with an early onset of a disorder (e.g., depression) are different from those that serve to maintain the disorder. Even then, the specification of an age of onset need not be made so precisely that it creates a false distinction that only valid cases meet this precise threshold, as may have happened with ADHD (see Nigg & Barkley, Chapter 2, this volume). Such efforts to impose precision where none exists may have backfired by hampering studies of teens and adults having the same disorder who cannot adequately recall such a precise onset, and by presuming that cases having qualitatively identical symptoms and impairments but later onsets are invalid instances of a disorder.

Although research supports the notion of continuity of disorders, it does not support the continuity of identical symptoms over time (i.e., "homotypic correspondence"). Continuity over time for patterns of behavior rather than for specific symptoms is the norm. For example, although externalizing disorders in boys are stable over time, the ways in which these behavioral patterns are expressed are likely to change dramatically over the course of development (Olweus, 1979). Even with wide fluctuations in the expression of behavior over time, "children may show consistency in their general adaptive or maladaptive pattern of organizing their experiences and interacting with the environment" (Garber, 1984, p. 34). Several research findings can be used to illustrate this notion of consistent "patterns of organization." For example, early, heightened levels of behavioral inhibition may affect later adjustment by influencing the way in which a child adapts to new and unfamiliar situations and the ensuing person–environment interactions over time (Kagan, 1994a). Another example of a consistent pattern of organization involves early attachment quality and the development of internal working models that children carry with them into their later relationships (Bowlby, 1988; Goldberg, 1991). Internal working models of self and relationships may remain relatively stable over time, at the same time that the behavioral expressions of these internal models change with development. From a neuroscientific perspective, Pennington and Ozonoff (1991) argue that certain genes and neural systems also play a significant predisposing role in influencing the continuity of psychopathology, and that the "discontinuities at one level of analyses—that of observable behavior—may mask continuities at deeper levels of analysis; those concerned with the mechanisms underlying observable behavior" (p. 117).

Given that developmental continuity is reflected in general patterns of organization over time rather than in isolated behaviors or symptoms, the relationships between early adaptation and later psychopathology are not likely to be direct or uncomplicated. The connections between psychopathology in children and adults are marked by *both* continuities and discontinuities. The degree of continuity–discontinuity will vary as a function of changing environmental circumstances and transactions between a child and the environment that affect the child's developmental trajectory.

Developmental Pathways

The concept of "developmental pathways" is crucial for understanding continuities and discontinuities in psychopathology. Such pathways are not directly observable, but function as metaphors that are inferred from repeated assessments of individual children over time and used as a framework for synthesis and integration (Loeber, 1991; Pickles & Hill, 2006). A pathway, ac-

cording to Loeber (1991), "defines the sequence and timing of behavioral continuities and transformations and, ideally, summarizes the probabilistic relationships between successive behaviors" (p. 98). In attempting to identify developmental pathways as either "deviant" or "normal," it is important to recognize that (1) different pathways may lead to similar expressions of psychopathology (i.e., "equifinality"); and (2) similar initial pathways may result in different forms of dysfunction (i.e., "multifinality"), depending on the organization of the larger system in which they occur (Cicchetti & Rogosch, 1996; Lewis, 2000; Loeber, 1991).

Research findings related to child maltreatment provide an example of a developmental pathway to maladaptive outcomes, with the important qualification that most children who are abused do not exhibit these negative outcomes. The question of why some children seem particularly susceptible to the impact of abuse has led to the search for susceptibility factors, such as child genetic markers (see Wekerle et al., Chapter 16, this volume). However, it is known that physically abused children are more likely to develop insecure attachments, to view interpersonal relationships as coercive and threatening, to become vigilant and selectively attend to hostile cues, to classify others instantly as threatening or nonthreatening, and to acquire aggressive behavioral strategies for solving interpersonal problems (see Cicchetti & Manly, 2001). These children bring representational models to peer relationships that are negative, conflictual, and unpredictable. They process social information in a biased and deviant manner, and develop problems with peer relationships that involve social withdrawal, unpopularity, and overt social rejection by peers (Dodge, Pettit, & Bates, 1994). In another example of a developmental pathway, the diagnosis of conduct disorder typically precedes the initiation of use of various substances, and this use in turn precedes the diagnosis of alcohol dependence in adolescents (Kuperman et al., 2001). Tragically, this can, in turn, exacerbate risk for persistant antisocial behavior by virtue of the reciprocal influences of alcohol dependence on antisocial behavior and vice versa (Barkley, Fischer, Smallish, & Fletcher, 2004).

The systematic delineation of developmental pathways not only offers several advantages for the study of the etiology and outcomes of childhood disorders, but may also suggest strategies for intervention. Loeber (1991, p. 99) describes these advantages as "attempts to capture the changing manifestations and variable phenotype of a given disorder" over time. In this way, the study of developmental pathways includes etiological considerations, the assessment of comorbidities as they accrue over time, and a sensitivity to diverse outcomes (e.g., White, Bates, & Buyske, 2001).

Risk and Resilience

Previous studies of child psychopathology focused on elucidating the developmental pathways for deviancy and maladjustment, to the relative exclusion of those for competency and adjustment (but see, for exceptions, Luthar, 1993; Rutter, 1985, 1987, 1994b; Rutter & Rutter, 1993). However, a significant number of children who are at risk do *not* develop later problems. There is a growing recognition of the need to examine not only risk factors, but also those conditions that protect vulnerable children from dysfunction and lead to successful adaptations despite adversity (Cicchetti & Garmezy, 1993; Masten & Wright, 2010).

"Resilience," which refers to successful adaptation in children who experience significant adversity, has now received a good deal of attention (Luthar, Cicchetti, & Becker, 2000). Early patterns of adaptation influence later adjustment in complex and reciprocal ways. Adverse conditions, early struggles to adapt, and failure to meet developmental tasks do not inevitably lead to negative outcomes. Rather, many factors can provide turning points whereby success in a particular developmental task (e.g., educational advances, peer relationships) shifts a child's course onto a more adaptive trajectory. Conversely, numerous events and circumstances, and underlying dynamic biological systems, may shape a child's developmental trajectory toward maladaptation (e.g., a dysfunctional home environment, peer rejection, difficulties in school, parental psychopathology, intergenerational conflict, and genetic effects).

Although the term "resilience" has not been clearly operationalized, it is generally used to describe children who (1) manage to avoid negative outcomes and/or to achieve positive outcomes despite being at significant risk for the development of psychopathology; (2) display sustained competence under stress; or (3) show recovery from trauma (Werner, 1995). Risk is usually defined in terms of child characteristics that are known to be associated with negative outcomes—for example, difficult temperament (Ingram & Price, 2001; Rothbart, Ahadi, & Evans, 2000)—and/or in terms of a child's exposure to extreme or disadvantaged environmental conditions (e.g., poverty or abuse). Individual children who are predisposed to develop psychopathology, and

who show a susceptibility to negative developmental outcomes under high-risk conditions, are referred to as "vulnerable." Genetic makeup and temperament are two factors that are presumed to contribute to susceptibility for children who are exposed to high-risk environments (Rutter, 1985; Seifer, 2000).

Further complicating such models are recent findings suggesting that certain genetic variants and temperament traits may serve not simply as markers of vulnerability to high-risk environments, but as markers of differential susceptibility to an array of positive and negative contexts (Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2011). The notion of differential susceptibility to the environment means that some individual-difference factors will be linked to both especially negative *and* positive outcomes for children, depending on whether the early environment is harsh or one of nurturing support. In contrast, other children lacking such markers of plasticity (Ellis & Boyce, 2008) will tend to have intermediate outcomes regardless of the quality of the early environment. These two types of children (i.e., those highly responsive to their environments vs. those more resistant to environmental influence) have been compared to the delicate orchid and the hardy dandelion (Ellis & Boyce, 2008), with the so-called "dandelion" children exhibiting resilience in the context of early adversity.

Research on resilience has lacked a consistent vocabulary, conceptual framework, and methodological approach (Luthar et al., 2000; Masten, 2011; Rutter, 2000). It is particularly important to note that resilience is not defined as a universal, categorical, or fixed attribute of a child, but rather as a number of different types of dynamic processes that operate over time. Individual children may be resilient in relation to some specific stressors but not others, and resilience may vary over time and across contexts (Rutter, 2012). Models of resilience have increasingly begun to address the complex and dynamic relationships between the child and his or her environment, to incorporate the theoretical and empirical contributions of developmental psychology, and to acknowledge the multiple factors related to normal and deviant behavior (Rutter, 2006; Shiner & Masten, 2012).

One problem in research on resilience has been an absence of agreed-upon criteria for defining positive developmental outcomes (see Kaufman, Cook, Arny, Jones, & Pittinsky, 1994, for a review of the ways in which positive outcomes in studies of resilience have been operationalized). For example, there is currently debate as to whether the criteria for defining resilience and adaptation should be based on evidence from external criteria (e.g., academic performance), internal criteria (e.g., subjective well-being), or some combination of these (see Masten, 2001). Variations across studies in the source of information (e.g., parent or teacher); the type of assessment method (e.g., interview, questionnaire, observation); the adaptational criteria used; and the number and timing of assessments can easily influence the proportion of children who are designated as resilient or not in any particular investigation (Kaufman et al., 1994; Masten, 2001). In addition, there is also some confusion about, and circularity in, how the term "resilience" has been used, in that it has been used to refer both to an outcome and to the cause of an outcome. Furthermore, in instances in which resilience is used to refer to qualities of children that are putative markers of the capacity for positive adaptation despite adversity, it is important that such markers reflect capture more than the simple absence of vulnerability in order for them to have unique incremental validity for child outcomes beyond models of risk (see next section).

Several different models of resilience have also been proposed, the most common ones being a compensatory model, a challenge model (e.g., stress inoculation), and a protective-factors model (Garmezy, Masten, & Tellegen, 1984). Years of research suggest that resilience is not indicative of any rare or special qualities of a child per se (as implied by the term "the invulnerable child"), but rather is the result of the interplay of normal developmental processes such as brain development, cognition, personality development, caregiver–child relationships, regulation of emotion and behavior, and the motivation for learning (Masten, 2001). Some researchers have argued that resilience may be more ubiquitous than previously thought, and that this phenomenon is part of the "ordinary magic" and makeup of basic human adaptation (Masten, 2001; Sheldon & King, 2001). It is when these adaptational systems are impaired, usually through prolonged or repeated adversity, that the risk for childhood psychopathology increases.

Finally, the possibility that children may actually benefit from exposure to mild to moderate levels of stress has been proposed (e.g., Rutter, 2012; Taleb, 2012), but is not well understood from the standpoint of empirical research. In brief, the notion behind this hypothesis is that the experience of stress enables children to develop coping and other skills that permit them to

manage future stressors more successfully; if so, overly protective, hypervigilant parenting styles would have a negative impact on children, in part by preventing them from having such experiences. While this idea has common-sense appeal and complements exposure-based approaches to treating anxiety and other psychological problems, it has yet to accrue much in the way of research attention; it thus represents an important future direction in work on how stress influences child development.

Protective and Vulnerability Factors

Various protective and vulnerability factors have been found to influence children's reactions to potential risk factors or stressors (Kim-Cohen & Gold, 2009; Luthar, 2006). These include factors within the child, the family, and the community (Osofsky & Thompson, 2000; Werner & Smith, 1992). An example of a within-child risk factor would be cases in which individual differences in genetic risk moderate associations between adversity and negative outcomes (e.g., Brody et al., 2014). Common risk factors that have been found to have adverse effects on a child encompass both acute stressful situations and chronic adversity; they include such events as chronic poverty, poor caregiving, parental psychopathology, death of a parent, community disasters, homelessness, reduced social support, decreased financial resources, family breakup, parental marital/couple conflict, and perinatal stress (Brennan et al., 2008; Deater-Deckard & Dunn, 1999; Luecken & Lemery, 2004; Repetti, Taylor, & Seeman, 2002; Rutter, 1999; Tebes, Kaufman, Adnopoz, & Racusin, 2001).

Protective factors within a child that have been identified include an "easy" temperament (i.e., a child who is energetic, affectionate, cuddly, good-natured, and/or easy to deal with), which makes the child engaging to other people; early coping strategies that combine autonomy with help seeking when needed; high intelligence and scholastic competence; effective communication and problem-solving skills; positive self-esteem and emotions; high self-efficacy; genetic factors (i.e., Dodge & Sherrill, 2007); and the will to be or do something (Fredrickson, 2001; Gilgun, 1999). An example of possible protective factors within the child is seen in findings that high respiratory sinus arrhythmia in conjunction with high skin conductance—taken as indices of a child's ability to self-regulate via self-soothing, focused attention, and organized and goal-directed behavior—can buffer children from the increases in internalizing symptoms associated with exposure to parental marital conflict (El-Sheikh et al., 2013).

At a family level, protective factors that have been identified include the opportunity to establish a close relationship with at least one person who is attuned to the child's needs; positive parenting; availability of resources (e.g., child care); a talent or hobby that is valued by adults or peers; and family religious beliefs that provide stability and meaning during times of hardship or adversity (Werner & Smith, 1992). Protective factors in the community include extrafamilial relationships with caring neighbors, community elders, or peers; an effective school environment, with teachers who serve as positive role models and sources of support; and opening of opportunities at major life transitions (e.g., adult education, voluntary military service, church or community participation, a supportive friend or marital/relationship partner).

In summary, early patterns of adaptation influence later adjustment in complex and reciprocal ways. Adverse conditions, early adaptational struggles, and failure to meet developmental tasks do not inevitably lead to a fixed and unmalleable dysfunctional path (Rutter, 2007a). Rather, as noted earlier, many different factors can act to alter a child's developmental course for the better. Conversely, numerous events and circumstances may serve to alter this course for the worse.

The interrelated issues of developmental continuities–discontinuities; of developmental pathways; of risk, resilience, and antifragility; and of vulnerability and protective factors are far from being resolved or clearly understood. The multitude of interdependent and reciprocal influences, mechanisms, and processes involved in the etiology and course of child psychopathology clearly suggest a need for more complex theories (e.g., chaos theory, nonlinear dynamic models) (Granic, 2005; Glantz & Johnson, 1999), research designs, and data-analytic strategies (Rutter, 2007b; Singer & Willett, 2003).

Contextual Influences

Messick (1983) cogently argued that any consideration of child psychopathology must consider and account for three sets of contextual variables: (1) the child *as* context—the idea that unique child characteristics, predispositions, and traits influence the course of development; (2) the child *of* context—the notion that the child comes from a background of interrelated family, peer,

classroom, teacher, school, community, and cultural influences; and (3) the child *in* context—the understanding that the child is a dynamic and rapidly changing entity, and that descriptions taken at different points in time or in different situations may yield very different information.

Research has increasingly come to recognize the reciprocal transactions between the developing child and the multiple social and environmental contexts in which development and psychopathological symptoms occur (Deater-Deckard, 2001; Dirks, De Los Reyes, Briggs-Gowan, Cella, & Wakschlag, 2012). Understanding context requires a consideration of events that impinge directly on the child in a particular situation at a particular point in time; extrasituational events that affect the child indirectly (e.g., a parent's work-related stress); and temporally remote events that continue to affect the child through their representation in the child's current cognitive–affective database.

Certainly, relatively straightforward aspects of the physical context are known to affect child development (e.g., diet, lead; Chandramouli, Steer, Ellis, & Emond, 2009; Grantham-McGregor & Baker-Henningham, 2005). However, defining context has been, and continues to be, a matter of some complexity. The context of maltreatment provides an illustration of difficulties in definition. Maltreatment can be defined in terms of its type, timing, frequency, severity, and chronicity in the family (e.g., Manly, Kim, Rogosch, & Cicchetti, 2001). Each of these parameters and their interaction may contribute to child outcomes, but in different ways. For example, Manly, Cicchetti, and Barnett (1994) studied different types of maltreatment and found that outcomes generally did not differ for children who were categorized as neglected versus abused. However, a regression analysis indicated that neglect accounted for more of the variance in child problems than other types of abuse did. In this study, sexually abused children were also found to be more socially competent than children exposed to other forms of maltreatment. This may reflect a lack of chronicity associated with sexual abuse, or it may suggest that problems related to sexual abuse may not reveal themselves until later periods in a child's development, when issues concerning sexuality become more salient. Other studies have found that psychological maltreatment and emotional abuse account for most of the distortions in development attributed to maltreatment in general, and have the most negative consequences for a child (Crittenden, Claussen, & Sugarman, 1994).

The example of maltreatment illustrates how contexts for development encompass heterogeneous sets of circumstances, and how child outcomes may vary as a function of (1) the configuration of these circumstances over time, (2) when and where outcomes are assessed, and (3) the specific aspects of development that are affected. More precise definitions are needed if the impact of maltreatment—or, for that matter, any contextual event (e.g., parent disciplinary styles, family support, intellectual stimulation, nutrition)—is to be understood.

Even for those forms of child psychopathology for which there are strong neurobiological influences, the expression of the disorder is likely to interact with contextual demands. For example, Iaboni, Douglas, and Baker (1995) found that although the overall pattern of responding shown by children with ADHD was indicative of a generalized inhibitory deficit, the self-regulatory problems of these children became more evident with continuing task demands for inhibition and/or deployment of effort. Likewise, tasks having high interest value or high external incentives may moderate these children's typically deficient performance on less interesting or low-incentive tasks (Carlson & Tamm, 2000; Slusarek, Velling, Bunk, & Eggers, 2001).

Child psychopathology research has increasingly focused on the role of the family system, the complex relationships within families, and the reciprocal influences among various family subsystems (Fiese, Wilder, & Bickham, 2000). There is a need to consider not only the processes occurring within disturbed families, but the common and unique ways in which these processes affect both individual family members and subsystems. Within the family, the roles of the mother–child and marital/couple subsystems have received the most research attention to date, with less attention given to the roles of siblings (Hetherington, Reiss, & Plomin, 1994) and fathers (Phares, Rojas, Thurston, & Hankinson, 2010). For the most part, research into family processes and child psychopathology has not kept pace with family theory and practice, and there is a need for the development of sophisticated methodologies and valid measures that will capture the complex relationships hypothesized to be operative in disturbed and normal family systems (Bray, 1995; Bray, Maxwell, & Cole, 1995). This task is complicated by a lack of consensus concerning how healthy family functioning or family dysfunction should be defined; what specific family processes are important to assess (Mash & Johnston, 1995); or the extent to which such measures of fam-

ily environment reflect true environmental effect or shared genetic influences between parent and child (Plomin, 1995).

DEFINING CHILD PSYCHOPATHOLOGY

There has been, and continues to be, a lack of consensus concerning how psychopathology in children should be defined (Angold & Costello, 2009; Rutter, 2011). Despite ongoing debate, for pragmatic purposes, researchers and clinicians typically define child psychopathology using standardized diagnostic systems such as the most recent revision of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association [APA], 2013a) and the *International Classification of Diseases*, 10th revision (ICD-10; WHO, 2010). The diagnostic criteria utilized in DSM-5 are the ones most commonly used in North America, and these are presented for the individual disorders described in each subsequent chapter of this volume. However, the increased use and acceptance of DSM-5 and its predecessors should not be taken as an indication of widespread agreement regarding the fundamental nature of what constitutes psychopathology in children or the specific criteria used to define it (cf. Coghill & Sonuga-Barke, 2012; Hudziak et al., 2007; Rutter, 2011). In many ways, the acceptance and use of DSM-5 seems to reflect a degree of resignation on the part of many researchers and clinicians concerning the prospects for developing a widely agreed-upon alternative approach. Nevertheless, alternative approaches are being advanced that apply current research findings toward the development of classification frameworks for psychopathology (Insel et al., 2010; Sanislow et al., 2010), as discussed later in this chapter.

Several fundamental questions have characterized most discussions concerning how child psychopathology should be defined:

1. Should child psychopathology be viewed as a disorder that occurs within the individual child (e.g., disorder of the brain, psychological disturbance), as a relational disturbance, as a reaction to environmental circumstances, or (as is likely) some combination of all these?

2. Does child psychopathology constitute a condition qualitatively different from normality (aberration), an extreme point on a continuous trait, a delay in the rate at which a normal trait would typically emerge, or some combination of the three? How are "subthreshold" problems to be handled?

3. Can homogeneous disorders be identified? Or is child psychopathology best defined as a configuration of co-occurring disorders or as a profile of traits and characteristics?

4. Can child psychopathology be defined as a static entity at a particular point in time, or do the realities of development necessitate that it be defined as a dynamic and ongoing process that expresses itself in different ways over time and across contexts?

5. Is child psychopathology best defined in terms of its current expression, or do definitions also need to incorporate nonpathological conditions that may constitute risk factors for later problems? This question is especially relevant when considering disorder and risk for disorder in infants and toddlers (see Lyons-Ruth, Zeanah, Benoit, Madigan, & Mills-Koonce, Chapter 15, this volume).

There are currently no definitive answers to these questions. More often, the way in which they are answered reflects theoretical or disciplinary preferences and utility, such as specific purposes and goals (e.g., defining samples for research studies, or determining program or insurance eligibility).

Psychopathology as Adaptational Difficulty

As we have noted earlier, a common theme in defining child psychopathology has been that of adaptational difficulty or failure (Garber, 1984; Mash, 1998). Sroufe and Rutter (1984) note that regardless of whether "particular patterns of early adaptation are to a greater or lesser extent influenced by inherent dispositions or by early experience, they are nonetheless patterns of adaptation" (p. 23). Developmental competence is reflected in a child's ability to use internal and external resources to achieve a successful adaptation (Masten, Burt, & Coatsworth, 2006; Waters & Sroufe, 1983), and problems occur when the child fails to adapt successfully. Even with wide variations in terminology and proposed explanatory mechanisms across theories, there is general agreement that maladaptation represents a pause, a regression, or a deviation in development (Garber, 1984; Simeonsson & Rosenthal, 1992).

In conceptualizing and defining psychopathology as adaptational difficulty, it is also essential to conceptualize and identify the specific developmental tasks and challenges that are important for children at various ages and periods of development, and the many contextual variables that derive from and surround the child (Garber, 1984; Luthar, Burack, Cicchetti, & Weisz, 1997; Mash, 1998). In this regard, the study of psychopathology in children and the study of development and context are for all intents and purposes inseparable (Cicchetti & Aber, 1998).

In determining whether a given behavior should be considered to be deviant in relation to stage-salient developmental issues, Garber (1984) stresses the need to understand several important parameters. The first, "intensity," refers to the magnitude of behavior as excessive or deficient. The second, "frequency," refers to the severity of the problem behavior, or how often it does or does not occur. Third, the "duration" of behavior must be considered. Some difficulties are transient and spontaneously remit, whereas others persist over time. To these parameters, we would add a qualitative parameter reflecting how grossly atypical the behavior may be (e.g., some of the complex compulsions seen in Tourette's disorder), such that even low-intensity, low-frequency, and short-duration behavior may be so bizarre as to constitute "psychopathology." It is crucial that the intensity, frequency, duration, and atypicality of the child's behavior be appraised with respect to what is considered normative for a given age (e.g., the developmental appropriateness of a behavior). The final parameter of deviance concerns the "number of different symptoms" and their "configuration." Each of these parameters is central to research and theory, and to one's specific definition of adaptational failure, regression, stagnation, or deviation.

Social Judgment

The diagnosis of psychopathology in children is almost always a reflection of both the characteristics and behavior of the child *and* of significant adults and professionals (Lewis, 2000). Research findings utilizing behavior problem checklists and interviews indicate that there can be considerable disagreement across informants (e.g., parents, teachers, professionals) concerning problem behaviors in children (Achenbach, McConaughy, & Howell, 1987; Feiring & Lewis, 1996; Youngstrom, 2013). Mothers typically report more problems than do fathers (e.g., Achenbach et al., 1991), and across a range of domains, teachers identify more problems than other informants do in assessing the same domains. For example, in a study with maltreated children, only 21% were classified as resilient by teachers, whereas 64% were so classified based on reports from other sources (Kaufman et al., 1994).

Issues regarding disagreement–agreement among informants are complicated by the fact that the amount of agreement will vary with the age and sex of the child (Offord, Boyle, & Racine, 1989), the nature of the problem being reported on (e.g., internalizing vs. externalizing; De Los Reyes & Kazdin, 2005), the method used to gather information (e.g., interview vs. questionnaire), and the informants being compared. For example, Tarullo, Richardson, Radke-Yarrow, and Martinez (1995) found that both mother–child and father–child agreement was higher for preadolescent than for adolescent children; in a meta-analysis, Duhig, Renk, Epstein, and Phares (2000) reported higher mother–father agreement for externalizing than for internalizing problems. Disagreements among informants create methodological difficulties in interpreting epidemiological data when such data are obtained from different sources, and also in how specific diagnoses are arrived at in research and practice. For most research studies, the practice tends to be to consider a symptom present if any informant endorses it as such (e.g., Costello, Mustillo, et al., 2003).

Also of importance is how disagreements among informants are interpreted (De Los Reyes, 2011). For example, disagreements may be viewed as (1) reflections of bias or error on the part of one informant; (2) evidence for the variability of children's behavior across the situations in which they are observed by others; (3) lack of access to certain types of behavior (i.e., private events) on the part of one informant; (4) denial of the problem; or (5) active distortion of information in the service of some other goal (e.g., defensive exclusion, treatment eligibility).

Parental psychopathology may "color" descriptions of child problems—as may occur when abusive or depressed mothers provide negative or exaggerated descriptions of their children (Gotlib & Hammen, 1992; Mash et al., 1983; Richters, 1992; Youngstrom, Izard, & Ackerman, 1999), or when dismissive/avoidant adult informants deny the presence of emotional problems at the same time that professionals observe a high level of symptoms (Dozier & Lee, 1995). These latter types of problems in reporting may be especially likely, given

the frequent lack of correspondence between the expression and the experience of distress for many child and adult disturbances. Hypothesized relationships between parental psychopathology and reports of exaggerated child symptoms have received mixed support. For example, some studies have failed to find evidence for distorted reports by depressed mothers (Tarullo et al., 1995). However, recent work (Durbin & Wilson, 2012) examining maternal ratings of child behavior also coded by objective raters found that mothers' lifetime psychiatric diagnoses and personality traits were associated with their reports of child emotional behavior, and that for some emotions, mothers' mental health and dispositional variables were more strongly related to their reports of their children's emotions than were objective indices of the children's observable emotional behavior. Related work (Hayden, Durbin, Klein, & Olino, 2010) indicates that maternal characteristics, such as mothers' own personality traits, influence the extent to which they successfully encode and/or report on analogous child behaviors. Intriguingly, the extent to which informant discrepancies are present regarding child behavior may predict poor child outcomes, above and beyond individual informants' reports of children (De Los Reyes, 2011). Thus, while it is well known that informant discrepancies exist, the meaning of these discrepancies and their implications for child outcomes requires further study.

APPROACHES TO CONCEPTUALIZING CHILD PSYCHOPATHOLOGY

The types of problems for which children are referred for treatment are reflected in the different approaches that have been used to conceptualize and classify these problems. Among the more common of these approaches are the following:

1. General and specific behavior problem checklists, which enumerate individual child symptoms—for example, the Child Behavior Checklist (Achenbach & Rescorla, 2001) and the Children's Depression Inventory 2 (Kovacs, 2010).
2. Dimensional approaches, which focus on symptom clusters or syndromes, derived from behavior problem checklists—for example, the Child Behavior Checklist and Profile (Achenbach, 1993; Achenbach & Rescorla, 2001).
3. Categorical approaches, which use predetermined diagnostic criteria to define the presence or absence of particular disorders—for example, DSM-5 (APA, 2013a) and ICD-10 (WHO, 2010).[5]
4. A multiple-pathway, developmental approach, which emphasizes developmental antecedents and competencies both within the child and the environment that contribute to (mal)adjustment and (mal) adaptation (Sroufe, 1997).

Issues related to the use of these different classification approaches are discussed in a later section of this chapter. What follows is a brief overview of the types of problem behaviors, dimensions, and disorders that occur during childhood and that are the topics of this volume's other chapters.

Individual Symptoms

For the most part, individual behavioral and emotional problems (i.e., symptoms) that characterize most forms of child psychopathology occur in almost all children at one time or another during their development (e.g., Achenbach & Edelbrock, 1981; Achenbach et al., 1991; MacFarlane et al., 1954). When taken in isolation, specific symptoms have generally shown little correspondence to a child's overall current adjustment or to later outcomes. This is the case even for many symptoms hypothesized to be significant indicators of psychopathology in children in earlier decades—for example, thumbsucking after 4 years of age (Friman, Larzelere, & Finney, 1994). Usually the age-appropriateness, clustering, and patterning of symptoms are what serve to define child psychopathology, rather than the presence of individual symptoms.

Many of the individual behavior problems displayed by children referred for treatment are similar to those that occur in less extreme forms in the general population or in children of younger ages. For example, Achenbach and colleagues (1991) found that although referred children scored higher than nonreferred children on 209 of 216 parent-rated problems, only 9 of the 209 items showed effects related to clinical status that were considered to be large (accounting for more than 13.8% of the variance), according to criteria specified by Cohen (1988). Examples of parent-reported individual symptoms that were more common in referred than in nonreferred children and that accounted for 10% or more of the variance in clinical status included "sad or

depressed," "uncooperative," "nervous," "high-strung, or tense," "feels he/she can't succeed," "feels worthless or inferior," "disobedient at school," "easily distracted," "lies," "fails to finish things he/she starts," "defiant," and "doesn't get along with other kids" (Achenbach et al., 1991). As can be seen, even the problems that best discriminated between referred and nonreferred children are relatively common behaviors that occur to some extent in all children; they are not particularly strange or unusual behaviors. In addition, most *individual* problem behaviors (approximately 90% of those on behavior problem checklists) do not, by themselves, discriminate between groups of clinic-referred and nonreferred children. Nondiscriminating items include some problems for children in both groups that are relatively common (e.g., "brags," "screams") and others that occur less frequently (e.g., "sets fires," "bowel movements outside the toilet").

Dimensions of Child Psychopathology

A second approach to describing child psychopathology identifies symptom clusters or "syndromes" derived through the use of multivariate statistical procedures, such as factor analysis or cluster analysis (e.g., Achenbach, 1993, 1997; McDermott, 1993; McDermott & Weiss, 1995). Research has identified two broad dimensions of child psychopathology—one reflecting "externalizing" or "undercontrolled" problems, and the other reflecting "internalizing" or "overcontrolled" problems (Reynolds, 1992). The externalizing dimension encompasses behaviors often thought of as directed at others, whereas the internalizing dimension describes feelings or states that are commonly viewed as "inner-directed." The presense of these two dimensions may account for the pervasive comorbidity found between internalizing (e.g., depression and anxiety) and externalizing (e.g., oppositional and conduct problems) disorders; moreover, extensions of this research applied to adults suggest that a similar structure may characterize adult psychopathology (Krueger & Markon, 2006; although see Kotov et al., 2011), thus supporting the lifespan continuity of this dimensional structure. Within the two broad dimensions of externalizing and internalizing disorders, there may be further subdimensions or syndromes, including anxious/depressed (e.g., "crying," "fearful of multiple situations"), withdrawn/depressed (e.g., "enjoys little," "withdrawn"), somatic complaints (e.g., "feels dizzy," "tired"), social problems (e.g., "lonely," "gets teased"), thought problems (e.g., "hears or sees things"), attention problems (e.g., "problems sitting still or attending"), rule-breaking behavior (e.g., "steals," "swears"), and aggressive behavior (e.g., "argumentative," "physically aggressive") (Achenbach & Rescorla, 2001).

Categories of Child Psychopathology

The DSM-5 diagnostic system (APA, 2013a) provides comprehensive coverage of the general types of symptom clusters displayed by children characterized as having mental disorders. To illustrate, DSM-5 categories that apply to children are listed in Tables 1.1–1.3. These tables are not intended to be exhaustive of all DSM-5 diagnoses that may apply to children. Rather, they are intended to provide an overview of the range and variety of disorders that typically occur during childhood. Specific DSM-5 disorders and their subtypes are discussed in detail in the subsequent chapters of this volume.

Table 1.1 lists the DSM-5 categories for neurodevelopmental disorders, including intellectual disability, communication disorders (e.g., language disorder), autism spectrum disorder, ADHD, specific learning disorder, and motor disorders. Most of these disorders are early-emerging, often co-occurring conditions characterized by deficits and delays in attaining developmental milestones, and are associated with a range of impairments in multiple domains of functioning (e.g., social, academic). An array of specifiers, such as age of onset and severity, can be applied to provide further detail to the clinical description of individual patients and to aid prediction of the disorder's course. Whether the disorder is accompanied by a medical or genetic condition or an environmental factor with potential etiological significance (e.g., fetal alcohol exposure) can also be noted as part of the diagnosis.

Table 1.2 is a noncomprehensive list of DSM-5 categories for other disorders that can be diagnosed in children or adolescents (e.g., schizophrenia, depressive disorders, bipolar and related disorders, anxiety disorders). It is noteworthy that, unlike its immediate predecessors, the DSM-5 does not contain a separate section on disorders of infancy and childhood; instead, disorders previously located in this section in DSM-IV are now found in the section for neurodevelopmental disorders (e.g., ADHD) or are integrated in other sections throughout the manual (e.g., separation anxiety

TABLE 1.1. DSM-5 Categories for Neurodevelopmental Disorders

Intellectual disabilities
Intellectual disability (intellectual developmental disorder)
Global developmental delay
Unspecified intellectual disability
Communication disorders
Language disorder
Speech sound disorder
Childhood-onset fluency disorder (stuttering)
Social (pragmatic) communication disorder
Unspecified communication disorder
Autism spectrum disorder
Autism spectrum disorder
Attention-deficit/hyperactivity disorder
Attention-deficit/hyperactivity disorder
Other specified attention-deficit/hyperactivity disorder
Unspecified attention-deficit/hyperactivity disorder
Specific learning disorder
Specific learning disorder
Motor disorders
Developmental coordination disorder
Stereotypic movement disorder
Tourette's disorder
Persistent (chronic) motor or vocal tic disorder
Provisional tic disorder
Other specified tic disorder
Unspecified tic disorder
Other neurodevelopmental disorders
Other specified neurodevelopmental disorder
Unspecified neurodevelopmental disorder

TABLE 1.2. Select DSM-5 Categories for Other Disorders Diagnosed in Infancy, Childhood, or Adolescence

Schizophrenia spectrum and other psychotic disorders
Schizotypal personality disorder; schizophrenia; schizoaffective disorder; schizophreniform disorder; delusional disorder; brief psychotic disorder
Bipolar and related disorders
Bipolar I disorder; bipolar II disorder; cyclothymic disorder
Depressive disorders
Disruptive mood dysregulation disorder; major depressive disorder, single episode or recurrent episodes; persistent depressive disorder (dysthymia)
Anxiety disorders
Separation anxiety disorder; selective mutism; specific phobia; social anxiety disorder (social phobia); panic disorder; agoraphobia
Obsessive–compulsive and related disorders
Obsessive–compulsive disorder; body dysmorphic disorder; hoarding disorder; trichotillomania (hair-pulling disorder); excoriation (skin-picking) disorder
Trauma- and stressor-related disorders
Reactive attachment disorder; disinhibited social engagement disorder; posttraumatic stress disorder; acute stress disorder; adjustment disorders
Feeding and eating disorders
Pica; Rumination disorder; avoidant/restrictive food intake disorder; anorexia nervosa; bulimia nervosa; binge-eating disorder
Elimination disorders
Enuresis; encopresis
Disruptive, impulse-control, and conduct disorders
Oppositional defiant disorder; intermittent explosive disorder; conduct disorder; antisocial personality disorder; pyromania; kleptomania
Substance-related and addictive disorders
Substance use disorders; substance-induced disorders

disorder). This change was made with the goal of emphasizing a lifespan approach to conceptualizing mental disorders, and in recognition of the fact that many disorders can and do manifest themselves across the lifespan (APA, 2013b). Although it is true that boundaries drawn between disorders of childhood and other age groups are arbitrary, and potentially hamper tests of psychopathology continuity over time, the long-term implications of this significant change to DSM organization are unclear. The addition of a specific section dedicated to disorders of childhood to DSM-III is widely regarded as having played a critical role in increasing research interest in childhood disorders; whether removing this distinction will result in a decrease in the level of attention being paid to disorders of children remains to be seen.

Finally, Table 1.3 is a noncomprehensive list of DSM-5 categories for other conditions that are not defined as mental disorders, but may be a focus of clinical attention. We have focused on those with the greatest relevance for childhood or adolescence, in that they emphasize relational problems, maltreatment, and academic and adjustment difficulties.

TABLE 1.3. DSM-5 Categories for Other Conditions That May Be a Focus of Clinical Attention

Relational problems
Problems related to family upbringing (e.g., parent–child relationship problem; child affected by parental relationship distress)
Other problems related to primary support group (e.g., disruption of family by separation or divorce; uncomplicated bereavement)
Abuse and neglect
Child maltreatment and neglect problems (e.g., confirmed and suspected physical and sexual abuse; confirmed and suspected neglect; encounters for mental health services for these problems)
Educational and occupational problems
Educational problems (e.g., academic problems)
Housing and economic problems
Housing problems (e.g., homelessness; inadequate housing)
Economic problems (e.g., lack of adequate food or safe drinking water; extreme poverty; low income)

APPROACHES TO THE CLASSIFICATION AND DIAGNOSIS OF CHILD PSYCHOPATHOLOGY

There is general agreement in medicine, psychiatry, and psychology regarding the need for a system of classifying childhood disorders. However, major areas of contention have arisen around such issues as which disorders should be included in the system, what the optimal strategies are for organizing and grouping disorders, and which specific criteria should be used to define a particular disorder (Achenbach, 1985; Achenbach & Edelbrock, 1989; Mash & Barkley, 2007; Sonuga-Barke, 1998).

The two most common approaches to the diagnosis and classification of child psychopathology involve the use of (1) "categorical" classification systems that are based primarily on informed clinical consensus, an approach that has dominated and continues to dominate the field (APA, 1994, 2000, 2013a); and (2) empirically based "dimensional" classification schemes derived through the use of multivariate statistical techniques (Achenbach, 1993, 1997; Achenbach & Rescorla, 2001). In addition, alternative and/or derivative approaches to classification have been proposed to address perceived deficiencies associated with the use of categorical and dimensional approaches. These have included developmentally based measures (Garber, 1984; Mohr & Regan-Kubinski, 1999; Sroufe, 1997), laboratory and performance-based measures (Frick, 2000), prototype classification (Cantor et al., 1980; Shaffner, 2012), and behavioral classification/functional analysis based on behavioral excesses, deficits, and faulty stimulus control (Mash & Hunsley, 1990; Ringdahl & Falcomata, 2009). Although each of these alternative approaches has something to offer to the classification of childhood disorders, they are generally underdeveloped and unstandardized, and have not been widely accepted or used in either research or practice.

In addition to these alternatives, the limitations of diagnostic systems derived from expert consensus (e.g., DSM-5) have led to both a call for greater emphasis on the underlying neurobiological substrates of psychopathology in classification, and a response, by virtue of the development of the Research Domain Criteria (RDoC; Insel et al., 2010; Sanislow et al., 2010). The RDoC initiative, which was spearheaded by the National Institute of Mental Health, aims to generate research on the biological substrates of psychopathology, with

the goal of developing future classification schemes that map more clearly onto the underlying pathophysiology of disorder. Multiple workshops were held in 2010–2012 with the goal of defining various domains of functioning (e.g., cognitive systems, arousal/regulatory systems), which were further broken down into constructs (e.g., attention, circadian rhythms) that have units of analysis with genetic, molecular, neural, and behavioral levels (Morris & Cuthbert, 2012), although the primary focus of RDoC is on neural circuitry (Insel et al., 2010). It is already known that many if not all of these levels of analysis will cut across disorders as they are traditionally defined, which can be taken as evidence for the failure of current diagnostic systems to "carve nature at its joints" and for the need for the RDoC framework.

One long-term goal of the RDoC initiative is that genetic sequencing, brain imaging, and other laboratory-based approaches will supplant diagnostic systems based on clinical consensus, play a central role in clinical assessments, and directly inform treatment (Insel, 2013; Insel et al., 2010). This is clearly a highly ambitious goal, given the currently limited ability of genetic and neuroimaging findings to predict treatment response or other important clinical outcomes; at present, most constructs with the capacity to predict clinical outcomes (e.g., age of onset, negative life events) would be considered "psychological" or "behavioral" rather than biological. Furthermore, embedded within the RDoC initiative is the notion that mental disorders are disorders of the brain, and can be best understood, and ultimately treated, through the application of clinical neuroscience methodologies and genomics. This viewpoint could be considered reductionistic; at the least, it is an empirical stance that may or may not ultimately be supported by data. Thus, while the core premise behind RDoC (i.e., that contemporary diagnostic systems do not map closely onto etiology, although it would be desirable for them to do so) is not especially controversial, the perceived preeminence of biological approaches to disorder may be to some in the field.

To date, no single classification scheme for childhood disorders has established adequate validity (Cantwell, 1996; Mash & Barkley, 2007; Rutter & Uher, 2012). Many researchers and clinicians have expressed and continue to express concerns that current diagnostic and classification systems (1) underrepresent disorders of infancy and childhood; (2) are inadequate in representing the interrelationships and overlap that exist among many childhood disorders; (3) are not sufficiently sensitive to the developmental, contextual, and relational parameters that are known to characterize most forms of psychopathology in children; and (4) are heterogeneous with respect to etiology (Jensen & Hoagwood, 1997; Kagan, 1997; Rice, 2010).

Categorical Approaches

Categorical approaches to the classification of childhood disorders have included systems developed by the Group for the Advancement of Psychiatry (1974), the WHO (2010), the APA (2013a), and the Zero to Three/National Center for Clinical Infant Programs (2005a). Although a detailed review of all these systems is beyond the scope of this chapter, a brief history of the APA's development of the DSM approach is presented to illustrate the issues associated with categorical approaches, the growing concern for more reliable classification schemes for childhood disorders, and the evolving conceptualizations of childhood disorders over the past 60 years. Discussion of the DSM approach in relation to specific child and adolescent disorders appears in the chapters that follow. Also, the *Diagnostic Classification of Mental Health and Developmental Disorders of Infancy and Early Childhood-Revised*, or *Diagnostic Classification: 0–3R* (DC:0–3R; Zero to Three/National Center for Clinical Infant Programs, 2005a), is described to illustrate a categorical approach that attempts to integrate developmental and contextual information into the diagnosis of infants' and young children's problems.

Development of the DSM Approach

One of the first efforts to collect data on mental illness was in the U.S. census of 1840, which recorded the frequency of a single category of "idiocy/insanity." Forty years later, seven categories of mental illness were identified: dementia, dipsomania, epilepsy, mania, melancholia, monomania, and paresis (APA, 1994). Much later (in the 1940s), the WHO classification system emerged with the manuals of the ICD, whose sixth revision included, for the first time, a section for mental disorders (APA, 1994; Cantwell, 1996).

In response to perceived inadequacies of the ICD system for classifying mental disorders, the APA's Committee on Nomenclature and Statistics developed DSM-I in 1952 (APA, 1952). There were three major categories of dysfunction in DSM-I—"organic brain syndromes," "functional disorder," and "mental defi-

ciency" (Kessler, 1971)—under which were subsumed 106 categories. The term "reaction" was used throughout the text, which reflected Adolf Meyer's psychobiological view that mental illness involves reactions of the personality to psychological, social, and biological factors (APA, 1987). Children were largely neglected in the early versions of DSM (Cass & Thomas, 1979; Silk et al., 2000). In fact, DSM-I included only one child category of "adjustment reactions of childhood and of adolescence," which was included under the heading of "transient situational disorders."

As reflected in the use of the term "reaction," psychoanalytic theory had a substantial influence on the classification of both child and adult psychopathology (Clementz & Iacono, 1993). In part, this was due to the fact that the first classification system to focus on childhood psychopathology was developed by Anna Freud in 1965 (see Cantwell, 1996). Although the term "reaction" was eliminated from DSM-II (APA, 1968), a separate section was reserved for classifying neuroses, and diagnoses could be based on either an assessment of the client's presenting symptomatology or inferences about his or her unconscious processes (Clementz & Iacono, 1993). Once again, apart from conditions subsumed under the adult categories, DSM-II gave little recognition to childhood difficulties except for mental retardation and schizophrenia—childhood type (Cass & Thomas, 1979).

As a formal taxonomy, DSM-III (APA, 1980) represented a substantial departure from, and advance over, earlier editions of the DSM. The first and second editions contained only narrative descriptions of symptoms, and clinicians had to draw on their own definitions for making a diagnosis (APA, 1980); thus interrater reliability of psychiatric diagnoses was quite poor. DSM-III, in which explicit inclusion, exclusion, and duration criteria for each disorder were included, represented a landmark shift of the field aimed at achieving greater diagnostic reliability (Achenbach, 1985; APA, 1980). Moreover, unsubstantiated etiological inferences that were heavily embedded in psychoanalytic theory were dropped, more child categories were included, and a greater emphasis was placed on empirical data (Achenbach, 1985). These changes reflected the beginnings of a conceptual shift in both diagnostic systems and etiological models away from an isolated focus of psychopathology as existing within the child alone, and toward an increased emphasis on his or her surrounding context. DSM-III was revised in 1987 (DSM-III-R) to help clarify the inconsistencies and ambiguities that arose in its use. For example, empirical data at that time did not support the category of attention deficit disorder *without* hyperactivity as a unique symptom cluster (Routh, 1990), and this category was removed from DSM-III-R. DSM-III-R was also developed to be polythetic, in that a child could be diagnosed with a certain subset of symptoms without having to meet all criteria. This was an important change, especially in light of the heterogeneity and rapidly changing nature of most childhood disorders (Mash & Barkley, 2007). Relative to its predecessors, far greater emphasis was also placed on empirical findings in the development of DSM-IV, particularly for the child diagnostic categories.

In order to bridge the planned 12-year span between DSM-IV and DSM-5, a revision (DSM-IV-TR) of DSM-IV was published in 2000 (APA, 2000). DSM-IV-TR was limited to text revisions (e.g., associated features and disorders, prevalence) and was designed mainly to correct any factual errors in DSM-IV, make sure that information was still current, and incorporate new information since the time the original DSM-IV literature reviews were completed in 1992. In 2013, after a considerable delay, DSM-5 was released.

Although contemporary versions of DSM have included numerous improvements over previous DSMs—with their greater emphasis on empirical research, and more explicit diagnostic criteria sets and algorithms—criticisms have also been raised (e.g., Hyman, 2010; Rutter, 2011; Uher & Rutter, 2012). First, although DSM-5 incorporates greater dimensional representation of disorders than its predecessors, it still relies largely on a categorical scheme that may not always optimally serve children's needs. For example, it may be necessary for a child to meet specific diagnostic criteria for specific learning disorder in order to qualify for a special education class. However, if the child's problems are subclinical, or the child's problems relate to more than one DSM category, then he or she may be denied services (Achenbach, 2000). Useful approaches to the goal of incorporating the strengths of dimensional operationalizations of disorder (e.g., increased information) with those of categorical approaches (e.g., ease of communication) have been proposed (e.g., Kamphuis & Noordhof, 2009) and should be applied more frequently in the field.

Another problem with DSM-5 relates to the wording and the lack of empirical adequacy for certain criterion sets. For example, the words "often" in the criteria for ADHD and conduct disorder, and "persistent" and "excessive" in the criteria for separation anxiety disorder,

are not clearly defined. This ambiguity poses a particular problem when one considers that the primary sources of assessment information are often a child's parents, whose perception and understanding of these terms may be idiosyncratic or inaccurate. This ambiguity and other factors may contribute to the unreliability or unsuitability of the DSM for diagnosing certain childhood disorders (e.g., Nicholls, Chater, & Lask, 2000).

A further difficulty with DSM-5 diagnostic criteria is the lack of emphasis on the situational or contextual factors surrounding and contributing to various disorders. This is a reflection of the fact that DSM-5 continues to view mental disorder as individual psychopathology or risk for psychopathology, rather than in terms of problems in psychosocial adjustment. One problem with respect to the atheoretical nature of DSM is that it has perhaps mistakenly fostered the assumption that a description of symptoms is sufficient for diagnosis, without taking into account natural history, psychosocial correlates, biological factors, or response to treatment (Cantwell, 1996). However, the consideration in DSM-5 of such factors as culture, age, and gender associated with the expression of each disorder is laudable, as is the increased recognition of the importance of family problems and extrafamilial relational difficulties.

Other concerns exist, including the extent to which comorbidity is an artifact of the DSM's polythetic criteria (Angold, Costello, & Erkanli, 1999; Nottelmann & Jensen, 1995), or whether the pendulum has swung too far from not identifying psychopathological conditions in children to overly liberal diagnostic practices that label relatively healthy children as disordered (Silk et al., 2000). It is also the case that ongoing changes in diagnostic criteria based on new findings and other considerations (e.g., eligibility for services) are likely to influence prevalence estimates for many childhood disorders. For example, current estimates of the prevalence of autism spectrum disorder (e.g., Kogan et al., 2009) are substantially higher than even fairly recent, previous ones (e.g., Fombonne, 1999; Tanguay, 2000); this increase is primarily due to a broadening of the criteria used to diagnose autism spectrum disorder, as well as increased recognition of milder forms of the disorder and changes in case-finding approaches (Costello, Foley, & Angold, 2006).

Development of the DC:0–3R System

In addition to the limitations noted above, DSM-5 does not provide in-depth coverage of the mental health and developmental problems of infants and young children, for whom such problems are frequently nested within the context of the family. To address this perceived deficiency, DC:0–3 and DC:0–3R, the current version, were developed by the Diagnostic Classification Task Force of the Zero to Three/National Center for Clinical Infant Programs (1994, 2005a). The revised version, developed after a decade's use of the original, primarily differs from the DC:0–3 in terms of its increased use of specific criteria to operationalize disorders, and thus increase interrater reliability (Zero to Three/National Center for Clinical Infant Programs, 2005b; Postert, Averbeck-Holocher, Beyer, Müller, & Furniss, 2009), although few data are available to speak to whether this aim was achieved. The DC:0–3R is intended to provide a comprehensive system for classifying problems during the first 3–4 years of life (Zero to Three/National Center for Clinical Infant Programs, 2005b). Unlike DSM-5, DC:0–3R is based on the explicit premise that diagnosis must be guided by the principle that infants and young children are active participants in relationships within their families. Hence descriptions of infant–caregiver interaction patterns, and of the links between these interaction patterns and adaptive and maladaptive patterns of infant and child development, constitute an essential part of the diagnostic process.

In explicitly recognizing the significance of relational functioning, DC:0–3R includes a relationship classification as a separate axis (Axis II) in its multiaxial approach (Axis I, clinical disorders; Axis III, medical and developmental disorders and conditions; Axis IV, psychosocial stressors; Axis V, emotional and social functioning). The formal classification of relationships is based on observations of parent–child interaction and information about the parent's and child's subjective experience. In classifying DC:0–3R Axis II, evidence for parental over-/underinvolvement, anxiety/tension, and anger/hostility are rated, and the clinician assesses the intensity, frequency, and duration of difficulties in the relationship, classifying these as either perturbation, disturbance, or disorder. Axis V of DC:0–3R, emotional and social functioning, includes the ways in which infants or young children organize their affective, interactive, and communicative experiences. Axis V assessment is based in large part on direct observations of parent–child interaction. The various levels include social processes such as mutual attention, mutual engagement or joint emotional involvement, reciprocal interaction, and affective/ symbolic communication. Problems may reflect constrictions in range of affect

within levels or under stress, or failure to reach expected levels of emotional development.

DC:0–3R differs significantly from other classification systems in recognizing the significance of early relational difficulties and the need to integrate diagnostic and relational approaches in classifying child psychopathology. In addition, the dimensions and specific processes that are used for classification (e.g., negative affect, unresponsivity, uninvolvement, lack of mutual engagement, lack of reciprocity in interaction) include those that have been identified as important in many developmental and clinical research studies on early relationships, and the system is decidedly more sensitive to developmental and contextual parameters than DSM-5. However, although promising, DC:0–3R is still relatively untested and suffers from many of the same criticisms that have been noted for DSM-5 (Eppright, Bradley, & Sanfacon, 1998). Nevertheless, the scheme provides a rich descriptive base for exploring the ways in which psychopathology is expressed during the first few years of life, and it calls attention to the need to examine potential continuities between early problems and later individual and/or family disorders (Postert et al., 2009).

Dimensional Approaches

Dimensional approaches to classification assume that a number of relatively independent dimensions or traits of behavior exist, and that all children possess these to varying degrees. These traits or dimensions are typically derived through the use of multivariate statistical methods, such as factor analysis or cluster analysis (Achenbach, 1993). Empirically derived schemes are more objective, usually more reliable, and more informative than clinically derived classification systems. However, several problems are also associated with their use, including their complexity, as well as the dependency of the derived dimensions on sampling, method, and informant characteristics, and on the age and sex of the children (Mash & Barkley, 2007). As a result, there can be difficulties in integrating information obtained from different methods, from different informants, over time, or across situations. Dimensional approaches have also shown a lack of sensitivity to contextual influences, although there have been efforts to develop dimensional classification schemes based on item pools that include situational content (e.g., McDermott, 1993). Moreover, in many applied contexts, "categorical" decisions regarding treatment must be made, such whether to engage in treatment. Thus most dimensional measures typically provide thresholds to indicate points at which symptoms are clinically significant to facilitate decisions regarding whether treatment should be implemented, effectively reducing such measures to categorical approaches. Nevertheless, dimensional measures of severity and/or chronicity can provide important clues regarding how intensive treatment should be (e.g., watchful monitoring vs. psychotherapy vs. combined medication and psychotherapy, in the case of depressive symptoms; Klein, 2008).

The growth in the use of multivariate classification approaches in child and family assessment has been fueled by the extensive work of Thomas Achenbach and his colleagues (see the website for the Achenbach System of Empirically Based Assessment, *www.aseba.org*) with the various parent, teacher, youth, observer, and interview versions of the Child Behavior Checklist and Profile (Achenbach, 1993; Achenbach & Rescorla, 2001), and by the development of similar assessment batteries (e.g., the Behavior Assessment System for Children, Second Edition; Reynolds & Kamphaus, 2004). For a comprehensive discussion of these approaches and the use of empirically derived classification schemes more generally, the reader is referred to Achenbach (1993), Hart and Lahey (1999), and Mash and Barkley (2007).

It should also be noted that there has been a trend toward greater convergence of the categorical and dimensional approaches to classification. Many of the items that were retained in DSM-IV child categories were derived from findings from multivariate studies, and the process that led to the development of DSM-IV treated most childhood disorders as dimensions, albeit the use of cutoff scores on item lists arbitrarily created categories out of these dimensions (Spitzer et al., 1990). DSM-5 has continued this trend with a greater emphasis on dimensional measures of psychopathology across development.

Performance-Based Diagnostic Information

Performance-based information and/or observational measures provide additional sources of diagnostic information that may be sensitive to differences among children exhibiting similar self- or other-reported symptoms (Frick, 2000; Kazdin & Kagan, 1994). These measures assess children's performance on standardized tasks, usually ones that reflect basic biological, cognitive, affective, or social functioning.

For example, tasks involving behavioral observations of fear and avoidance, recall memory under stressful conditions, delayed response times to threatening stimuli, and the potentiation of the blink reflex following exposure to a threatening stimulus have all been suggested as potentially useful in diagnosing groups and/or subgroups of children with anxiety disorders (Kazdin & Kagan, 1994; Vasey & Lonigan, 2000). Similarly, tests of behavioral inhibition (e.g., the stop-signal paradigm) and tasks involving sustained attention (e.g., the continuous-performance test) have proven useful for research on children with ADHD (Rapport, Chung, Shore, Denney, & Isaacs, 2000). Measures of low resting heart rate as an early biological marker for later aggressive behavior (Raine, Venables, & Mednick, 1997); facial emotion recognition tasks and gambling tasks in identifying children with psychopathic tendencies (Blair, Colledge, & Mitchell, 2001; Blair, Colledge, Murray, & Mitchell, 2001); and a variety of cognitive tasks for children with autism spectrum disorder (Klinger & Renner, 2000) have also been found to have diagnostic value.

A study by Rubin, Coplan, Fox, and Calkins (1995) illustrates the utility of performance-based diagnostic information. These researchers differentiated groups of preschool children on the two dimensions of "emotionality" (i.e., threshold and intensity of emotional response) and "soothability" (i.e., recovery from emotional reaction based on soothing by self and others), and on their amount of social interactions with peers. Children's dispositional characteristics and behavioral styles were used to predict outcomes. Asocial children with poor emotion regulation had more internalizing problems. In contrast, social children with poor emotion regulation were rated as having more externalizing difficulties. When behavioral and emotional dimensions were incorporated into classification, it was possible to make finer predictions—for example, that only a certain type of asocial children (i.e., reticent children with poor emotion regulation) would display later problems.

The use of performance-based measures in diagnosis is predicated on the availability of reliable and valid performance indicators for groups of children with known characteristics. Although such data are available in varying amounts for a wide range of disorders, there is a need to validate such findings for the purposes of diagnosis and against other sources of information. It is also the case that performance criteria for these measures are based on information obtained from children who were themselves previously identified using other diagnostic procedures. This raises the question of nonindependence and representativeness of samples. There is also little normative information available regarding the base rates of children in the general population who exhibit certain patterns of responding on these tasks.

ISSUES IN CLASSIFICATION

Categories, Dimensions, or Both?

Psychological studies of child psychopathology have tended to conceptualize behavior, affect, and cognition on quantitative/continuous dimensions, whereas child psychiatry has tended to conceptualize child psychopathology in categorical terms. Both approaches are relevant to classifying childhood disorders, in that some disorders may be best conceptualized as qualitatively distinct conditions and others as extreme points on one or more continuous dimensions. However, there is ongoing debate regarding which childhood disorders are best conceptualized as categories and which as dimensions (Coghill & Sonuga-Barke, 2012). It has been suggested that many childhood disorders, such as anxiety, depression, ADHD, and the disruptive behavior disorders, appear to reflect dimensions of personality rather than categorical conditions (e.g., Werry, 2001). For example, childhood ADHD symptom clusters of inattention–disorganization and hyperactivity–impulsivity have been related to personality dimensions of low conscientiousness and low agreeableness, respectively (Nigg et al., 2001). Furthermore, children naturally vary in terms of their capacity to attend and in terms of how active they are (e.g., Rothbart, 2007), and in many other dimensional behaviors that overlap with clinical conditions (e.g., temperamental fearfulness and anxiety disorders—Goldsmith & Lemery, 2000; positive and negative emotionality and depression—Klein, Durbin, & Shankman, 2009). Even autism spectrum disorder, which has frequently been viewed as categorically distinct, can be conceptualized as an extreme version of a more normative style of approaching and understanding the world and other people (Baron-Cohen, 2000; Lawson, Baron-Cohen, & Wheelwright, 2004). For disorders that reflect underlying dimensions, the concern is that the practice of categorical diagnosis creates arbitrary distinctions between normality and abnormality (e.g., children who score just below the cutoff for a diagnosis may meet full criteria

at another assessment due to random fluctuations, and often show impairment comparable to that of children who meet full criteria). Since any classification scheme represents a construction rather than a reality, it seems unlikely that most disorders will fall neatly into one designation or the other (Lilienfeld & Marino, 1995). Whether or not particular conditions are construed as qualitatively distinct categories, as continuous dimensions, or as both will probably depend on the utility, validity, and predictive value of particular groupings and subgroupings for certain purposes related to understanding and remediating child psychopathology (e.g., Kendall, Brady, & Verduin, 2001). Regardless of the particular approach one adopts for the classification of childhood psychopathology, diagnostic decisions need to be based on a comprehensive assessment of the individual child—one that incorporates sensitivity to, and understanding of, the complexity of multiple antecedents, developmental considerations, comorbidity, continuity–discontinuity, and the constantly changing nature of the child (Frick, Barry, & Kamphaus, 2010; Mash & Hunsley, 2007). Given the general trend for cognitive-behavioral approaches to be the most effective available for childhood disorders (Mash & Barkley, 2006), functional analysis of child behavior should also play a key role.

Comorbidity

An issue that has important ramifications for theory and research in defining and classifying child psychopathology is comorbidity (Achenbach, 1995; Angold, Costello, & Erkanli, 1999; Carey & DiLalla, 1994; Caron & Rutter, 1991; Sonuga-Barke, 1998). "Comorbidity" generally refers to the manifestation of two or more disorders that co-occur more often than would be expected by chance alone. For example, although the base rates for ADHD and conduct disorder in the general population are less than 10% for each disorder, epidemiological studies have found that among children diagnosed with ADHD, approximately 50% are also diagnosed with conduct disorder (Kazdin & Johnson, 1994; Loeber & Keenan, 1994). Comorbidity has been reported to be high in community samples and even higher in clinic samples (Bird et al., 1988; Caron & Rutter, 1991; Costello, Mustillo, et al., 2003). Some of the more commonly co-occurring child and adolescent disorders include conduct disorder and ADHD, autism spectrum disorder and intellectual disability, and child/adolescent depression and anxiety disorders.

There is continuing debate regarding the definition and nature of comorbidity (Angold, Costello, & Erkanli, 1999; Blashfield, McElroy, Pfohl, & Blum, 1994; Cunningham & Ollendick, 2010; Lilienfeld, Waldman, & Israel, 1994; Meehl, 2001; Robins, 1994; Rutter, 1994b; Sameroff, 2000). Some researchers contend that the term is wholly inadequate because it does not distinguish accurately between manifest conditions seen in organic medicine (e.g., diseases) and latent conditions described in mental health (e.g., syndromes and disorders (Lilienfeld et al., 1994). Others argue that the dispute over whether one should use the term "comorbidity," "co-occurrence," or "covariation" is largely a semantic one (Rutter, 1994b; Spitzer, 1994; Widiger & Ford-Black, 1994).

Several possible reasons why comorbidity may be exaggerated or artificially produced have been identified in the literature (Angold, Costello, & Erkanli, 1999; Lilienfeld et al., 1994; Rutter, 1994b; Verhulst & van der Ende, 1993; Wolff & Ollendick, 2006). There may be a sampling bias that occurs when estimates of disorder prevalence are derived from treatment-seeking or clinic samples. In such cases, the clinic samples will contain a disproportionately large number of subjects who display comorbid conditions, as the probability of being referred to mental health services is higher for a child with a comorbid condition than for a child with only one disorder. Related to this sampling bias are various other referral factors that may inflate the degree of co-occurring disorders among clinic samples. Clinics and clinicians specializing in treatment of more complicated cases, for example, may be more likely to receive referrals in which comorbid conditions are present. In addition, children with internalizing difficulties such as depression are more likely to be referred by their parents or the school system if they also show externalizing symptoms, largely because externalizing problems are viewed as more disruptive by referral sources.

Comorbidity may also reflect various sources of nosological confusion arising from the manner in which different childhood disorders have been conceptualized and organized. For instance, Widiger and Ford-Black (1994) claim that excessive rates of co-occurrence seemed to appear concomitantly with the changes that occurred in DSM-III (e.g., increased coverage, divisions of diagnostic categories, the provision of separate and multiple axes). Another example is that DSM-5 makes it possible to have multiple diagnoses in the absence of multiple syndromes (Cantwell, 1996; Robins, 1994). One source of confusion stems from the overlap-

ping criterion sets within contemporary classification schemes (Drabick & Kendall, 2010; Rutter, 2010). In DSM-5, diagnoses are based on a set of polythetic criteria that include specific symptom constellations. In many cases, the presence of concomitant symptoms of a different kind are ignored, resulting in an increased likelihood that the accompanying symptoms will be represented in a different diagnostic category (Caron & Rutter, 1991). Sonuga-Barke (1998) argues, however, that although earlier diagnostic systems steered clear of comorbidity by using a hierarchical set of exclusionary criteria, "these approaches were abandoned because they clearly led to a misrepresentation of the structure of disorder" (p. 119). For example, they led to low base rates of disorders and poor interrater agreement.

Apart from the various artifactual contributors to comorbidity, there are also indicators in support of "true" comorbidity (Rutter, 1994b). It is possible that general propensities toward and/or struggles with adaptation are at the core of every disorder, but that the expression of the phenotype is contingent upon a myriad of environmental conditions and person–environment interactions (Caron & Rutter, 1991). Consistent with this notion, Lilienfeld and colleagues (1994) maintain that comorbidity in childhood disorders may be partly a function of developmental level—that is, of underlying processes that have not yet achieved full differentiation. Differing rates of comorbidity with age may also reflect the fact that the appearance of one disorder or problem may precede the appearance of the other, as is the case for anxiety preceding depression (Brady & Kendall, 1992) or for impulsivity preceding attentional problems (Hart et al., 1995). Still another possibility is that comorbidity reflects "a more amorphous early expression of psychopathology in young children that does not crystallize into more definitive psychopathology until later in life" (Cantwell, 1996, p. 4). Comorbidity can also arise as a result of a causal association in which the severity of one disorder may lead to or greatly increase the later risk for another disorder (e.g., ADHD and oppositional defiant disorder) or a shared underlying cause, such as common genetic influences (e.g., conduct disorder and depression) or neurobiological processes (e.g., anxiety and depression). In the case of shared etiology, poorly drawn boundaries between disorders may contribute to the appearance of multiple co-occurring disorders, when the reality is that two disorders are different manifestations of the same underlying neural circuit disruptions (Morris & Cuthbert, 2012).

In summary, it would appear that some cases of comorbidity are the results either of ambiguity in the definition of dysfunctionality that is used, or of artifactual/methodological issues. However, as Kazdin and Kagan (1994) note, "the broader point is still relevant and not controverted with specific diagnostic conundrums—namely, multiple symptoms often go together in packages" (p. 40). This is not to suggest that *all* disorders cluster together into packages; rather, the fact that many frequently do has important implications for how child psychopathology is conceptualized and treated. The complexity of comorbidity behooves researchers to move beyond singular models and to examine multiple expressions, etiologies, and pathways of childhood dysfunction (Beauchaine, Hinshaw, & Pang, 2010; Burt, Krueger, McGue, & Iacono, 2001; Kazdin & Johnson, 1994).

THE DEVELOPMENTAL PSYCHOPATHOLOGY PERSPECTIVE

The developmental psychopathology perspective aims to provide a useful working framework for conceptualizing and understanding child psychopathology. This approach integrates multiple theories (e.g., psychodynamic, behavioral, cognitive, biological, family systems, and sociological), each of which focuses on different sets of variables, methods, and explanations (Achenbach, 2000), to provide a template and principles for understanding the processes underlying how and why psychopathology in children emerges, how it changes over time, and how it is influenced by a child's developmental capacities and by the contexts in which development occurs (Cicchetti & Toth, 2009). Long described as a macroparadigm that subsumes several theoretical approaches (Cicchetti, 1984; Cicchetti & Cohen, 1995; Lewis, 2000; Luthar et al., 1997; Rutter & Sroufe, 2000; Sameroff, 2000), "developmental psychopathology" has been defined as "*the study of the origins and course of individual patterns of behavioral maladaptation*, whatever the age of onset, whatever the causes, whatever the transformations in behavioral manifestation, and however complex the course of the developmental pattern may be" (Sroufe & Rutter, 1984, p. 18; original emphasis). Put simply, developmental psychopathology provides a general framework for understanding both normal development and its maladaptive deviations. Its main focus is an elucidation of developmental processes and their functioning through

an examination of extremes in developmental outcome and of variations between normative outcomes and negative and positive extremes. Developmental psychopathology does not focus exclusively on the study of childhood disorders, but serves to inform the understanding and treatment of disorders through the study of a full range of developmental processes and outcomes.

A developmental psychopathology perspective is consistent with both transactional and ecological views, and assumes that within ongoing change and transformation there exist coherence and predictability for adaptive and maladaptive development (Campbell, 1989; Cicchetti & Toth, 1997). This perspective also emphasizes the importance of endogenous (e.g., genetic, neurobiological) and exogenous (e.g., family, social, and cultural factors) and the interaction of the two in predicting and understanding developmental changes (Achenbach, 2000; Lewis, 2000). In this way, developmental psychopathology attempts to address the complex influences surrounding the development of the child across the lifespan. In attempting to do so, it draws on knowledge from multiple fields of inquiry (including psychology, psychiatry, sociology, education, criminology, epidemiology, and neuroscience) and attempts to integrate this knowledge within a developmental framework (Rutter & Sroufe, 2000).

The focus of developmental psychopathology is on normal developmental patterns, continuities and discontinuities in functioning, and transformational interactions over different developmental periods that produce adaptive or maladaptive outcomes. The processes underlying both healthy and pathological development are seen as stemming from idiosyncratic transactions between a child and his or her unique context (Achenbach, 2000; Sroufe & Rutter, 1984). Thus a central tenet of this approach is that to understand maladaptive behavior adequately, one needs to view it in relation to what may be considered normative for a given period of development (Edelbrock, 1984). Significant challenges for research, then, are to differentiate those developmental deviations that are within normative ranges from those that are not, and to ascertain which among the plethora of interacting variables account for developmental deviation. A developmental psychopathology perspective is also guided by several other principles, including the notion that the individual child plays an active role in his or her own developmental organization, that developmental outcomes are best predicted through consideration of prior experience and recent adaptations examined in concert, and that transitional turning points or sensitive periods in development represent times when developmental processes are most susceptible to positive and/or negative self-organizational efforts (Cicchetti & Tucker, 1994).

Until recently, the developmental psychopathology perspective has been more of a conceptual enterprise than a well-validated approach (Lewis, 2000). However, in a very short period of time, it has proven to be an enormously useful framework for understanding and guiding research in child psychopathology, and it represents an important shift in thinking away from single causal hypotheses toward a view based on complex and multiple pathways of influence: "After each effort to support an explanatory model by collecting a set of data, the results have required modifications in the model, forcing the field to evolve from a concern with causes and effects to an increasing appreciation of the probabilistic interchanges between dynamic individuals and dynamic contexts that comprise human behavior" (Sameroff, 2000, p. 297).

Within the integrative framework of developmental psychopathology, efforts are made to understand the different pathways through which similar forms of psychopathology emerge, and the reasons why seemingly similar developmental pathways may lead to different outcomes. Numerous disorder- and problem-focused theories have been proposed. These models are empirically based and are sensitive to the specific characteristics and processes that research has identified as important for understanding a particular disorder or problem. A few examples of representative models include Barkley's (2004, 2012a) theory of "inhibitory and executive dysfunction," which initially proposed behavioral inhibition as the primary and central deficit underlying the attentional, cognitive, affective, and social difficulties of children with ADHD. The subsequent iteration of this theory has now expanded this idea to include other executive functions, such as working memory, besides the inhibitory deficits as being central to this disorder (Barkley, 2004, 2012a). These initial deficits produce numerous effects at increasing spatial and temporal distances into the social ecology of the individual that comprise the extended phenotype of the disorder (Barkley, 2012b). Another example is the Cummings and Davies (1996, 2010; Davies & Cummings, 1994) "emotional security hypothesis," which proposes that emotional insecurity resulting from a number of sources (e.g., maternal depression, marital conflict) may lead to child difficulties in self-regulation, efforts to overregu-

late others, and maladaptive relational representations. Crick and Dodge's (1994) model of social information-processing deficits in aggressive children provides yet another example, which views aggression as a outcome of a child's use of biased or distorted interpretational processes in social situations.

Other theories that have been proposed to account for these and other problems and disorders are presented in the subsequent chapters of this volume. The growth in the number of such theories reflects an increasing trend toward models that focus on the processes underlying specific forms of child psychopathology, rather than on child psychopathology in general. However, most contemporary causal models that emphasize specific disorders have not conducted the necessary empirical tests to determine the specificity of putative etiological factors, despite the fact that that there are likely to be common factors (e.g., personality, genetic risks, family discord/stress) that increase risk for many different types of disorder (Epkins & Heckler, 2011). Identifying how etiological influences are similarly versus differentially related to disorders is an important task for future research.

GENERAL THEORIES OF CHILD PSYCHOPATHOLOGY

Several major theories have been proposed to account for the emergence of psychopathology in children (see Table 1.4). These include psychodynamic (Dare, 1985; Fonagy & Target, 2000; Shapiro & Esman, 1992), attachment (Atkinson & Goldberg, 2004; Bowlby, 1973, 1988), behavioral/reinforcement (Bijou & Baer, 1961; Skinner, 1953), social learning (Bandura, 1977, 1986), interpersonal (Gotlib & Hammen, 1992; Joiner & Coyne, 1999; Rudolph, Flynn, & Abaied, 2008); cognitive (Beck, 1964; Beck, Rush, Shaw, & Emery, 1979; Evraire, Dozois, & Hayden, in press; Ingram, Miranda, & Segal, 1998), constitutional/neurobiological (e.g., Cappadocia, Desrocher, Pepler, & Schroeder, 2009; Heim & Nemeroff, 2001; Matthys, Vanderschuren, & Schutter, 2013; Tripp & Wickens, 2009), affective (Davidson, 2000; Rubin, Cheah, & Fox, 2001), and family systems (Cowan & Cowan, 2002; Davies & Cicchetti, 2004; Grych & Fincham, 2001) models. A detailed discussion of the basic tenets of each of these general theories is beyond the scope of this chapter. For comprehensive discussions of these theories, the reader is directed to original sources and to specific references cited throughout this volume. What follows is a discussion of several general points related to some of these theories.

TABLE 1.4. General Models Used to Conceptualize Child Psychopathology

Psychodynamic models	Inborn drives, intrapsychic mechanisms, conflicts, defenses, psychosexual stages, fixation, and regression.
Attachment models	Early attachment relationships; internal working models of self, others, and relationships in general.
Behavioral/reinforcement models	Excessive, inadequate, or maladaptive reinforcement and/or learning histories.
Social learning models	Vicarious and observational experience, reciprocal parent–child interactions.
Interpersonal models	Interactional styles, social skills deficits, social difficulties, stressful interpersonal environments.
Cognitive models	Distorted or deficient cognitive structures and processes.
Constitutional/neurobiological models	Temperament, genetic influences, structural and functional neurobiological mechanisms.
Affective models	Dysfunctional emotion-regulating mechanisms.
Family systems models	Intra- and intergenerational family systems, and the structural and/or functional elements within families.

Note. Models are highlighted in terms of their relative emphasis.

Each general theoretical approach reflects a diversity of viewpoints. For example, psychodynamic theory encompasses traditional Freudian and Kleinian psychoanalytic constructs and their many derivatives as reflected in ego-analytic and object relations theory (Fonagy & Target, 2000; Lesser, 1972). Behavioral/reinforcement perspectives include traditional operant/classical conditioning constructs, mediational mod-

els, and contemporary theories of learning (Klein & Mower, 1989; Krasner, 1991; Viken & McFall, 1994). Cognitive theories include cognitive-structural models, models of cognitive distortion, and models of faulty information processing (Clark, Beck, & Alford, 1999; Ingram et al., 1998; Kendall & Dobson, 1993). Family systems theories include systemic, structural, and social learning models (Jacob, 1987). Therefore, when one is discussing any theory, it is critical to distinguish among the different perspectives encompassed by the approach.

Many theories of child psychopathology are derivatives of earlier approaches. For example, psychodynamic theories dominated thinking about child psychopathology for the first half of the 20th century. These theories contributed to our understanding of child psychopathology through their emphasis on the importance of relationships, early life experiences, mental mechanisms, and unconscious processes, and they spawned a number of other models—for example, attachment theory (Rutter, 1995). The emergence of attachment theory reflected a shifting of attention from the more traditional psychoanalytic role of intrapersonal defenses to that of interpersonal relationships (Bretherton, 1995). Similarly, the emergence of social learning theory reflected disenchantment with nonmediational models of learning and a growing interest in the role of symbolic processes.

A number of general points can be made regarding theories of child psychopathology:

1. Each theory offers an explanation regarding the etiology of child psychopathology. The strength of each theory rests on its specificity in predicting various forms of psychopathology and its degree of empirical support.

2. The varying degrees of support for each conceptualization suggest that no single model can fully explain the complexities involved in understanding child psychopathology. In light of this, increased understanding may accrue if greater integrative and collaborative efforts are undertaken.

3. Many explanations of childhood disorders implicitly or explicitly assume a simple association between a limited number of antecedents and a given disorder. However, as we have discussed, the concept of multiple pathways that lead to different outcomes depending on the circumstances represents a more viable framework in light of current research findings.

4. Although the testing of specific models is consistent with the spirit of parsimony, far greater attention needs to be given to the unique contexts and conditions under which a particular model does or does not apply.

5. Research on dysfunction frequently examines static conditions and influences such as the expression of a disorder at a given age or the influence of a specific stressor. However, evidence indicates that the expression and etiology of psychopathology in children are continuously changing over time, and theories need to account for these types of changes.

Current models are becoming increasingly sensitive to the many different components of childhood dysfunction. Indeed, constitutional, behavioral, cognitive, emotional, and social factors cross a number of theoretical domains; this is reflected in the emergence of hybrid models (e.g., cognitive-behavioral, social information processing, cognitive-neuropsychological), as well as the inclusion of family and ecological constructs across many different theories. Behavioral models, which have frequently been characterized as having a narrow emphasis on conditioning principles, are also becoming increasingly sensitive to systems influences (Viken & McFall, 1994).

Four interrelated theoretical approaches have received increased attention in current research on child psychopathology: (1) attachment theory, (2) cognitive theories, (3) emotion theories, and (4) constitutional/neurobiological theories. Each of these approaches is highlighted in the sections that follow.

Attachment Theory

Bowlby's (1973, 1988) theory of attachment is based on both an ethological and a psychoanalytic perspective (Cassidy & Shaver, 2008; Cicchetti, Toth, & Lynch, 1995). Nevertheless, Bowlby rejected the psychoanalytic ideas that individuals pass through a series of stages where fixation at or regression to an earlier state can occur, and that emotional bonds are derived from drives based on food or sex. Drawing on ethology and control theory, Bowlby and his successors replaced Freudian concepts of motivation based on psychic energy with cybernetically controlled motivational–behavioral systems organized as plan hierarchies (Bowlby, 1973; Bretherton, 1995). Within attachment theory, instinctive behaviors are not rigidly predetermined, but rather become organized into flex-

ible goal-oriented systems through learning and goal-corrected feedback. Motivational–behavioral systems (e.g., attachment, exploration) regulate time-limited consummatory behaviors and time-extended instinctive behaviors that maintain an organism in relation to its environment. Attachment belongs to a group of stress-reducing behavioral systems that operate in conjunction with physiological arousal-regulating systems. The child is motivated to maintain a balance between familiarity-preserving, stress-reducing behaviors, and exploratory and information-seeking behaviors. Self-reliance develops optimally when an attachment figure provides a secure base for exploration (Bretherton, 1995).

It is via the attachment relationship that the infant develops an "internal working model" of the self and others. Bowlby (1988) argued that the development of psychopathology is directly related to the inability of the caregiver to respond appropriately to the child's needs. This assertion is, however, a point of contention among researchers. Sroufe (1985), for example, has questioned the direct role of parental influence, arguing that infant temperament and the reciprocal interaction of a "difficult temperament" with parental response may better account for the variance in the attachment relationship and its ensuing insecure attachment difficulties. On the basis of a review of several studies examining infant temperament and attachment, Sroufe suggests that although some studies have supported the notion that differences between secure and insecure attachments may be due to temperament, the bulk of evidence suggests that infants change their attachment patterns with different caregivers.

In postulating an association between early attachment and later psychopathology, one must exercise caution, in that there does not appear to be one specific subtype of attachment that leads to one particular childhood disorder. Rather, the trajectory for developmental pathways and manifestations of psychopathology emerges as the result of environmental experience, biological predispositions, and learning. When one is identifying possible developmental paths as factors related to subsequent psychopathology, the concept of the child's internal working model is useful; however, it is important to bear in mind that the internal working model represents a set of active constructions that are subject to change, and that the association with later psychopathology is probabilistic rather than absolute.

Rutter (1995) has highlighted a number of key issues surrounding attachment, including (1) the need to identify mechanisms involved in proximity-seeking behavior; (2) broadening the basis for measuring attachment to include dimensions as well as categories; (3) studying relationship qualities that may not be captured by "insecurity"; (4) understanding the relationship between temperament and attachment; (5) dealing with how discrepant relationships are translated into individual characteristics; (6) operationalizing internal working models; (7) defining attachment quality across the lifespan, and determining whether or not meanings are equivalent at different ages; (8) determining how one relationship affects others; and (9) identifying the boundaries of attachment vis-à-vis other aspects of relationships. Several issues—the association between attachment and later functioning; the linkage between parenting and attachment quality; the adaptive value of secure attachment (e.g., insecure attachment does not equal psychopathology); disorders of attachment associated with abuse and neglect; and the diffuse attachments associated with institutionalization—are all in need of further investigation. Bowlby's attachment theory has played an important role in focusing attention on the quality of parent–child relationships, the interaction between security in relationships and the growth of independence, the importance of placing emergent human relationships within a biological/evolutionary context (e.g., Kraemer, 1992), the concept of internal working models, and insecure early attachments (e.g., Barnett & Vondra, 1999) as the basis for the development of psychopathology (Rutter, 1995).

Cognitive Theories

Considerable research has focused on the role of cognition (i.e., mental processes that include attention, memory, learning, problem-solving and decision-making) in both adult and child psychopathology (Clark et al., 1999; Ingram et al., 1998; Ingram & Price, 2001). Several theoretical perspectives have been concerned with childhood cognitions. These have included cognitive-structural models (Ingram et al., 1998; Selman, Beardslee, Schultz, Krupa, & Poderefsky, 1986), information-processing approaches (Crick & Dodge, 1994; Ingram & Ritter, 2000; Taylor & Ingram, 1999), and cognitive-behavioral approaches (Braswell & Kendall, 2001; Dobson & Dozois, 2001; Meichenbaum, 1977). Representative examples of the information-processing and cognitive-behavioral approaches are described below. Recently cognitive theories have focused on the importance of positive cognitions, the role of cognitive

specificity, the role of context on cognitions, the impact of comorbidity, the use of information-processing risk paradigms, a movement away from simple cognitive diathesis–stress models to looking at information-processing mediators, and the need for theoretical integration.

Information Processing

Biased information processing has been implicated in a number of childhood disorders. For example, socially aggressive children have been found to display negative attributional biases (Dodge & Pettit, 2003; Schwartz & Proctor, 2000); children with anxiety disorders show attentional biases to threatening stimuli (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007; Waters, Henry, Mogg, Bradley, & Pine, 2010); and depressed children exhibit greater encoding biases for negative material, less endorsement and recall of positive information, and other forms of negative cognition (Abela & Hankin, 2008; Lakdawalla, Hankin, & Mermelstein, 2007). Research on information processing and child psychopathology has emanated from three streams: one focusing on deficits in basic information processing related to attention, memory, and other cognitive functions (e.g., Carter & Swanson, 1995); another related to social information processing (Crick & Dodge, 1994); and a third focusing on maladaptive cognition (e.g., Ingram et al., 1998; Ingram & Ritter, 2000; Taylor & Ingram, 1999).

Dodge's model as applied to socially aggressive boys illustrates the social information-processing approach (Dodge & Pettit, 2003; Dodge & Somberg, 1987). In the initial model, a series of thought processes and behaviors (i.e., encoding, interpretation, response search, response decision, and enactment) was postulated to occur during the course of appropriate social interactions and to be absent or distorted during inappropriate social interactions. The model has evolved, positing the same basic information-processing steps, but at each stage there is ongoing reciprocal interaction between the information-processing skills required during social transactions in context and the individual's "database" (a collection of social schemas, memories, social knowledge, and cultural values or rules) (Crick & Dodge, 1994; Dodge & Pettit, 2003). Instead of a linear processing model, there are postulated to be cyclical feedback loops connecting all stages of processing. Increased recognition of the influence of peer appraisal and response, emotional processes, and the development and acquisition of cognitive skills as important contributors to social adjustment are meaningful additions to the reformulated model. In addition to the enhanced sensitivity to developmental trajectories, the reformulated model emphasizes the role of early dispositions (e.g., temperament) and other factors (e.g., age, gender, social context) that serve to moderate the relationship between information processing and social adjustment. A number of studies have provided empirical support for the expanded model (Contreras, Kerns, Weimer, Getzler, & Tomich, 2000; Gomez & Gomez, 2000; Gomez, Gomez, DeMello, & Tallent, 2001).

Cognitive-Behavioral Theories

Cognitive-behavioral theories represent "a purposeful attempt to preserve the positive features of the behavioral approaches, while also working to incorporate into a model the cognitive activity and information-processing factors of the individual" (Kendall & MacDonald, 1993, p. 387; see also Braswell & Kendall, 2001), and cognitive vulnerabilities to depression and anxiety in particular are firmly established as central models of risk and treatment. Research on such cognitive models initially focused on adults, using a wide array of operationalizations of cognitive risk; this research has generated a vast corpus of results generally supporting the central tenets of cognitive theories, in that cognitive vulnerability has been found to be a diathesis that interacts with negative life events to predict increases in symptoms (Ingram et al., 1998).

Four elements of cognition are distinguished for the purpose of understanding the pathogenesis of psychiatric disturbances: cognitive structures, content, operations, and products (Beck et al., 1979; Dozois & Dobson, 2001; Ingram et al., 1998; Kendall & Dobson, 1993). "Cognitive structures" represent the way in which information is organized and stored in memory, and serve the function of filtering or screening ongoing experiences. "Cognitive content" (or propositions) refers to the information that is stored in memory (i.e., the substance of the cognitive structures). Together, cognitive structures and content make up what is termed a "schema." A schema stems from a child's processing of life experiences and acts as a guideline or core philosophy influencing expectations and filtering information in a fashion consistent with the child's core philosophy. As such, cognitive schemas have also been referred to as "filters" or "templates" (see Kendall & MacDonald, 1993). A schema is postulated to affect the relative ob-

served consistency in the child's cognition, behavior, and affect (Stark, Rouse, & Livingston, 1991). According to Beck's model, maladaptive schemas develop in early childhood and remain dormant until some untoward event triggers the latent schemas, and the individual begins to encode, process, and interpret information in a schema-congruent way. Individuals with a depression schema, for instance, process and interpret information about themselves, the world, and the future in a negatively biased fashion, whereas persons with an anxiety schema interpret environmental stimuli with a cognitive focus on future threat. In addition, what appears to be specific to depression is a lack of positive cognition (Gencoez, Voelz, Gencoez, Pettit, & Joiner, 2001). "Cognitive processes" or "cognitive operations" pertain to the manner by which the cognitive system functions. Thus cognitive processes, which are guided by schemas, suggest the mode by which an individual perceives and interprets both internal and external stimuli. Finally, "cognitive products" are the ensuing thoughts that stem from the simultaneous and reciprocal interactions among the various components of the cognitive system.

Work testing cognitive models of depression has shifted in recent years toward the exploration of the utility of these models in adolescents and children (Abela & Hankin, 2008). Reviews of this literature support the claim that cognitive vulnerability in youth is an important prospective predictor of depressive symptoms (e.g., Hankin et al., 2009), usually when examined in conjunction with stressful life events. More specifically, most studies have focused on testing whether the interaction between negative cognition and stress predicts elevations in children and adolescents' depressive symptoms. These studies have shown that stressful life events show stronger associations with depression when youth possess negative cognitive styles (such as maladaptive attributional styles), information-processing biases favoring enhanced processing of negative stimuli, and other aspects of depressive cognition (Abela & Hankin, 2008; Lakdawalla et al., 2007).

A potentially useful distinction can be made between "cognitive deficits" and "cognitive distortions." Kendall (1993) argues that this distinction is useful in describing, classifying, and understanding a variety of juvenile disorders. Children with "deficits" display an absence of thinking where it would be beneficial. Aggressive youth, for example, frequently lack the ability to encode interpersonal information (Coy, Speltz, DeKlyen, & Jones, 2001; Pakaslahti, 2000; Schwartz & Proctor, 2000) or to solve social problems adequately (Crick & Dodge, 1994; Lochman & Dodge, 1994), and impulsive children often fail to think before they respond (Moore & Hughes, 1988). Conversely, children who display "distortions" typically do not lack the ability to organize or process information; rather, their thinking is described as biased, dysfunctional, or misguided (Kendall, 1993; Kendall & MacDonald, 1993). A depressed individual's negative view of him- or herself, the world, and the future is an example of distorted thinking. Kendall (1985, 1993) notes that the distinction between deficient and distorted thinking is relevant to the distinction that has been made between externalizing and internalizing disorders (cf. Achenbach, 2000). Generally, internalizing disorders are related to distortions in thinking, whereas externalizing disorders are more commonly associated with cognitive deficits. However, empirical evidence suggests that aggressive behaviors usually include both distortions and deficits (e.g., Lochman, White, & Wayland, 1991).

Cognitive models have both strengths and weaknesses. The theoretical model asserts that stable, latent schemas develop in childhood and are dormant until a triggering negative event; the model thus generates strong hypotheses regarding the assessment of cognitive risk and the work of therapy (Braswell & Kendall, 2001; Kendall, 1993). Importantly, these theories thus assert the stability of cognitive risk markers that emerge early in life. There is ongoing debate regarding when meaningful, stable aspects of cognitive vulnerability emerge (e.g., Abela & Hankin, 2011; Cole et al., 2008; Garber, 2010; Gibb & Coles, 2005; Hammen & Rudolph, 2003). Furthermore, work that speaks to the stability of childhood cognitive vulnerability is accruing (e.g., Cole et al., 2009: Hankin, 2008; Hayden, Olino, Mackrell, et al., 2013), and evidence is consistent with both stability and change (Hankin et al., 2009). This literature indicates that while some rank-order stability emerges in later childhood, significant change also occurs for some children. However, this work has focused on self-reported cognitive risk in later childhood and early adolescence, and across relatively brief follow-ups—factors that may serve to indicate increased stability compared to research on younger samples using laboratory-based measures and longer follow-up intervals. Further work on emerging cognitive risk in younger children, indexed via approaches that map more fully onto the array of methodologies indexing cognitive risk in depression, is clearly needed. If a period in development can be identified in which

children's cognitive vulnerability has both meaningful implications for disorder risk *and* evidence of some degree of plasticity, such a period could represent an important window for preventative efforts.

Another limitation of these models is that the developmental origins of emerging cognitive risk have yet to be fully explored, particularly in the context of broader models childhood cognitive risk. More specifically, relatively little research has attempted to identify early precursors of negative cognition implicated in disorder risk. In recent years, work tying negative cognition to early adversity (Gibb, 2002), parental psychopathology, emotional traits (Davidson et al., 2002; Hamburg, 1998; Hayden et al., 2006), and genetic risk (Gibb, Beevers, & McGeary, 2013; Hayden, Olino, Bufferd, et al., 2013) has begun to emerge, although more comprehensive models that test the possibility of dynamic interplay among multiple factors are still lacking.

Emotion Theories

Emotion and its regulatory functions are constructs that cross several conceptual models— including psychodynamic theory, with its concept of defense mechanisms; cognitive-behavioral theory, which stresses the role of thought patterns and behavior as determinants of emotion; attachment theory, with its premise that an internal working model is formed on the basis of early relations and continues to regulate emotion in subsequent relationships (Cassidy, 1994); and biological theories, which emphasize the structural and neurochemical correlates of emotion regulation (Pennington & Ozonoff, 1991; Posner & Rothbart, 2000). Emotion and its regulation played a central role in the conceptual paradigms of early models of child psychopathology. For example, psychoanalytic theory emphasized the regulation of emotions through the use of defense mechanisms, with an absence of such regulation leading to anxiety and psychopathology (see Cole, Michel, & Teti, 1994). By giving individuals the opportunity to avoid, minimize, or convert emotions, defense mechanisms were hypothesized to serve the function of regulating emotional experiences too difficult to manage at the conscious level.

Although the advent and growth of cognitive and behavioral models shifted attention away from an interest in affective processes, the study of emotional processes in child psychopathology has experienced a resurgence of interest (Arsenio & Lemerise, 2001; Belsky, Friedman, & Hsieh, 2001; Insel, 2003; Rubin et al., 2001), in recognition that children's emotional experience, expression, and regulation are likely to affect the quality of their thinking, social interactions, and relationships (e.g., Flavell, Flavell, & Green, 2001; Rubin et al., 2001; Schultz, Izard, Ackerman, & Youngstrom, 2001). From a functionalist perspective, emotions are viewed as playing a causal role in organizing and directing the way in which children react to environmental events. This perspective is illustrated by findings showing that induced negative child emotions increase children's distress, negative expectations, and appraisals of adult conflict, whereas induced positive emotions have the opposite effect (Davies & Cummings, 1995). Several discussions have focused on the development of emotion regulation and its ability to influence both adaptive and maladaptive functioning (Fredrickson, 2001; Kagan, 1994b; Mayer & Salovey, 1995; Thompson, 2011). In general, there is growing support for the view that emotionality and regulation are related to children's concurrent and long-term social competence and adjustment (Eisenberg, Fabes, Guthrie, & Reiser, 2000).

Emotion systems have as their primary functions the motivation/organization of behavior and communication with self and with others. Emotions represent patterns that include at least several of the following components: (1) activating neural, sensory–motor, cognitive, and/or affective stimulus events; (2) dedicated neural processes; (3) changes in physiological responses; (4) changes in motoric/expressive behavior; (5) related cognitive appraisals; and (6) concomitant alterations in subjective experiences or feeling states (Cicchetti, Ackerman, & Izard, 1995; Izard, 1993; Kagan, 1994b).

Different theories have viewed child psychopathology as emanating from the following: (1) unrestrained emotions (i.e., emotions that are unconnected to cognitive or affective–cognitive control processes); (2) deficits or distortions in cognitions and behaviors that interfere with emotion modulation (i.e., emotions connected to cognitive processes and behavior that are situationally inappropriate); (3) emotional interference with planful cognitive processes (i.e., emotional flooding); (4) dysfunctional patterns of emotion processing and communication, involving problems with recognition, interpretation, and expression; and (5) difficulties in coordinating emotional and cognitive processes in the regulation of emotion (Cicchetti, Ackerman, & Izard, 1995).

Emotion dysfunction may emanate from several sources, including variations in biological vulnerabil-

ity and stress. In studying child psychopathology, it is important not to focus on negative emotions without also recognizing several other factors: the beneficial and buffering effects of positive emotions (Fredrickson, 2001; Masten, 2001; Tugade & Fredrickson, 2004; Wichers et al., 2007); the adaptive value and facilitating effects of negative emotions of moderate or at times even extreme intensity; and the ongoing importance of emotion content and meaning for a child's behavior. Also, since negative emotions are neither topographically nor functionally unidimensional, it is important to identify the *discrete* emotions and emotional patterns underlying different forms of child psychopathology (Cicchetti, Ackerman, & Izard, 1995). For example, the negative affect that is associated with depression may involve sadness, anger, or guilt, in the same way that negative behaviors in depressed children may be both aggressive/confrontational and depressive/distressed (Hops, 1995).

It may be useful to distinguish between the two dimensions of "emotion reactivity" and "emotion regulation." "Reactivity" refers to individual differences in the threshold and intensity of emotional experience, whereas "regulation" describes processes that operate to control or modulate reactivity (e.g., attention, inhibition, approach–avoidance, coping styles) (Rubin et al., 1995). According to Rubin and colleagues (1995), this distinction is important because it highlights the need to focus on the dynamic interaction between general temperament and specific regulatory mechanisms, and in turn the need to recognize that emotional arousal (reactivity) can serve to inhibit, facilitate, or disrupt behavior. The distinction can also be made between problems in regulation and problems in dysregulation, with regulation problems involving weak or absent control structures or structures overwhelmed by disabling input, and dysregulation involving existing control structures that operate in a maladaptive manner and direct emotion toward inappropriate goals (Cicchetti, Ackerman, & Izard, 1995). Functions of emotion involve the emotion knowledge of self and others in identifying feelings and behavior, including monitoring of self and environment. Absent or weak monitoring may result in dissociated emotional and cognitive processes and emotional leakage, whereas excessive monitoring may lead to a narrow sampling of emotional signals and excessive use of specific emotions in communication (Cicchetti, Ackerman, & Izard, 1995).

Of interest to the present chapter is the manner in which emotion regulation has been defined and conceptualized with respect to psychopathology (Keenan, 2000). The processes of emotion regulation include the attenuation or deactivation of an ongoing emotion, the amplification of an ongoing emotion, the activation of a desired emotion, and the masking of emotional states (Cicchetti, Ackerman, & Izard, 1995). Thompson (1994) defines emotion regulation as consisting of "the extrinsic and intrinsic processes responsible for monitoring, evaluating, and modifying emotional reactions, especially their intensive and temporal features, to accomplish one's goals" (p. 27). This definition highlights several important characteristics of emotion regulation. First, it involves enhancing, maintaining, or inhibiting emotional arousal for the purpose of meeting one's goals. Second, there are both internal and external factors that influence the development and use of emotion-regulating strategies. Finally, there is a temporal dimension: Sometimes there are sudden and transitory changes in emotional arousal that must be dealt with (e.g., acute or state anxiety), whereas at other times there are longer-lasting ramifications of emotional arousal created by years of experience (e.g., chronic or trait anxiety; Kagan, 1994b; Terr, 1991). However, an important conceptual issue that is central to the question of what is currently known about the role of emotion regulation in child development and psychopathology concerns the extent to which research has adequately differentiated between emotion experience (i.e., the strength of an initial emotional response) and regulatory processes (i.e., processes that modulate this initial response). Although emotion and emotion regulation are theoretically distinct, Campos, Frankel, and Camras (2004) have cogently argued that the processes that underpin the two overlap almost entirely, and that adequately differentiating between them for the purposes of assessment is a potentially intractable problem. Indeed, a review of the literature indicates that many studies methodologically conflate high emotionality (e.g., the expression of high levels of negative emotions) with deficits in regulatory processes by using indicators that apply to both constructs (see Lewis, Zinbarg, & Durbin, 2010, for an eloquent discussion of these considerations). In order for a better understanding of the incremental utility of emotion regulation for psychopathology to emerge, greater efforts to differentiate it from near-neighbor constructs are essential.

The development of emotion regulation or dysregulation is thought to derive both from innate predispositions and from socialization. At the level of constitutional factors are various neural circuits and temperamental

characteristics. For example, inhibited children appear to bring a high state of reactivity into their environment, particularly in novel or unfamiliar situations. This biological propensity is thought to be the result of a number of neurological factors that include interrelating messages sent to and from neuroanatomical structures (vis-à-vis neuroelectricity and neuropharmacology) to the central and peripheral nervous system (Fox, Henderson, Marshall, Nichols, & Ghera, 2005). Cognitive and language development also contribute to emotion regulation. Growth in cognitive development allows the child increasingly to differentiate and cope with a diverse set of emotion-arousing stimuli. The development of emotion language also affords an opportunity for the communication of emotion meaning to others and its management through self-regulatory mechanisms (Cole et al., 1994; Thompson, 1994).

Finally, emotion regulation is also embedded within the unique context of the child. Socialization influences within the family, peer group, and culture are important in the development and expression of emotion, and may support or hinder emotion regulation in a variety of ways. One important influence is the way in which parents respond to the child's initial expressions of emotion, and how emotions are communicated in the context of the ongoing interactions between the parents and child (Cassidy, 1994; Volling, 2001). The development of emotion regulation may also come about through the modeling of appropriate or inappropriate emotional expression (e.g., Shipman & Zeman, 2001). Finally, the rules or boundaries of emotional expression, which are established by both the family and the community at large, also influence the development of emotion regulation (Cole et al., 1994).

Emotion dysregulation begins with context-specific efforts at self-regulation, which may then develop into more stable patterns of responding and thereby contribute to the development of psychopathology. The determination of emotion regulation as adaptive or maladaptive varies with the circumstances, but it generally involves the degree of flexibility of the response, the perceived conformity of the response to cultural and familial rules and boundaries, and the outcome of the response relative to the child's and parents' short- and long-term goals (Thompson, 1994).

Some forms of emotion dysregulation may be adaptive in one environment or at one time, but maladaptive in other situations or at other points in development (Fischer et al., 1997; Thompson & Calkins, 1996). For example, in discussing children who have been emotionally and sexually abused, Terr (1991) describes the process of "numbing" (a symptom of a posttraumatic stress reaction), which serves to protect a child from overwhelming pain and trauma. However, when numbing becomes a characteristic way of coping with stressors later in life, it may interfere with adaptive functioning and with long-term goals. Another example stems from studies on attachment quality. In response to attachment figures that are rejecting or inconsistent, infants may develop an insecure/avoidant attachment in which emotional expression is minimized. Such an infant's reduced emotional expression, while serving the strategic function within the attachment relationship of minimizing loss by reducing investment in the relationship, may establish a pattern of emotional responding that is maladaptive for the development of subsequent relationships (Cassidy, 1994).

In summary, emotion theorists conceptualize the development of emotion regulation as involving a variety of increasingly complex developmental tasks. The degree of interference with these tasks depends on the characteristics of the child and his or her environment, as well as on their interaction. Emotion dysregulation is believed to be the consequence of interference in the associated developmental processes. Dysregulation is associated with a wide range of emotions; depending on the overall context, it may or may not become a stylistic pattern, and it may or may not lead to later psychopathology.

Genetic/Neurobiological Theories

In attempting to understand child psychopathology, genetic/neurobiological theorists recognize individual differences in genetically based, neurobiological characteristics and processes. From this perspective, mental disorders are represented in the brain as a biological entity (Insel et al., 2010). The goal of research in this field is therefore to characterize the genetic, structural, and functional brain bases of psychopathology. Diverse lines of research, including family and twin studies, molecular genetic, neurobiological, neurophysiological, and neuroanatomical studies, suggest a heritable, neurobiological basis for many childhood disorders, including ADHD, autism spectrum disorder, adolescent depression, pediatric bipolar disorder, social withdrawal, some anxiety disorders, and obsessive–compulsive disorder, to name a few. Research on brain structure and function using neuroimaging procedures has implicated specific brain regions for ADHD (e.g., Frodl

& Skokauskas, 2012; Peterson et al., 2009), anxiety disorders (De Bellis et al., 2002; McClure et al., 2007), autism spectrum disorder (Di Martino et al., 2009), and many other disorders, as reviewed in subsequent chapters. There is also increasing interest in neural network perspectives on disorder, as few disorders (if any) arise from a single brain region; such work has aimed to characterize both functional (Gaffrey, Luby, Botteron, Repovš, & Barch, 2012) and structural connectivity (e.g., Zielinski et al., 2012) between brain regions that work in conjuction to influence processes relevant to psychopathology (e.g., self-referential processing; Hamilton et al., 2011).

Neuroimaging studies tell us that one region or another may be involved, but they do not tell us why, and the findings for particular disorders are not always consistent from study to study, for children of different ages, or for boys versus girls. Furthermore, much of this work has failed to meet the standards of other types of research in the field of developmental psychopathology. For example, very little neuroimaging research adequately disentangles the time course by which disorder is linked to brain structure and function (i.e., differences in brain structure and activity can emerge as both causes and consequences of a disorder; longitudinal work is needed to address this possibility). In addition, many of these studies have used small samples, and other methodological inconsistencies raise questions about the robustness of some findings (Vul & Pashler, 2012). Research into specific neurotransmitters has also provided promising leads, although findings have also been inconsistent. One of the difficulties in research in this area is that many forms of child psychopathology involve the same brain structures and neurotransmitters, making it difficult to assess the specificity of their contributions to particular disorders. Such findings may reflect the limitations of existing categorical diagnostic systems, as discussed earlier in the section describing the RDoC initiative (Insel et al., 2010).

With respect to genetic influences on child psychopathology, familial aggregation has been viewed as an important initial step in providing evidence for genetic mechanisms. Once familial clustering is demonstrated, twin studies, adoption studies, segregation analyses, and linkage studies can be conducted (cf. Szatmari, Boyle, & Offord, 1993). "Familial aggregation" refers to the nonrandom clustering of disorders or characteristics within a given family, relative to the random distribution of these disorders or characteristics in the general population (Szatmari et al., 1993). This paradigm rests on the premise that if there is a genetic component to a given disorder, the frequency of the phenotype (or manifest pathology) will be higher among biological relatives of the proband than in the general population (Lombroso, Pauls, & Leckman, 1994).

Twin studies are beneficial in helping to ascertain the contribution of genetic factors in the etiology of child psychopathology. The twin study approach emerged from the long-standing "nature versus nurture" or "genes versus environment" debate (Lombroso et al., 1994). Although twin studies provide a powerful research strategy for examining the role of genetic influences in both psychiatric and nonpsychiatric disorders, numerous methodological issues necessitate that caution be exercised in interpreting findings. For example, although Willerman (1973) found a concordance rate for hyperactivity of approximately 70%, this does not necessarily mean that 70% of the variance in hyperactivity is accounted for by genetic variation. Research suggests, for instance, that monozygotic twins spend more time together, frequently engage in similar activities, and have many of the same friends in common (Torgersen, 1993). Thus the common or shared environment presents a potential confound in any twin study, and unless twins are reared apart, or dizygotic twins are employed as the comparison group, it becomes difficult to separate the effects of genetic and environmental influences. Moreover, mutations can occur very early in cell proliferation in one twin fetus that result in phenotypic discordance (Czyz, Morahan, Ebers, & Ramagopalan, 2012). While such differences are clearly of genetic origin, they would be classified as "environmental" in parsing the variance in the trait under study. Representativeness and generalizability to the general population are other problems with twin studies (Lombroso et al., 1994; Torgersen, 1993). Growing up with a sibling of an identical age, for example, introduces its own special challenges (e.g., competition between siblings, greater dependency on each other) that make the twin environment unique.

Adoption studies have been used to circumvent some of the problems with twin and familial aggregation studies. They explicitly attempt to control for environmental variation in the heritability equation. The assumption behind this strategy is that when a disorder has a genetic etiology, the frequency of its expression should be greater among biological relatives than among adoptive relatives. Conversely, when environmental factors assume a larger role in the etiology of

psychopathology, the frequency of the disorder would be expected to be greater among the parents of adoptive relatives than among biological parents (Lombroso et al., 1994; Torgersen, 1993).

Several reasons may be advanced to account for the sparse number of investigations using the adoptive strategy. One obstacle has been the difficulty of obtaining reliable information regarding the biological parents of adoptees. The timing of adoption placements also represents a potential confound. Since children are typically adopted at different ages, it is difficult to determine what environmental influences the biological parents may have had during the earliest years of life (Lombroso et al., 1994). Similarly, many children are placed in residential settings prior to adoption; these conditions, which may affect a child's development, would be unaccounted for by an adoptive strategy. A confound analogous to the problem of timing is the high probability of being placed in an adoptive home that is similar to the home environment of the biological family. For instance, adoption agencies are quite strict in their criteria for adequate placements, and the adoptive home must, at a minimum, meet current middle-class standards (Torgersen, 1993).

However, while the aforementioned designs (i.e., family, twin, and adoption studies) play a vital role in providing evidence for the heritability of a disorder, and thus laying the groundwork for future research on genetic etiology, they are not equipped to identify specific genetic variants that play a role in the pathogenesis of disorder. The identification of etiologically relevant genes (i.e., those implicated in the pathophysiology of disorder) has the potential to greatly enhance our understanding of a disorder, as well as potential treatment mechanisms (Stodgell, Ingram, & Hyman, 2000). Toward this goal, the past few decades have witnessed rapid advances in researchers' ability to derive vast amounts of information on individual differences in genetic factors potentially relevant to disorder risk, and psychopathologists have accordingly availed themselves of these technologies. As a result, specific genetic variants have been implicated in virtually all forms of psychopathology (e.g., Allen et al., 2008; Gizer, Ficks, & Waldman, 2009; Levinson, 2006).

Unfortunately, replication of molecular genetic findings remains a significant concern, and there is disagreement regarding the best way forward in the search for the genetic bases of psychopathology (Hudziak & Faraone, 2010; Willcutt et al., 2010). Concerns raised in regard to efforts to model links between single genes and disorder include (1) the fact that such designs fail to capture the polygenic basis of psychopathological phenomena; (2) the arguably low likelihood that diagnostic syndromes are adequate phenotypes for molecular genetic study; (3) the probability that some variants operate in a context-dependent manner (i.e., the case of gene–environment interaction, or G×E); relatedly, (4) the fact that gene function is a dynamic phenomenon influenced by the environment, other genetic variants, and multiple epigenetic processes not captured by studies that assess genotype–phenotype associations only; and (5) the possibility that many cases of disorder are related to yet-to-be identified rare variants, making the a priori selection of candidate genes misguided. We address these points in the following few paragraphs.

Genome-wide association studies have emerged as a means of capturing polygenic influences on psychopathology, although their replication record appears variable, and overall effect sizes have been criticized for their small magnitude (Manolio, 2010; McCarthy et al., 2008); furthermore, it is unclear how to incorporate such studies within frameworks that also capture environmental influences on disorder, as well as G×E. With respect to concerns regarding the use of diagnostic phenotypes, many investigators interested in the molecular basis of disorder elect to avoid the use of these entirely, focusing instead on endophenotypes (Gottesman & Gould, 2003), or markers of disorder risk that are thought to lie more proximal to the actions of genes than diagnostic outcomes. For example, endophenotypes related to neuropsychological function (such as reaction time variability, time reproduction, and response inhibition) have been applied to the genetic investigation of ADHD (e.g., Nigg, 2010), and biases in memory may be a promising endophenotype for depression risk (e.g., Hayden et al., 2006; Hayden, Olino, Bufferd, et al., 2013), although variability across studies in terms of how endophenotypes have been operationalized has made replication attempts difficult.

Regarding the conditional effects of genes, one of the more controversial directions in psychiatric genetics is the emergence over the past decade of studies testing G×E, which attempt to capture the interplay between specific genetic variants and environmental risk factors in producing psychopathological outcomes (Kendler, 2011; Uher, 2011). Although the earliest of these seminal studies focused on psychiatric disorder in adults (e.g., Caspi et al., 2003), this literature has frequently focused on the role of early childhood adversity in potentiating the effect of genetic risk variants on

later disorder; this may account for the tremendous appeal of this approach to developmental psychopathologists, who tend to have a keen interest in the dynamic relationship between endogenous child and contextual risk factors. Moreover, studies identifying G×E hold the promise of accounting for the poor rate of replication of studies seeking to identify single-gene main effects, if many genetic influences are context-dependent or conditional. It is therefore not surprising that journals have been flooded with studies testing G×E across development.

Unfortunately, many of these studies are plagued by the same limitations found in poorer-quality molecular genetic association studies (e.g., small sample sizes; testing genetic influences on relatively complex, biologically implausible phenotypes), and may represent false-positive findings (Duncan & Keller, 2011). Also, attempts to model single-gene effects on complex psychiatric phenotypes, even within the context of environmental risk, may be misplaced. For many of the more popular G×E models, meta-analyses have been conducted that have supported (Karg, Burmeister, Shedden, & Sen, 2011; Kim-Cohen et al., 2006) and refuted (e.g., Risch et al., 2009) these findings. It has been argued that poor measurement approaches (e.g., self-report questionnaires) to the phenotype and the environmental context limit the ability of studies to detect true G×E (Monroe & Reid, 2008). Furthermore, Brown (2012) recently noted that studies of adults in which support for a G×E involving the serotonin transporter genotype and stress was evident were those in which adult stress could be interpreted as a marker of childhood adversity, suggesting that research on G×E should focus on developmental periods of greater plasticity (i.e., childhood), as this is when environmental moderation of genetic effects is unfolding. In conclusion, while it seems unquestionable that genetically influenced responses to the environment are an important force in risk for psychopathology, the question of how best to model this interplay has yet to be resolved.

Aside from these concerns, few would argue that the fact that studies of G×E are attempting to model an unknown, underlying biological process through statistical methods is an unimportant limitation. In other words, tests of G×E statistically model the conditional effects of genes without knowledge of the biological mechanisms through which these conditional effects emerge (Mill, 2011). While accurate genotyping of the loci implicated in psychopathology risk is now relatively affordable, a host of dynamic processes (see Mill, 2011, for an overview of these) known as "epigenetic influences" that further shape the actions of genes are less well understood or readily characterized to date, although these appear to play a more important role in gene function than previously thought. An emerging body of research is exploring epigenetic markers in psychiatric disorders and related processes in humans (Petronis, 2010); however, it is unclear whether the noninvasive methods available for human epigenetic research adequately reflect epigenetic processes in the human brain, which are presumably the most relevant to mechanisms of psychopathology.

Finally, it has been argued that, in sharp contrast to the widely held notion that disorder arises from the summed influence of many genes with small individual effects, individual rare variants with a large, harmful impact on neural function play a key role in the genetic basis for psychiatric disorder (McClellan & King, 2010). Although such rare variants by definition do not account for a large number of cases of disorder, the hope is that through their study, a better understanding of the pathophysiology of disorder can be gained. This is a relatively new approach that, due to its novelty, is difficult to evaluate in terms of the insights it has yielded to date.

SUMMARY AND CONCLUSIONS

In this introductory chapter, we have described a developmental–systems framework for child psychopathology that emphasizes three central themes: (1) the need to study child psychopathology in relation to ongoing normal and pathological developmental processes; (2) the importance of context in determining the expression and outcome of childhood disorders; and (3) the role of multiple and interacting events and processes in shaping both adaptive and maladaptive development. The research findings presented in the subsequent chapters of this volume illustrate the importance of these themes for understanding children and adolescents displaying a wide range of problems and/or disorders.

A developmental–systems framework eschews simple linear models of causality and advocates for a greater emphasis on systemic and developmental factors and their interactions in understanding child psychopathology. Multiple etiologies and their interplay represent the norm for most forms of child psychopathology. For example, in the study of conduct disorder, genetic in-

fluences, constitutional factors, insecure attachment relationships, impulsivity, biased cognitive processing, parental rejection, a lack of parental supervision, interpersonal difficulties, and many other influences have been implicated. However, many of these influences have also been implicated in other disorders, and not all children who exhibit such risks develop conduct disorder. There is a need for research that will help to disentangle the role of these multiple sources of influence and their interactions in relation to different childhood disorders.

We have argued that all forms of child psychopathology are best conceptualized in terms of developmental trajectories, rather than as static entities, and that the expression and outcome for any problem will depend on the configuration and timing of a host of surrounding circumstances that include events both within and outside a child. For any dynamically changing developmental trajectory, there also exists some degree of continuity and stability in structure, process, and function across time. Understanding such continuity and stability in the context of change represents a challenge for future research; it necessitates that psychopathology in children be studied over time, from a number of different vantage points, utilizing multiple methods, and drawing on knowledge from a variety of different disciplines.

Given the complexities associated with a developmental–systems framework for understanding child psychopathology, there is a clear need for theories to guide our research efforts. We have argued that a developmental psychopathology perspective provides a broad macroparadigm for conceptualizing and understanding childhood disorders in general, and that complementary disorder- and problem-specific theories are also needed to account for the specific configurations of variables commonly associated with particular disorders. Such problem-specific theories are presented in the subsequent chapters of this volume. The conceptualization of child psychopathology in terms of developmental trajectories, multiple influences, probabilistic relationships, and diverse outcomes suggests that some influences are likely to be common to many different disorders and that others are probably specific to particular problems. Our theories need to account for both types of influence.

As we have seen, childhood disorders constitute a significant societal problem, and in the absence of an empirically grounded knowledge base, unsubstantiated theories have frequently been used as the basis for developing solutions to these problems. There is a pressing need for further longitudinal research to inform our intervention and prevention efforts. If such work is to succeed in capturing the multiple interacting influences and changes over time outlined in this chapter, such research will require new ways of conceptualizing childhood disorders; greater collaboration across disciplines; and the use of novel technologies, sophisticated designs, and complex statistical tools. Considerable advances have been made in all of these areas since earlier editions of this book appeared. The chapters in the present volume provide a state-of-the-art review and critique of current definitions, theories, and research for a wide range of childhood disorders. They also identify current needs and forecast likely future directions for research into child psychopathology.

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NOTES

1. As a matter of convenience, we use the terms "children" and "child" in this chapter and volume to refer to children of all ages, from infancy through adolescence. The diversity within this wide age range will necessitate the use of more specific designations of age and developmental level as appropriate to each discussion. We use the terms "child psychopathology" and "developmental psychopathology" interchangeably in this chapter and in this volume. Other terms that have been used to describe problems during childhood are "abnormal child psychology," "childhood disorders," "atypical child development," "childhood behavior disorders," "childhood emotional and behavioral problems," and "exceptional child development." These differences in terminology reflect the many disciplines and theoretical perspectives that are concerned with understanding and helping disturbed children.

2. We recognize that theory and research in child psychopathology need to be put to the test in the applied arena. However, in this volume we do not consider in any detail the range of assessment, treatment, or prevention strategies available for the problems under discussion. Our decision not to address assessment, treatment, and prevention in this volume was based on two factors. First, we perceived a need for a

substantive review of what we currently know about childhood disorders. Many current treatments for childhood disorders are relatively untested (Kazdin, 2000; Mash & Barkley, 2006), and it was felt that future efforts to test treatment approaches would benefit from a detailed discussion of our current knowledge base for child psychopathology. Second, we wished not to dilute the discussion of theory and research in child psychopathology by attempting to provide cursory coverage of assessment and intervention. Instead, we refer the reader to companion volumes to this one, which have as their primary focus child assessment (Mash & Barkley, 2007) and child treatment (Mash & Barkley, 2006), respectively.

3. A complete discussion of the scope and complexity of issues surrounding the concept of harmful dysfunction is beyond the scope of this chapter. The reader is referred to papers in the *Journal of Abnormal Psychology* (see Clark, 1999, for an overview) and in *Behaviour Research and Therapy* (Houts, 2001; McNally, 2001; Wakefield, 1999a, 1999b, 2001) for excellent discussions of these and related issues.

4. ICD-10 is currently under revision, and ICD-11 is expected to appear in 2015. For information about ICD-11, see its website (*www.who.int/classifications/icd/revision/icd-11faq/en*).

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PART II

ADHD, CONDUCT DISORDERS, AND SUBSTANCE USE DISORDERS

CHAPTER 2

Attention-Deficit/Hyperactivity Disorder

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OVERVIEW

Inattention and impulsivity can occur in a wide range of psychopathologies. For example, substance use, gambling, and antisocial behavior are all associated with impulsivity even in adults. Anxiety or depression can make someone have trouble concentrating at any age. Furthermore, it is normal for little children to be active, energetic, impulsive (acting without thinking of the consequences), and frequently inattentive (not concentrating or having their mind wander on to whatever is nearby). Even in adulthood, most people have trouble concentrating if they are overloaded with too many things to do or a lot of pressure to hurry—a common complaint for people today. Finally, spontaneity and creativity are actually healthy, even though they may often bring impulsivity or off-topic thinking in their wake.

Yet for some individuals their activity level, difficulty controlling impulses (actions or emotional/verbal expression), or inattention are so extreme that they cannot keep up in society. Children with attention-deficit/hyperactivity disorder (ADHD) are so active or impulsive that they cannot sit still, are constantly fidgeting, talk when they should be listening, interrupt people all the time, can't stay on task, don't seem to be listening to others, and constantly lose things. They may often accidentally injure themselves, may be unable to stay seated in the classroom, or may be so inattentive that they cannot learn. They are no longer simply spontaneous by design, but are now out of control in their spontaneity, unable to rein themselves in on a consistent basis. Indeed, these children may be so emotionally volatile or poorly controlled that they are difficult to parent or teach. When they reach adulthood, many continue to have difficulties: They are unable to get work done, get into frequent traffic accidents, or aggravate others in conversations by being off topic or intruding at the wrong time. When things get this bad, individuals are no longer simply expressing the *joie de vivre* of typical children or of outgoing and optimistic adults. They are highly likely to be impaired in social, cognitive, academic, familial, and eventually occupational domains. These impairments can be extensive, and we detail them later. Figure 2.1 depicts our general framework for ADHD; it shows why we consider ADHD extremely important in regard to being a developmental gateway, emanating from multiple early risk factors, and setting the stage for a range of poor life outcomes.

As this volume goes to press, it has been nearly 240 years since Melchior Adam Weikard in 1775 (see Barkley & Peters, 2012) first described disorders of attention in the medical literature. His work was followed a generation later by Alexander Crichton's more elaborate

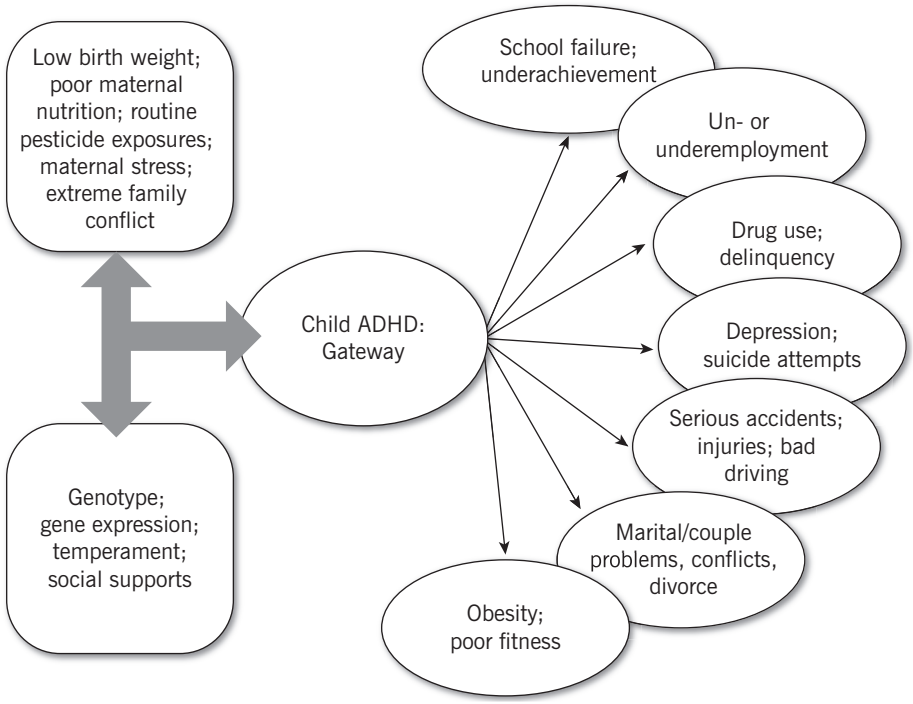

FIGURE 2.1. ADHD as a risk gateway: It likely stems in most instances from multiple prenatal and early developmental risk factors, and it amplifies risk for a wide range of outcomes related to cascading effects of poor self-control throughout life.

descriptions in his medical textbook in 1798 (see Palmer & Finger, 2001). It has also been just over 200 years since Benjamin Rush (1812/1962) provided the first American medical description of extremely impulsive children similar to today's children with ADHD; just over 75 years since the discovery that amphetamine-like drugs could help them (Bradley, 1937); just over 45 years since the first official diagnostic criteria for hyperkinetic reaction of childhood were formulated by the American Psychiatric Association (APA) in the second edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-II; APA, 1968); and nearly 35 years since the first formal diagnostic criteria for attention deficit disorder were promulgated in DSM-III (APA, 1980), both officially revising and narrowing the older construct of minimal brain dysfunction (Taylor, 2011). The current volume's publication comes just after the publication of DSM-5 (APA, 2013), marking the latest update in diagnostic criteria and accompanying advisory and descriptive text for mental disorders in psychiatry. The 11th revision of the *International Classification of Diseases* (ICD-11) by the World Health Organization (see *www.who.int/classifications/icd/revision/icd11faq/en*) is expected to follow in 2015 and to have some continued differences from DSM-5. The primary difference historically has been that the ICD definition has been narrower (i.e., has identified fewer children) than the DSM definition. We focus here on the DSM-5 formulation.

As the preceding history indicates, diagnostic labels for these children (and now adults) and the corresponding conceptions of what is wrong with them have changed several times in the past 200-plus years, even as the literature has progressed from rare to extensive scrutiny of this syndrome. Even so, the clinical descriptions have remained remarkably consistent in their essential features over the past century and longer. This constellation of behavior problems may constitute one

of the most well-studied childhood disorders of our time. Nevertheless, these children remain an enigma: Many laypeople are still struggling to accept the notion that the disorder may be a biologically rooted developmental disability or the result of a subtle brain injury, when nothing seems physically wrong.

It is striking that in DSM-5, ADHD is classified as a neurodevelopmental disorder—alongside autism spectrum disorder, specific learning disorder, communication disorders, and intellectual disabilities. This grouping has come about not only because ADHD shares with these other conditions an early onset and persistent course. Like these other conditions, ADHD is often accompanied by other delays and has been associated with enduring alterations in neural development; it also often co-occurs or overlaps with other subtle problems in language, motor, and social development.

This chapter provides an overview of the nature of this disorder; summarizes key aspects of its colorful history in Western society; and describes its diagnostic criteria, its developmental course and outcomes, and what is known about its causes. Along the way, we note key issues that a critical professional needs to bear in mind, and we make some guesses about what the future may hold for this disorder. As will become evident, despite the disorder's current label, the central difficulty is more complex than simply a problem in attention.

HISTORICAL CONTEXT

It is interesting to speculate as to whether ADHD is actually a psychiatric condition of relatively recent historical onset that may have been very rare in ancient times (like anorexia nervosa), or a disorder that seems to have affected our species for several thousand years (like schizophrenia). If we could fill in this gap in historical knowledge, it would put useful constraints on theories of what causes ADHD. There is no obvious description that we know of in the ancient literature, despite the distinct personality types described by Galen. Literary references to individuals having serious problems with inattention, hyperactivity, and poor impulse control can be found in Shakespeare, who alluded to a malady of attention in *King Henry VIII*. As we have noted above, the modern history of ADHD-like medical desciptions can be traced back over 200 years; this early history has been expertly detailed by Taylor (2011) but should be supplemented by more recent discoveries in that history, as discussed below. Here we draw upon his work and more recent articles with a few additional highlights.

As we have noted earlier, the first description of disorders of attention now appears to be the one in a medical textbook by Melchior Adam Weikart in German in 1775 (or even 1770; see Barkley & Peters, 2012). Weikart described adults and children who were inattentive, distractible, impersistent, overactive, and impulsive—characteristics appearing similar to today's description of ADHD. Weikart's account was followed by descriptions of ADHD-like symptoms in a textbook by the Scottish physician Alexander Crichton (Crichton, 1798; see Palmer & Finger, 2001), who may well have studied with Weikart in his medical training. Crichton described patients with "extreme mental restlessness." Next, the famous American physician Benjamin Rush (1812/1962) mentioned a syndrome involving inability to focus attention. In the mid-1800s, German pediatrician Heinrich Hoffman published a book for children, *Der Struwwelpeter* (Hoffman, 1865), which described both a very impulsive, fidgety child he called "Fidgety Phil" and a very inattentive child he called "Johnny Head-in-Air" (see Stewart, 1970); both are recognizable to contemporary clinicians. William James (1890/1950), in *The Principles of Psychology*, described a normal variant of character that he called the "explosive will," which may resemble the difficulties experienced by those who today are described as having ADHD.

As noted by Bader and Hidjikhani (2013), in France the concept of ADHD may have originated in the notion of "mental instability" introduced in the late 19th century under the leadership of Désiré Magloire Bourneville (1885 or 1886, 1895) at the Hospital Bicêtre in Paris. Bourneville observed children and adolescents who had been labeled "abnormal" and placed in medical and educational institutions. Charles Baker, a student of Bourneville, made the first clinical description of hyperactive and impulsive symptoms in four children in his 1892 thesis, according to Bourneville (1895); attention problems were also mentioned in one case in this work. In Great Britain, serious clinical interest in children with ADHD was generated by the physician George Still (1902) in three lectures before the Royal Academy of Physicians. Still described a cohort of 20 children in his clinical practice whom he defined as having a deficit in "volitional inhibition" (p. 1008), which led to a "defect in moral control" (p. 1009) over their own behavior. By 1908, the term "minimal brain damage" had entered the medical lexicon (Taylor,

2011) to represent a group of substantial ADHD-like behavioral disturbances in children who showed no evidence of gross brain damage. In Spain, the physician Rodriguez-Lafora (1917) wrote about his interests in childhood mental illness and described a group of children having psychopathic constitutions, a subset of whom he called the "unstables." His description of them was a close match for the modern view of ADHD (Bauermeister & Barkley, 2010), including inconstancy of attention, excessive activity, and impulsive behavior, as well as the observation that these children frequently got carried away by their adventurous temperaments.

After the great encephalitis epidemics of 1915–1920, it was observed that some children who survived these brain infections had many behavioral problems with defiance, impulsivity, and overactivity; these descriptions do not perfectly match the current conceptualization of ADHD, but have notable similarities (Ebaugh, 1923; Hohman, 1922; Stryker, 1925). These cases and others known to have arisen from birth trauma, head injury, toxin exposure, and infections (see Barkley, 2006) eventually cemented the idea of a "brain-injured child syndrome" (Strauss & Lehtinen, 1947), often associated with intellectual disability. This label would eventually be applied to children manifesting these same behavioral features, but without evidence of brain damage or retardation (Dolphin & Cruickshank, 1951; Strauss & Kephardt, 1955). This concept evolved into "minimal brain damage" and eventually "minimal brain dysfunction" (MBD), as challenges were raised to the original label because of the dearth of evidence for obvious brain injury in most cases (see Kessler, 1980, for a more detailed history of MBD).

In a serendipitous step forward, Bradley (1937) discovered that children with hyperactive behavior and other attributes of MBD showed remarkable improvement in response to stimulant medication (Benzedrine). Although physicians did not begin regularly prescribing stimulants for MBD until the 1950s and 1960s, Bradley's discovery probably also affected conceptions of the disorder, and shifted interest away from cognitive and learning problems toward hyperactivity.

Psychiatric classifications did not formally enter the medical lexicon until after World War II, and the first formal definition of what is now ADHD did not appear until 1980, but the stage was set now for the gradual emergence of the modern conception. By the late 1950s, labels such as as "hyperkinetic impulse disorder" or "hyperactive child syndrome" (Burks, 1960; Chess, 1960) were also in use. The disorder was thought to arise from cortical overstimulation, due to poor thalamic filtering of stimuli entering the brain (Knobel, Wolman, & Mason, 1959; Laufer, Denhoff, & Solomons, 1957). Despite a continuing belief among many clinicians and researchers of this era that the condition had some sort of neurological origin, the influence of psychoanalytic thought and psychosocial theories was also prominent. When DSM-II (APA, 1968) appeared, childhood disorders were noted for the first time. All childhood disorders were described as "reactions," to emphasize their believed exogenous causation, and the hyperactive child syndrome became "hyperkinetic reaction of childhood."

The view that the disorder was not caused by brain damage seemed to follow an argument made somewhat earlier by the prominent child psychiatrist Stella Chess (1960). It set off a major rift between professionals in North America and those in Europe. Even today, there continue to be divergent traditions of how to understand and treat ADHD in the United States and in Europe: European practice guidelines tend to favor psychological intervention as the first line of treatment and medication as the second line, while American practice guidelines tend to reverse this order. Moreover, professionals in Europe continued to view hyperkinesis for most of the latter half of the 20th century as a relatively rare condition of extreme overactivity, and revisions of the ICD have continued to refer to the syndrome as "hyperkinetic disorder." Historically, in North America, Canada, and Australia, such children were diagnosed with ADHD (a developmental disorder), whereas in Europe for much of the late 1900s they were viewed as having a conduct problem or disorder (a behavioral disturbance believed to arise largely out of family dysfunction and social disadvantage). The fundamental tension between viewing these children as having either a neurobiological or a behavioral/psychosocial problem is apparent in arguments about ADHD to varying extents to the present day. Interestingly, the tension can to some extent be resolved conceptually by acknowledging recent findings that ADHD and conduct disorder do indeed have relatively different configurations of genetic and environmental influences. For example, shared environment plays a larger role in conduct problems and aggression than it does in the etiology of ADHD (Burt, 2009). However, for the clinician, whether to prioritize the ADHD or the conduct problems when they co-occur is a difficult choice on which the traditions still tend to differ. We return to this in our integrative remarks later.

By the 1970s, inspired by progress in cognitive and experimental psychology in operationally defining attention, research emphasized the problems with

sustained attention and impulse control in addition to hyperactivity (Douglas, 1972). Douglas (1980, 1983) theorized that MBD involved major deficits in (1) the investment, organization, and maintenance of attention and effort; (2) the ability to inhibit impulsive behavior; and (3) the ability to modulate arousal levels to meet situational demands. Together with these tdeficits went an unusually strong inclination to seek immediate reinforcement. Douglas's emphasis on attention, along with the numerous studies of attention, impulsiveness, and other cognitive sequelae that followed (for reviews, see Douglas, 1983; Douglas & Peters, 1978), may have eventually led to renaming the disorder "attention deficit disorder" (ADD) in DSM-III (APA, 1980). At that time, the syndrome was redefined in narrower terms than those previously used for MBD, and the term MBD was abandoned.

Also notable in DSM-III was that clinical recognition was also given to children who were inattentive, but not necessarily hyperactive. Thus DSM-III specified criteria for two subtypes of ADD: "with hyperactivity" and "without hyperactivity" (although criteria for this second subtype were not proposed). Little research existed at the time that would have supported such a distinction, but the suggestion stimulated research on possible differences between groups of children with ADD. We return to this question about inattentive children and subtypes below.

Even so, concern arose within a few years of the ADD label's creation that the important features of hyperactivity and impulse control were being deemphasized, when in fact they were critically important to differentiating the disorder from other conditions and to predicting later developmental risks (Barkley, 2006; Weiss & Hechtman, 1993). Furthermore, the newly applied technique of computerized factor analysis suggested that the three symptom groups as proposed in DSM-III (inattention, hyperactivity, and impulsivity) were not statistically valid. Therefore, the disorder was renamed "attention-deficit hyperactivity disorder" in DSM-III-R (APA, 1987), and a single list of items incorporating all three symptoms was specified. The condition of ADD without hyperactivity was retained and renamed "undifferentiated ADD"—but it was relegated to an appendix of the manual, away from the main diagnostic section on ADHD, and was still presented without defining operational criteria. The reason given was that insufficient research existed to guide the construction of diagnostic criteria for it at that time.

During the 1980s, reports focused instead on problems with motivation generally, and on an insensitivity to response consequences specifically (Barkley, 1989b; Glow & Glow, 1979; Haenlein & Caul, 1987). Research was demonstrating that under conditions of continuous reward, the performances of children with ADHD were often indistinguishable from those of typical children on various lab tasks, but that when reinforcement patterns shifted to partial and hence delayed reward or to extinction (no-reward) conditions, the children with ADHD showed significant declines in their performance relative to control children (Douglas & Parry, 1983, 1994; Parry & Douglas, 1983). It was also observed that deficits in the control of behavior by rules characterized these children (Barkley, 1989b).

Beginning in the late 1980s, researchers employed information-processing paradigms to study ADHD, and found that problems in perception and information processing were not as evident as were problems with motivation and response inhibition (Barkley, Grodzinsky, & DuPaul, 1992; Schachar & Logan, 1990; Sergeant, 1988; Sergeant & Scholten, 1985a, 1985b). The problems with hyperactivity and impulsivity were also believed to form a single dimension of behavior for all practical purposes (Achenbach & Edelbrock, 1983; Goyette, Conners, & Ulrich, 1978; Lahey et al., 1988), which others described as "disinhibition" (Barkley, 1994, 1997a, 1997b). All of this led to further work on item sets and factor analyses. The result was that when DSM-IV was published (APA, 1994), ADHD was once again described as reflecting two distinct yet correlated dimensions or domains of behavior: One set of symptoms was provided for inattention, and another set of symptoms for hyperactive–impulsive behavior.[1] Unlike DSM-III-R, DSM-IV thus once again permitted the full-fledged diagnosis of a subtype of ADHD that consisted principally of problems with attention (ADHD, predominantly inattentive type), and for the first time provided specific diagnostic criteria for this group—although the conceptual definition was somewhat different from that in DSM-III (because DSM-III had allowed these children to be impulsive but not hyperactive). DSM-IV also permitted, for the first time, the distinction of a subtype of ADHD that consisted chiefly of hyperactive–impulsive behavior without significant inattention (ADHD, predominantly hyperactive–impulsive type). Children having significant problems from both item lists were described as having ADHD, combined type.

Several developments in the literature became notable as the 21st century began. Theoretical conceptions of ADHD continued to broaden in scope. These revisions included interest in more broadly defined at-

tentional features, such as working memory and temporal information processing, that extend well beyond formal definitions of attention and are in part captured by the umbrella term "executive functioning" (Barkley, 1997a; Castellanos, Sonuga-Barke, Milham, & Tannock, 2006). This term often refers to those cognitive abilities involved in goal-directed behavior and problem solving (Barkley, 2013). There was also a revival of interest in dopamine response theories, which focused on reward or reinforcement mechanisms (Sagvolden, Johansen, Aase, & Russell, 2005; Tripp & Wickens, 2008). Particularly notable, in our view, was the growing emphasis on "multiple-pathway models" of ADHD. This perspective suggests that both attention-related theories and motivation-related theories have captured a piece of the truth. Perhaps the inattentive–disorganized symptom domain is best seen as emanating from breakdowns in dorsal prefrontal–striatal neural circuits and executive functioning or cognitive control, whereas the hyperactive–impulsive symptom domain is best seen as related to problems in ventral–prefrontal–limbic neural circuits involved in reward valuation, regulation, and resolution of conflicts in consequences. Alternatively, perhaps different children with ADHD have different reasons for their behaviors: Some may have problems primarily with cognitive control, others primarily with reward response. We take up this idea again later when we consider future directions in the field. (Meantime, for more discussion of these ideas, see Nigg, Hinshaw, & Huang-Pollock, 2006; Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005; Sonuga-Barke, 2005.)

It was not until almost 20 years after DSM-IV appeared that DSM-5 was published (APA, 2013). During this interim period, in addition to developments in theory, technology revolutionized research on child psychopathology. For the first time, ADHD was associated with massive research on structural and functional brain imaging, involving the use of such devices such as magnetic resonance imaging (MRI) in children. That period of time also saw an explosive increase in molecular genetic studies of ADHD. Together, these literatures provided new and tantalizing evidence for biological correlates of ADHD. The authors of DSM-5 thus considered numerous potential improvements to the criteria. Yet, in the end, few substantive changes were made.[2] The same 18 items and the same two behavioral domains (inattention and hyperactivity–impulsivity) are still in force. Indeed, the literature of the last 20 years has provided powerful evidence for the clinical utility and validity of distinguishing these two symptom domains—which, despite being highly correlated, predict different impairments and are likely to have different neural correlates (Willcutt et al., 2012). In particular, symptoms of inattention–disorganization tend to predict such outcomes as academic problems, certain driving difficulties, and peer neglect. Symptoms of hyperactivity–impulsivity tend to predict aggression, peer rejection, and speeding citations, among other difficulties.

Also historically significant has been the further description of a potential second attention disorder, originally believed to be a subtype or at least a subset of ADHD and typically ensconced by clinicians in the DSM-IV category of ADHD, predominantly inattentive type. This condition was first identified in efforts to distinguish DSM-III ADD without hyperactivity from ADD with hyperactivity. It appears that the first description of a subset of children without hyperactivity as being more drowsy, sluggish, and daydreamy appeared in a paper by Lahey, Schaughency, Strauss, and Frame (1984) comparing children in the two ADD groups. Results for studies evaluating such distinctions were mixed (see Milich, Balentine, & Lynam, 2001); yet some investigators repeatedly identified a subset of children having this quite different pattern of inattention and hypoactivity that came to be called by Carlson, Lahey, and Neeper (1986) "sluggish cognitive tempo" (SCT). Its symptoms included staring, daydreaming, drowsiness, mental fogginess/confusion, and slow processing of information, as well as appearing lethargic, hypoactive, and even sleepy. Subsequent studies of children (Barkley, 2013; Bauermeister, Barkley, Bauermeister, Martinez, & McBurnett, 2012) and adults (Barkley, 2012b) led those authors to suggest that SCT is a separate disorder from ADHD, but one that coexists with it in 35–50% of all cases of each. SCT is discussed in more detail later in this chapter.

DESCRIPTION AND DIAGNOSIS

Core Symptoms

As already highlighted, research employing factor analysis has repeatedly identified two distinct yet substantially correlated behavioral dimensions underlying the various behavioral symptoms thought to characterize ADHD (see note 1; also see Burns, Boe, Walsh, Sommers-Flanagan, & Teegarden, 2001; DuPaul, Power, Anastopoulos, & Reid, 1998; Lahey et al., 1994;

Pillow, Pelham, Hoza, Molina, & Stultz, 1998; for a review, see Willcutt et al., 2012). These two dimensions have been identified across various ethnic and cultural groups (Beiser, Dion, & Gotowiec, 2000). They have excellent reliability and discriminant validity (Willcutt et al., 2012), and thus ADHD can be thought of as a syndrome having two distinct but correlated components.

Attention

We have just noted that inattention in DSM is not formally defined relative to the experimental psychology literature. There, attention represents a multidimensional construct (Bate, Mathias, & Crawford, 2001; Mirsky, 1996; Strauss, Thompson, Adams, Redline, & Burant, 2000), and thus several qualitatively distinct problems with attention may be evident in children (Barkley, 2001c). The dimension impaired in ADHD reflects an inability to sustain attention or persist at tasks or play activities, to remember and follow through on rules and instructions, and to resist distractions while doing so. It also seems to involve problems in planning and staying organized, as well as in timeliness and problems in staying alert. One view is that this dimension actually reflects problems in cognitive control, effortful control, or executive function—particularly in working memory—rather than in other types of attention, such as orienting, focusing–executing, or alertness (Barkley, 1997a; Oosterlan, Scheres, & Sergeant, 2005; Seguin, Boulerice, Harden, Tremblay, & Pihl, 1999; Wiers, Gunning, & Sergeant, 1998).

Parents and teachers frequently complain that these children do not seem to listen as well as they should for their age, cannot concentrate, are easily distracted, fail to finish assignments, are forgetful, and change activities more often than others (DuPaul, Power, et al., 1998). Research employing objective measures corroborates these complaints through observations of exhibiting more off-task behavior and less work productivity; looking away more often from assigned tasks (including television); showing less persistence at tedious tasks (such as continuous-performance tasks); being slower and less likely to return to an activity once interrupted; being less attentive to changes in the rules governing a task; and being less capable of shifting attention across tasks flexibly (Borger & van der Meere, 2000; Hoza, Pelham, Waschbusch, Kipp, & Owens, 2001; Lorch et al., 2000; Luk, 1985; Newcorn et al., 2001; Seidman, Biederman, Faraone, Weber, & Ouellette, 1997; Shelton et al., 1998). This inattentive behavior distinguishes these children from those with learning disabilities (Barkley, DuPaul, & McMurray, 1990) or other psychiatric disorders (Chang et al., 1999; Swaab-Barneveld et al., 2000). Although inattentive behaviors are also seen in other conditions, co-occurring conditions do not explain inattention in ADHD (Klorman et al., 1999; Murphy, Barkley, & Bush, 2001; Newcorn et al., 2001; Nigg, 1999; Seidman, Biederman, et al., 1995).

Hyperactive–Impulsive Behavior

Like attention, impulsivity is a multidimensional construct (Nigg, 2000; Olson, Schilling, & Bates, 1999). Several different literatures in psychology have explored the definition of impulsivity in ratings of both personality and behavior, as well as in laboratory paradigms such as speed of responding to cues, delay aversion, and temporal discounting of future rewards. Thus one can think of impulsivity as being related to disinhibition, although there are distinctions to be made between impulsivity and disinhibition as we elaborate along the way.

To understand disinhibition, think of an impulse as a behavior that is "ready to go"—either because a child just did it (e.g., a young child repeats a behavior that just got adults to laugh, even after being told, "That's enough"—the behavior is primed and ready, and now takes effort to stop); because the child is answering quickly on a timed test; because the child has been thinking about it constantly and now has a chance to do it (e.g., the school bell rings and the child is free to leave his or her seat); or because a strong incentive cue has appeared (e.g., the ice cream truck stops in front of the house!).

However, a critical distinction, often lost in the literature, is that stopping an impulse can happen in two fundamental ways—both of which involve attention. The first way is that a child exerts effort or exerts cognitive control (i.e., the child applies attention and thus can voluntarily suppress or possibly inhibit the behavior). Very young children resist a temptation to grab a forbidden toy by looking away form the reward. Older children might be observed deliberately forcing themselves not to talk, for example. You, our readers, can imagine this by introspection: You have an urge to interrupt someone who is saying something wrong, but you force yourself to wait your turn, perhaps because you believe that courtesy is important.

A second way an impulse can be inhibited is due to a stronger impulse. Fear or anxiety can stop a behav-

ior, and, in the process, can capture attention involuntarily. A child who is horsing around in an unsupervised classroom may stop involuntarily—at least for a moment—when there is a loud knock on the door or when a bigger, unfamiliar child enters the room. You can imagine this by introspection when you hesitate to interrupt someone you are afraid to make angry (e.g., your boss, a police officer). Your impulse to avoid the angry response automatically stops you from talking, and now it takes deliberate effort to override the fear if you are going to talk.

But impulsivity can also be thought of as something involving not inhibition, but rather a heightened valuation of reward (Sagvolden et al., 2005). Each child or adult is presumed to give a certain salience or value to a future reward. This salience is influenced by many factors—how far in the future the reward lies, how certain or probable it is, how generally optimistic the individual is about the future, and others. That said, a discounting function can be estimated by comparing, for example, the choice of receiving $100 in a week to receiving $10 today. You might choose $100 in a week instead of $10 right now. However, you would probably choose $10 right now rather than $100 in 5 or 10 years. You have "discounted" the value of that future $100, due to how far away it is in time. This theory of impulsivity states that immediate rewards have unusually high influence relative to later rewards, and furthermore that they shape learning and behavior toward an impulsive style. Neurobiologically, this is thought to be rooted in dopaminergic systems. Cognitively, it can be thought of as a constant process of rapid decision making. In economics, it represents having a high time preference (a preference for consequences near in time). In the past 20 years, as well, there has been renewed interest in the behavioral description of impulsivity. Whiteside and Lynam (2001) have suggested that impulsivity consists of four behavioral components—positive urgency, lack of premeditation, lack of perseverance, and sensation seeking.

DSM-5 does not well capture these different kinds of impulsivity. It does not capture impulsive decision making (valuing of immediate rewards), nor does it very well capture different kinds of disinhibtion. Rather, the symptom items for impulsivity tend to reflect socially intrusive verbal behavior and/or impatience, while ignoring motor, cognitive, and emotional–motivational modalities for impulsive actions. Thus more work needs to be done in future editions of DSM to better capture impulsivity across the lifespan, as now reflected in the scientific literature. Work is also needed to determine which aspects of impulsivity best characterize ADHD and most closely mediate its various outcomes.

Clinically, children with ADHD manifest difficulties with excessive activity level and fidgetiness; less ability to stay seated when required; greater touching of objects; more moving about, running, and climbing than other children exhibit; playing noisily, talking excessively, and acting impulsively; interrupting others' activities; and being less able than others to wait in line or take turns in games (APA, 1994, 2013). Parents and teachers describe them as acting as if driven by a motor, incessantly in motion, always on the go, and unable to wait for events to occur. Research objectively documents them to be more active than other children (Barkley & Cunningham, 1979b; Dane, Schachar, & Tannock, 2000; Luk, 1985; Porrino et al., 1983; Shelton et al., 1998); to have considerable difficulties with stopping an ongoing behavior (Schachar, Tannock, & Logan, 1993; Milich, Hartung, Matrin, & Haigler, 1994; Nigg, 1999, 2001; Oosterlaan, Logan, & Sergeant, 1998); to talk more than others (Barkley, Cunningham, & Karlsson, 1983); to interrupt others' conversations (Malone & Swanson, 1993); to be less able to resist immediate temptations and delay gratification (Anderson, Hinshaw, & Simmel, 1994; Barkley, Edwards, Laneri, Fletcher, & Metevia, 2001; Olson et al., 1999; Rapport, Tucker, DuPaul, Merlo, & Stoner, 1986; Solanto et al., 2001); and to respond too quickly and too often when they are required to wait and watch for events to happen, as is often seen in impulsive errors on continuous-performance tests (Losier, McGrath, & Klein, 1996; Newcorn et al., 2001). Although less frequently examined, similar differences in activity and impulsivity have been found between children with ADHD and those with learning disabilities (Barkley, DuPaul, et al., 1990; Bayliss & Roodenrys, 2000; Klorman et al., 1999; Willcutt et al., 2001). Mounting evidence further shows that these inhibitory deficits are not a function of other psychiatric disorders that may overlap with ADHD (Barkley, Edwards, et al., 2001; Fischer, Barkley, Smallish, & Fletcher, 2005; Halperin, Matier, Bedi, Sharpin, & Newcorn, 1992; Murphy et al., 2001; Nigg, 1999; Oosterlaan et al., 1998; Seidman et al., 1997).

Developmentally, problems with impulsivity (and overactivity) are apparent first (at ages 3–4 years), emerging ahead of those related to inattention (at ages 5–7 years). The symptoms of SCT—a possibly distinct yet related attention disorder, as noted earlier—may

arise even later (ages 8–10) (Hart, Lahey, Loeber, Applegate, & Frick, 1995; Loeber, Green, Lahey, Christ, & Frick, 1992; Milich et al., 2001). Hyperactivity tends to decline normatively with age, and by adolescence hyperactive symptoms in ADHD may be seen in the form of extreme restlessness and a fast tempo, rather than in literally running about the room as in children. Impulsivity probably remains elevated relative to that of peers during development, but in DSM it is closely paired with hyperactivity, so that DSM symptoms of hyperactivity–impulsivity tend to decline normatively with development during childhood and into adolescence. In contrast, inattention and disorganization remain stable during the elementary grades as well as into adolescence (Hart et al., 1995). They eventually decline by adolescence (Fischer, Barkley, Fletcher, & Smallish, 1993b), though not to normative levels.

Why the inattention arises later than the disinhibitory symptoms and does not decline when the latter do over development remains an enigma. A parsiminous explanation may be that societal demands for cognitive control and attention escalate dramatically at ages 5–7 as children enter school. An interesting possibility from a developmental perspective arises from the asynchronous nature of neural development. Limbic and subcortical structures probably play a large role in hyperactivity and impulsivity (Sonuga-Barke, 2005) by driving reward sensitivity. These neural structures mature more rapidly than several cortical areas. In contrast, inattention and executive functioning probably rely on maturation of prefrontal cortices, which are slower to mature than the subcortical areas. Another possibility is that cognitive control and executive functioning rely on interacting long-range neural connections throughout the brain, which also are slow to mature fully (Shaw, Greenstein, et al., 2006).

Situational and Contextual Factors

It is important to recognize that although ADHD is a neurodevelopmental disorder, it is not like more dramatic disorders, such as Down syndrome, that are apparent in all situations. At the risk of reviving the MBD analogy, ADHD may be more analogous to a mild closed head injury, with no apparent physical damage yet subtle decrements in cognition, self-regulation, and other abilities that are noticeable under challenge. Thus, although in some cases of ADHD the syndrome is sufficiently dramatic that it is apparent "at a glance," for the most part the behavioral and cognitive problems seen in ADHD are context-dependent—apparent only in some situations and not all. Douglas (1972) long ago commented on the greater variability of task performances by children with ADHD compared to control children.

Several factors influence the ability of children with ADHD to sustain their attention to task performance, control their impulses to act, regulate their activity level, and/or produce work consistently. The performance of these children is worse (1) later in the day than earlier (Dane et al., 2000; Porrino et al., 1983; Zagar & Bowers, 1983); (2) in more complex tasks, where organizational strategies are required (Douglas, 1983); (3) when restraint is demanded (Barkley & Ullman, 1975; Luk, 1985); (4) under low levels of stimulation (Antrop, Roeyers, Van Oost, & Buysse, 2000; Zentall, 1985); (5) under more variable schedules of immediate consequences in the task (Carlson & Tamm, 2000; Douglas & Parry, 1983, 1994; Slusarek, Velling, Bunk, & Eggers, 2001; Tripp & Alsop, 1999); (6) under longer delay periods prior to reinforcement availability (Solanto et al., 2001; Sonuga-Barke, Taylor, & Heptinstall, 1992; Tripp & Alsop, 2001); and (7) in the absence of adult supervision during task performance (Draeger, Prior, & Sanson, 1986; Gomez & Sanson, 1994).

Besides the aforementioned factors, which chiefly apply to task performance, variability has also been documented across more macroscopic settings. For instance, children with ADHD exhibit more problematic behavior when persistence in work-related tasks is required (chores, homework, etc.) or where behavioral restraint is necessary, especially in settings involving public scrutiny (in church, in restaurants, when a parent is on the phone, etc.) than in free-play situations (Altepeter & Breen, 1992; Barkley, 2012a; Barkley & Edelbrock, 1987; DuPaul & Barkley, 1992). Although they will be more disruptive when their fathers are at home than during free play, children with ADHD are still rated as much less problematic when their fathers are at home than in most other contexts. Fluctuations in the severity of ADHD symptoms have also been documented across a variety of school contexts (Barkley & Edelbrock, 1987; DuPaul & Barkley, 1992). In this case, contexts involving task-directed persistence and behavioral restraint (e.g., the classroom) are the most problematic, with significantly fewer problems in contexts involving less work and behavioral restraint (at lunch, in hallways, at recess, etc.), and even fewer problems during special events (field trips, assemblies) (Altepeter & Breen, 1992).

Associated Developmental Impairments

Children with ADHD often demonstrate deficiencies in many other cognitive and emotional abilities. Among these are difficulties with (1) physical fitness, gross and fine motor coordination, and motor sequencing (Breen, 1989; Denckla & Rudel, 1978; Harvey & Reid, 1997; Kadesjo & Gillberg, 2001; Mariani & Barkley, 1997); (2) speed of color naming (Carte, Nigg, & Hinshaw, 1996); (3) verbal and nonverbal working memory and mental computation (Barkley, 1997b; Mariani & Barkley, 1997; Murphy et al., 2001; Zentall & Smith, 1993); (4) story recall (Lorch et al., 2000; Sanchez, Lorch, Milich, & Welsh, 1999); (5) planning and anticipation (Grodzinsky & Diamond, 1992; Klorman et al., 1999); (6) verbal fluency and confrontational communication (Grodzinsky & Diamond, 1992; Zentall, 1988); (7) effort allocation (Douglas, 1983; Nigg, Hinshaw, Carte, & Treuting, 1998; Sergeant & van der Meere, 1994; Voelker, Carter, Sprague, Gdowski, & Lachar, 1989); (8) developing, applying, and self-monitoring organizational strategies (Clark, Prior, & Kinsella, 2000; Hamlett, Pellegrini, & Connors, 1987; Purvis & Tannock, 1997; Zentall, 1988); (9) internalization of self-directed speech (Berk & Potts, 1991; Copeland, 1979; Winsler, 1998; Winsler, Diaz, Atencio, McCarthy, & Chabay, 2000); (10) adhering to restrictive instructions (Danforth, Barkley, & Stokes, 1991; Roberts, 1990; Routh & Schroeder, 1976); and (11) self-regulation of emotion (Barkley, 2010; Braaten & Rosen, 2000; Hinshaw, Buhrmester, & Heller, 1989; Maedgen & Carlson, 2000).

The last-mentioned difficulties, those with emotional control, may be especially salient in children having ADHD with comorbid oppositional defiant disorder (ODD) (Melnick & Hinshaw, 2000). Several studies have also demonstrated that ADHD may be associated with less mature or diminished moral development (Hinshaw, Herbsman, Melnick, Nigg, & Simmel, 1993; Nucci & Herman, 1982; Simmel & Hinshaw, 1993). Many of these cognitive difficulties appear to be specific to ADHD and are not a function of its commonly comorbid disorders, such as learning disabilities, depression, anxiety, or ODD/conduct disorder (CD) (Barkley, Edwards, et al., 2001; Clark et al., 2000; Klorman et al., 1999; Murphy et al., 2001; Nigg, 1999; Nigg et al., 1998). However, more recent work (Barkley, 2010) has begun to articulate more clearly the problems in emotion regulation that seem to accompany ADHD. Clinically, this means that children with ADHD are more likely to get angry, sad, explosive, or moody than those without ADHD. Formally, this can be measured as reductions in the efficiency of physiological regulation of emotion (Musser et al., 2011).

DIAGNOSTIC CRITERIA AND RELATED ISSUES

The most recent diagnostic criteria for ADHD as defined in DSM-5 (APA, 2013) are set forth in Table 2.1. Like those in DSM-IV, to which these are qute similar, the DSM-5 diagnostic criteria represent the best consensus of experts in the field and were approved after extensive reviews of the literature, data reanalyses, and field trials and several periods of public comment.

Even so, the criteria have not escaped controversy and are not without limitations. As noted earlier, there will continue to be controversy—and, we hope, new research—on the validity and boundaries of a putatively more homogeneous inattentive group; on irritability and emotional dysregulation; on measurement of impulsivity, especially in adulthood; and overall on different ways to capture heterogeneity in ADHD. The subtyping of ADHD in DSM-IV has been essentially carried forward to DSM-5, although the word "presentation" instead of "type" is used for each and they have been classed as modifiers to convey, as explained in the accompanying text to the criteria, that these presentations are quite unstable and that clinicians should not see them as permanent descriptors. The hyperactive–impulsive type from DSM-IV had limited validity beyond preschool age (see Willcutt et al., 2012), and this is likely to remain a concern even for the concept of a presentation rather than a subtype. The DSM-IV field trial found that those diagnosed with predominantly hyperactive–impulsive ADHD were primarily preschool-age children, whereas those with the combined type of ADHD were primarily school-age children. This picture has not changed much in the ensuing two decades, and the major review by Willcutt and colleagues (2012) has raised significant questions about the validity of this category after preschool.

The issue of developmental appropriateness of the criteria will continue to be a concern as well. The DSM-IV field trials, which remain the main basis for the criteria set and cutoff points, were conducted on children ages 4–16 years. Even for DSM-5, a proper field trial of adults was not conducted. Substantial reasons exist to expect a lower symptom threshold to be appropriate in adults, and DSM-5 has appropriately

TABLE 2.1. DSM-5 Diagnostic Criteria for Attention-Deficit/Hyperactivity Disorder

A. A persistent pattern of inattention and/or hyperactivity–impulsivity that interferes with functioning or development, as characterized by (1) and/or (2):

1. **Inattention:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

   Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

   a. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).
   b. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).
   c. Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).
   d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily sidetracked).
   e. Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).
   f. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework; for older adolescents and adults, preparing records, completing forms, reviewing lengthy papers).
   g. Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).
   h. Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).
   i. Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).

2. **Hyperactivity and impulsivity:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

   Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

   a. Often fidgets with or taps hands or feet or squirms in seat.
   b. Often leaves seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).
   c. Often runs about or climbs in situations where it is inappropriate. (**Note:** In adolescents or adults, may be limited to feeling restless).
   d. Often unable to play or engage in leisure activities quietly.
   e. Is often "on the go," acting as if "driven by a motor" (e.g., is unable to be or uncomfortable being still for extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).
   f. Often talks excessively.
   g. Often blurts out an answer before a question has been completed (e.g., completes people's sentences; cannot wait for turn in conversation).
   h. Often has difficulty waiting his or her turn (e.g., while waiting in line).
   i. Often interrupts or intrudes on others (e.g., butts into conversations, games, or activities; may start using other people's things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).

B. Several inattentive or hyperactive–impulsive symptoms were present prior to age 12 years.

C. Several inattentive or hyperactive–impulsive symptoms are present in two or more settings (e.g., at home, school, or work; with friends or relatives; in other activities).

D. There is clear evidence that the symptoms interfere with, or reduce the quality of, social academic, or occupational functioning.

(continued)

TABLE 2.1. *(continued)*

E. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

Specify whether:

314.01 (F90.2) Combined presentation: If both Criterion A1 (inattention) and Criterion A2 (hyperactivity–impulsivity) are met for the past 6 months.

314.00 (F90.0) Predominantly inattentive presentation: If Criterion A1 (inattention) is met but Criterion A2 (hyperactivity–impulsivity) is not met for the past 6 months.

314.01 (F90.1) Predominantly hyperactive/impulsive presentation: If Criterion A2 (hyperactivity–impulsivity) is met and Criterion A1 (inattention) is not met for the past 6 months.

Specify if:

In partial remission: When full criteria were previously met, fewer than the full criteria have been met for the past 6 months, and the symptoms still result in impairment in social, academic, or occupational functioning.

Specify current severity:

Mild: Few, if any, symptoms in excess of those required to make the diagnosis are present, and symptoms result in no more than minor impairments in social or occupational functioning.

Moderate: Symptoms or functional impairment between "mild" and "severe" are present.

Severe: Many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present, or the symptoms result in marked impairment in social or occupational functioning.

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provided a lower threshold for adults and older adolescents, but only by one symptom (five symptoms) versus the threshold for children (six symptoms). That work was based on secondary, as yet unpublished analyses of five different data sets. Other research indicates that an even lower cutoff may be most appropriate (perhaps as low as four symptoms; Barkley, Murphy, & Fischer, 2008). Furthermore, revised cutoffs or duration periods for preschoolers under age 4 may be needed. Finally, the validity of the three presentations in adults with the five-symptom cutoff is unknown.

Also as noted earlier, the criteria may not provide adequate coverage of impulsivity, especially for older adolescents and adults. More work will be needed to integrate various emerging measures of impulsivity with the criteria for ADHD in future editions of DSM.

It is important to note the language in the DSM-5 criteria, which is also echoed in the manual's text, about the importance of obtaining corroborating information from other sources besides the patient—particularly to verify cross-situational display of symptoms. This is an improvement over DSM-IV and is a point too easily overlooked in clinical practice. It is important because over- versus underreporting of symptoms is an important issue in this population (Barkley, Knouse, & Murphy, 2011; Edwards, Barkley, Laneri, Fletcher, & Metevia, 2001; Fischer, Barkley, Fletcher, & Smallish, 1993a; Henry, Moffitt, Caspi, Langley, & Silva, 1994; Mannuzza & Gittelman, 1986; Romano, Tremblay, Vitaro, Zoccolillo, & Pagani, 2001).

A different issue pertains to whether or not the criteria should be adjusted for the gender of the children being diagnosed. Research evaluating these and similar item sets demonstrates that male youngsters display more of these items, and do so to a more severe degree, than do female youngsters in the general population (Achenbach, 1991; DuPaul, Power, et al., 1998). Given that the majority of children in the DSM-IV field trial were boys (Lahey et al., 1994), the symptom threshold chosen in the DSM-IV and now carried forward to DSM-5, at least for children, is more appropriate to males. This results in girls' having to meet a higher threshold relative to other girls to be diagnosed as having ADHD than boys must meet relative to other boys. Gender-adjusted thresholds would seem to be in order to address this problem; yet such thresholds would evaporate the currently disproportionate male-to-female ratio of 2.5:1 found across studies (see below)

in children. They would also potentially obscure relevant etiological factors, such as hormonal regulation of neural development in relation to ADHD (Martel, 2013). In contrast, ADHD in adults does not show significant sex differences in the nature of the symptoms or in the ratio of diagnosis in men versus women (Barkley, 2011). Why the sex difference should attenuate by adulthood remains an enigma.

Age and Developmental Considerations

Preschoolers

A key area of controversy has been the diagnosis of ADHD in very young children (ages 2–3 years). The DSM-5 text (APA, 2013) points out that it is difficult to establish a valid diagnosis below age 4, but the criteria do not forbid doing so. Yet it is unclear whether a differentiation of inattention or impulsivity from irritability, defiance, aggression, or immaturity is possible at younger ages. The 6-month requirement for duration of problems is also likely to be problematic in preschoolers. Many children age 3 years (or younger) may have parents or preschool teachers who report concerns about the children's activity level or attention, but these concerns have a high likelihood of remission within 12 months (Beitchman, Wekerle, & Hood, 1987; Campbell, 2006; Lerner, Inui, Trupin, & Douglas, 1985; Palfrey, Levine, Walker, & Sullivan, 1985). It would seem that the 6-month duration specified in the DSM-5 criteria may be too brief for preschoolers, resulting in overidentification of children with ADHD in this age range (false positives). However, this same body of research found that for those children whose problems lasted at least 12 months or beyond age 4 years, the behavior problems were highly persistent and predictive of continuance into the school-age range. Such research suggests that the duration of symptoms be set at 12 months or more at least in preschoolers. This is another issue to be considered for the next edition of DSM.

Adults

As noted above, DSM-5 has lowered the cutoff point for adults from six symptoms to five, on the basis of analysis of five different data sets. A key problem with diagnosis in adults is determining the history. However, much is now known about adolescent and adult outcomes from longitudinal studies. We discuss the adult outcomes further in a subsequent section.

Subtypes

Despite the clear validation of the two-domain structure of ADHD, an ability to distinguish subtypes easily does not follow—and, despite the substantial literature, the picture on subtypes remains ambiguous. This would be expected, given that the two dimensions are highly correlated, sharing at least 50–64%+ of their variance. Several trends were noted in a comprehensive review commissioned to inform the authors of DSM-5 (Willcutt et al., 2012):

1. The DSM-IV subtype designations were not stable over time, at least when the single-reporter interview methods adopted in longitudinal studies were used. Thus a child could be diagnosed as having one subtype in one year and another subtype the next year.

2. The differences between the subtypes were primarily in degree rather than kind. Children with the combined type of ADHD had worse impairments than did children with the inattentive type, while the hyperactive–impulsive type, rare in children after preschool, was little studied.

3. Neurobiological studies (e.g., functional brain imaging or molecular genetics) that directly compared these subtypes were still almost nonexistent. DSM-5 therefore removed their designations as "types" and replaced them with clinical "presentations" that are intended to be seen as course specifiers, although because they still have distinct codes they may in fact simply function in a fashion similar to the DSM-IV subtypes. This was intended to weaken the tendency to reify the unstable types, while also leaving open the possibility for new data that might address biological differences between these presentations.

The Willcutt and colleagues (2012) review also revealed that there has been insufficient empirical study of children who are inattentive but not hyperactive. That is, children who have the DSM-IV inattentive subtype or the DSM-5 inattentive presentation can still be hyperactive—just not hyperactive enough to meet criteria for the combined presentation. Thus some observers believe that if there are indeed distinct subtypes, the DSM formulation may include "subthreshold com-

bined" children along with "true inattentive" children. The idea here is that the cutoff point is in the wrong place.

That claim is intuitively appealing but has been difficult to win, however, for two reasons. First, most studies use the DSM-IV subtypes, thus evading the question of whether the grouping is "wrong" in the first place. Second, regardless of the definitions used (prior to DSM-IV, various definitions were used because DSM-III provided no formal criteria for this group), the data tend to follow a severity pattern. That is, typically the correlates of inattention accrue to the inattentive group and the correlates of inattention and of hyperactivity accrue to the combined group, suggesting that subtypes are little more than arbitrary cutoff points on these behavioral dimensions that can mix in different ways.

Nonetheless, new evidence is emerging. One kind of evidence that children with the DSM inattentive type may include children with the subthreshold combined type came from Stawicki, Nigg, and von Eye (2006), who reviewed family history data. They found that across thousands of families pooled over multiple studies, children with the predominantly inattentive type of ADHD were likely to have relatives with both this type and the combined type, whereas children with the combined type were likely to have relatives with the combined type. DSM, by contrast, still allows up to five hyperactive–impulsive symptoms in children with the "inattentive" presentation. Although validation data remain sparse, initial evidence suggests that these children may indeed have more different, and not just less severe, cognitive problems in some domains than children who are at subthreshold levels for the combined presentation, with four or five symptoms of hyperactivity–impulsivity (Carr, Henderson, & Nigg, 2010; Milich et al., 2001). The presence of inattention only, with low levels of hyperactive–impulsive symptoms, is the condition that earlier investigators identified as SCT—and that later research suggests might even form a separate yet potentially comorbid attention problem, as noted above and discussed further below.

Overall, a key question for the field now requires scrutiny: Is it simply the case that more symptoms lead to more impairment, so that subtypes merely represent differences of degree and not of kind? Or are there true differences in kind, hidden within the current DSM parameters? This will remain a "hot topic" in the years to come, and perhaps the next edition of DSM will therefore have enough literature behind it to justify renewed recognition of purely inattentive, or inattentive–sluggish, children.

It is important to reiterate that in both DSM-IV and DSM-5, "inattention" and "impulsivity" are not formally defined. Indeed, impulsivity as currently understood is not well captured in the DSM-5 criteria, as discussed earlier. DSM-5 (like DSM-IV before it) provides for three impulsivity items that pertain primarily to verbal behavior and social intrusiveness. Current understandings of impulsivity instead emphasize the relative weighting of immediate over later reward during decision making (reminiscent of the ideas about ADHD in the 1980s, also described earlier). This type of behavior, however, is not well represented in DSM. Similarly, inattention in DSM is simply defined by off-task behavior or problems with concentrating. In formal terms, inattention may be due to low energy, poor working memory, problems with controlling sensory or cognitive interference, poor cognitive control, or poor self-regulation—all of which are more precise terms that capture forms or types of attention. Debate about how to assemble these different types of attention into an overall picture of different kinds of children with ADHD continues.

However, it is increasingly believed that ADHD probably reflects multiple underlying breakdowns in cognition and neurobiology. It is also likely that in a group of children with ADHD, not all will have the same neurobiology or the same cognitive dysfunction. A neurobiological subtyping or subgrouping of individuals with ADHD remains the sought-after "holy grail" in this field, as we elaborate subsequently under "Future Directions."

Although DSM-5 has commendably urged consideration of data from multiple informants, a key problem that the authors of DSM-5 have deferred to the future concerns how such information should be combined. Is a symptom present if any reporter endorses it? Should reports from different informants be averaged? Or are some reporters more valid than others for some symptoms at some ages? This degree of nuanced weighting of reporting would be the ideal, especially given the well-established limited agreement across parents and teachers (Achenbach, McConaughy, & Howell, 1987)—and it is increasingly feasible, with the worldwide spread of microcomputing technology such as that found on smart phones. Such disagreements among sources certainly reflect differences in a child's behavior as a function of true differential demands of

these settings. But they also reflect differences in the attitudes and judgments of different people. Clinicians are left to make difficult judgments about the reliability of the different reports and the likelihood of variation across settings in determining whether the appropriate formulation is ADHD, or whether situational problems at home or school may need to be addressed. The best discrimination of children with ADHD from other groups may be achieved by blending the reports of parents and teachers, such that one counts the number of different symptoms endorsed across *both* sources of information (Crystal, Ostrander, Chen, & August, 2001; Mitsis, McKay, Schulz, Newcorn, & Halperin, 2000), as was actually done in the earlier DSM-IV field trial (Lahey et al., 1994).

Many of these problematic issues are likely to be addressed in future editions of DSM. Even so, the present criteria are actually some of the best ever advanced for the disorder; they represent a vast improvement over the state of affairs that existed prior to 1980. The various editions of DSM also have spawned a large amount of research into ADHD—its symptoms, subtypes, criteria, and even etiologies—that probably would not have occurred had such criteria not been set forth for professional consumption and criticism. The most recent criteria provide clinicians with a set of guidelines that are specific, reliable, empirically justifiable, predictive, and based on the scientific literature.

Sluggish Cognitive Tempo

SCT is not recognized in DSM-5, and so there are no officially endorsed criteria for its clinical recognition. Saxbe and Barkley (2013) recently reviewed the literature for clinicians, and much of this discussion is based on their paper. The most salient symptoms of SCT (Barkley, 2012b, 2013; Carlson & Mann, 2002; Garner, Marceaux, Mrug, Patterson, & Hodgens, 2010; McBurnett, Pfiffner, & Frick, 2001; Penny, Waschbusch, Klein, Corkum, & Eskes, 2009) are as follows: A child (1) often daydreams, (2) has trouble staying awake/alert, (3) is mentally foggy/easily confused, (4) stares a lot, (5) is "spacey"/mind is elsewhere, (6) is lethargic, (7) is underactive, (8) is slow-moving/sluggish, (9) doesn't process questions or explanations accurately, (10) has a drowsy/sleepy appearance, (11) is apathetic/withdrawn, (12) is lost in thoughts, (13) is slow to complete tasks, and (14) lacks initiative/has trouble sustaining effort. The last two symptoms, however, are as likely to be associated with ADHD as with SCT in children or adolescents, and so they are not recommended for assisting with differential diagnosis between these two types of attention disorders (Barkley, 2013). But the remaining 12, among others (Penny et al., 2009), appear to be highly useful for making such distinctions.

SCT symptoms cluster into separate symptom dimension(s) from the two traditional yet highly intercorrelated ones of inattention and hyperactivity–impulsivity for ADHD both in children (Jacobson et al., 2012; Penny et al., 2009) and in adults (Barkley, 2011). Two (or more) symptom dimensions are often evident: (1) daydreaming/sleepiness and (2) being slow/sluggish/lethargic (Barkley, 2013; Penny et al., 2009). A third dimension, representing low initiation/persistence, may also be present (Jacobson et al., 2012) but may be as correlated with ADHD inattention symptoms as it is with SCT, thus making it less useful for case discrimination. The factors emerge regardless of approaches to measurement, and in both clinic-referred and community-based cases. Whether researchers have used parent and teacher ratings (Barkley, 2013; Bauermeister et al., 2012; Garner et al., 2010; Hartman, Willcutt, Rhee, & Pennington, 2004; Jacobson et al., 2012; Penny et al., 2009), observations of behavior at school (McConaughy, Ivanova, Antshel, Eiraldi, & Dumenci, 2009), and observations of behavior in clinical settings (McConaughy, Ivanova, Antshel, & Eiraldi, 2009), SCT symptoms are shown to be distinct from ADHD ones. This is true in adult self-reports as well (Barkley, 2012b). SCT symptoms are significantly but moderately correlated with the ADHD symptom dimensions, and particularly with the inattention dimension of ADHD; share approximately 10–25%+ of their variance. Yet SCT symptoms are substantially less correlated with ADHD symptoms than the two ADHD symptom dimensions are to each other (Barkley, 2012b, 2013; Penny et al., 2009). And SCT symptoms demonstrate a far lower relationship to hyperactive–impulsive symptoms than they do to inattention symptoms (Barkley, 2012b, 2013; Garner et al., 2010; Hartman et al., 2004; Jacobson et al., 2012; Penny et al., 2009; Wahlstedt & Bohlin, 2010). SCT symptoms are thus as independent of or partially coupled to ADHD symptoms as other symptom dimensions of child and adult psychopathology are to each other.

Unlike ADHD, SCT does not seem to be as serious and pervasive a disorder of executive functioning as ADHD is, whether tests of executive functioning

(Bauermeister et al., 2012; Wahlsted & Bohlin. 2010) or rating scales of such functioning in daily life (Barkley, 2012b, 2013) are used. Indeed, SCT may not be a disorder of executive functioning at all (Barkley, 2013).

SCT can overlap with ADHD. In the study of U.S. children by Barkley (2013), more than half (59%) of those participants qualifying for a designation of SCT also qualified as having ADHD. Where overlap existed, it was principally with those DSM-IV ADHD subtypes having significant inattention symptoms rather than with the hyperactive–impulsive subtype; this finding is consistent with earlier studies exploring this overlap in children (Garner et al., 2010; Penny et al., 2009; Skirbekk, Hansen, Oerbeck, & Kristensen, 2011) and adults (Barkley, 2012b). 39% of the children qualifying for ADHD of any type also qualified for SCT. Again, these findings agree with prior studies of children (Garner et al., 2010; Hartman et al., 2004) and adults (Barkley, 2012b). For instance, a recent survey of U.S. adults relying on self-report (Barkley, 2012b) found that 5.8% of the sample met criteria for high SCT symptoms. Approximately half (54%) of those participants qualifying for SCT also qualified for ADHD, based on their self-reported symptoms. About half of the individuals qualifying for ADHD of any type (46%) also qualified for SCT. The relationship of SCT to ADHD appears to be one of comorbidity between two relatively distinct but related or partially coupled disorders, such as anxiety and depression, and not one of subtyping within a single shared disorder.

The SCT dimension relates more closely to internalizing symptoms than do ADHD symptoms (Bauermeister et al., 2012; Becker & Langberg, 2012; Capdevila-Brophy et al., in press; Carlson & Mann, 2002; Garner et al., 2010; Hartman et al., 2004; Penny et al., 2009). This remains the case even after controlling for the contribution of ADHD symptoms (Bauermeister et al., 2012; Becker & Langberg, 2012; Penny et al., 2009). There is also a weaker association of SCT with externalizing symptoms or disorders, such as ODD, CD, or psychopathy, in children. ADHD, in contrast, is routinely linked to a higher risk for comorbidity with the externalizing symptom dimension generally, and specifically with ODD and CD, as discussed above.

Salient differences exist between SCT and ADHD in ratings of impairment in daily life activities (Barkley, 2012b, 2013). Space precludes a detailed discussion of these findings. Evidence shows that SCT is more associated with social withdrawal and peer neglect or oversight, whereas ADHD is associated with significant peer conflicts, aggression, bullying/victimization and rejection (Milich et al., 2001; Penny et al., 2009). Both disorders impair academic performance, but ADHD is far more closely associated with disruptive behavior in school and with greater impairment in domains outside school that require restraint and self-regulation, such as following rules, doing chores or homework, or driving. SCT, in contrast, is as impairing (if not more so) in educational work performance and occupational functioning as is ADHD, but it is less disruptive of driving.

In closing this discussion, it is worth noting that SCT may not be the best term for this disorder, as noted by Saxbe and Barkley (2013). First of all, it implies an understanding of the underlying neuropsychological deficits in SCT that actually remains unknown. Second, it carries some similar pejorative connotations to those that may be conveyed by the phrases "slow learner" or "having low intelligence," which is hardly the case. We would endorse such labels as "concentration deficit disorder," "developmental concentration disorder," or "focused attention disorder" as more generally and socially acceptable. They retain the emphasis on a problem with attention or arousal/alertness—a problem that is likely to be distinct from ADHD—but without any implication of underlying cognitive processes or denigration.

THEORETICAL CONSIDERATIONS

Theories of ADHD's core pathophysiology can be understood from both a psychological perspective and a neurobiological perspective. From a psychological perspective, many theories of ADHD have been proposed over the past century to account for the diversity of findings so evident in this disorder (for a more detailed review, see Barkley, 1999). However, within the psychological perspective they fall into two major groups of theories, depending on whether they emphasize some form of cognitive control ("top-down" theories) or emphasize motivational or energetic factors ("bottom-up" theories); recent theories combine these views. These different theories vary in their degree of comprehensiveness or the extent to which they are really a theory versus a hypothesis. Here, we note several of the key proposals. Table 2.2 lists the major modern theories of psychological mechanism, to make it easier to track them during this discussion.

Some of these theories have been discussed above (see "Historical Context"). Early top-down theories

TABLE 2.2. Examples of Modern Theories of Psychological Dysfunction in ADHD

Year	Author	Core concept	Type of theory
1972	Douglas	Attention	Top-down
1981	Barkley	Rule-governed behavior	Top-down
1997	Barkley	Response inhibition	Top-down
1972	Sagvolden	Reinforcement gradient	Bottom-up
1987	Haenlein & Caul	Reward response	Bottom-up
1997	Quay	Behavioral inhibition	Bottom-up
1988	Sergeant	Arousal/activation	Bottom-up
1992	Sonuga-Barke	Delay aversion	Bottom-up
1993	Schachar	Response inhibition	Top-down
2002	Castellanos & Tannock	Temporal processing and control	Hybrid
2005	Sagvolden	Reinforcement gradient/dopamine	Bottom-up
2005	Sonuga-Barke	Dorsal–ventral dual process	Hybrid
2005	Nigg & Casey	Cognitive and emotional processing	Hybrid

were Still's (1902) notion of defective volitional inhibition and moral regulation of behavior; Douglas's (1972, 1983) theory of deficient attention, inhibition, arousal, and preference for immediate reward; and Barkley's (1981, 1989b) idea of a deficit in rule-governed behavior. Classic or early bottom-up theories were ADHD as a deficit in sensitivity to reinforcement (Haenlein & Caul, 1987) or as involving a steep reward-discounting gradient (see Sagvolden et al., 2005, for a summary of the conclusions of their two decades of work on this idea). Quay (1997), relying on Gray's (1982) neuropsychological model of anxiety, proposed that ADHD arises from a deficit in the brain's behavioral inhibition system (what Nigg, 2000, called "motivational inhibition"). An influential integrative model designed to better locate the ADHD problem was provided by Sergeant (1988). According to this model, behavioral control arises from a specific interplay of "energetic factors" such as arousal (readiness to perceive a signal), activation (readiness to respond), and effort (motivation) with "executive functioning" (i.e., what today would be called "cognitive control"). Sergeant reviewed evidence that ADHD might be most particularly associated with problems in activation or arousal.

Meantime, relying on Logan's "race" model of inhibition, Schachar and colleagues (1993) refined the top-down theories by arguing for a central deficit in inhibitory processes in those with ADHD, but using a perspective we would call "top-down or controlled inhibition" (executive inhibition). In this model, an event or stimulus is hypothesized to trigger both an activating or primary response and an inhibitory response, creating a competition or race between the two as to which will be executed first. Disinhibited individuals, such as those with ADHD, are viewed as having slower initiation of inhibitory processes than typical children do. An extensive literature confirms that this is so, but does not resolve the degree to which this accounts for other symptoms of ADHD.

Refined and sophisticated versions of bottom-up motivational or reinforcement gradient theories have continued to emerge, driven by an improved neuroscience-based understanding of how dopamine signaling influences regulation. The most comprehensive articulation of this perspective has been provided by Sagvolden and colleagues (2005), who developed their model using an animal strain called the "spontaneously hypertensive" rat. These animals had a steeper discounting of future reinforcers than comparison strains. The application to ADHD relies on a detailed understanding of how reinforcement × delay gradients change the likelihood of impulsive behavior in different contexts. The most important point for our purposes is that the theory posits a specific failure of dopamine activity as driving the development over time of a hyperactive–impulsive style via countless repetitions of steep-gradient response contingency experiences. A nuanced alternative to this theory came from Tripp and Wickens (2008), who posited an abnormal dopamine response not for future reinforcers, but for present reinforcers.

A related conception has been offered by Sonuga-Barke (2005; Sonuga-Barke et al., 1992), who uses the term "delay aversion." In this variation of the theory, a need for stimulation makes absence of feedback (or absence of reinforcement of any kind) unusually unpleas-

ant for individuals with ADHD, leading them to take action to drive a response from the environment. This action, by provoking environmental or social response, would create the possibility of reward. However, most of the evidence related to that theory relies on findings of a steep reinforcement-learning or impulsive-choice reward gradient, thus overlapping with evidence for the reinforcement gradient theory.

The most comprehensive articulation of a top-down model has come from Barkley (1994, 1997a, 1997b, 2001b, 2001a, 2012c). He has outlined a theory of ADHD that attempts to integrate numerous observations into a more comprehensive theory, initially anchored on the well-established aspect of poor inhibition of prepotent responses. Figure 2.2 illustrates the original theory (Barkley, 1997a).

This theory proposes that self-regulation requires the ability to inhibit a behavioral response, and that four other executive functions are dependent upon this for their own effective execution. These four executive functions provide for self-regulation, bringing behavior progressively more under the control of time and the influence of future over immediate consequences. The interaction of these executive functions permits far more effective adaptive functioning oriented toward the social future (social self-sufficiency). In this model, problems with arousal regulation and reward discounting are "downstream" from a fundamental problem in behavioral inhibition. Like other theories, this theory is more relevant to the combined type/presentation of ADHD than to the purely inattentive type/presentation or SCT.

The five executive functions are believed to develop via a common process. All represent private, covert forms of behavior that at one time in early child development (and in human evolution) were entirely publicly observable and were directed toward others and the external world at large. With maturation, this outer-directed behavior becomes turned on the self as a means to control one's own behavior. Such self-directed behaving then becomes increasingly less observable to others as the suppression of the public, peripheral, musculoskeletal aspects of the behavior progresses. The child is increasingly able to act toward the self without publicly displaying the actual behavior being activated. This progressively greater capacity to suppress the publicly observable aspects of behavior is what is meant here by the terms "covert," "privatized," or "internalized." The child comes to be capable of behaving internally (in the brain) without showing that response through the peripheral muscles, at least not to the extent that it is visible to others. As discussed elsewhere (Barkley, 1997a, 2001a), this behavior-to-the-self can still be detected in very subtle, vestigial forms as slight shifts in muscle potential at those peripheral sites involving the muscles used in performing the public form of that behavior (e.g., when one engages in verbal thought, one still slightly moves the lips, tongue, larynx, etc.). In this sense, all of the executive functions follow the same general sequence as the internalization of speech (Diaz & Berk, 1992; Vygotsky, 1967/1987, 1978), which in this model forms the third executive function.

This theory has had several salutary effects, including stimulating a wealth of new research on executive functioning, better articulating the operational definition of an "executive function" (a form of self-directed behavior or self-regulation), identifying the kinds of executive functioning relevant to ADHD, and spurring theoretical perspectives to be more precise in explaining ADHD. More recently, Barkley has conceded that the central deficit in ADHD may be a deficiency not only in behavioral inhibition as initially proposed, but in metacognition (self-awareness and working memory) which was initially believed to be deficient secondary to the inhibition deficit (Barkley, 1997b). In the latest iteration of this theory (Barkley, 2012c), self-awareness (self-directed attention) has been added to this model as a foundational executive function developing alongside inhibition (self-restraint). These executive functions precede and eventually coexist with the others across development: nonverbal and verbal working memory (self-imagery and self-speech), emotional and motivational self-regulation, and planning/problem solving (private self-directed play).

Also in this recent version, Barkley views executive functioning as an inherently social neuropsychological adaptation, having evolved to address problems that have arisen in human group living social existence. He has borrowed the concept of an "extended phenotype" from evolutionary biology to explain how these executive functions can produce effects at considerable spatial, temporal, and social distances to form four levels of executive functioning in daily life. These levels are (1) instrumental/self-directed, comprising the executive functions just discussed; (2) adaptive/self-reliant, in which instrumental executive functions subserve the development of self-care, independence from others, and social self-defense; (3) tactical/reciprocal, in which the lower-level executive functions now contribute to

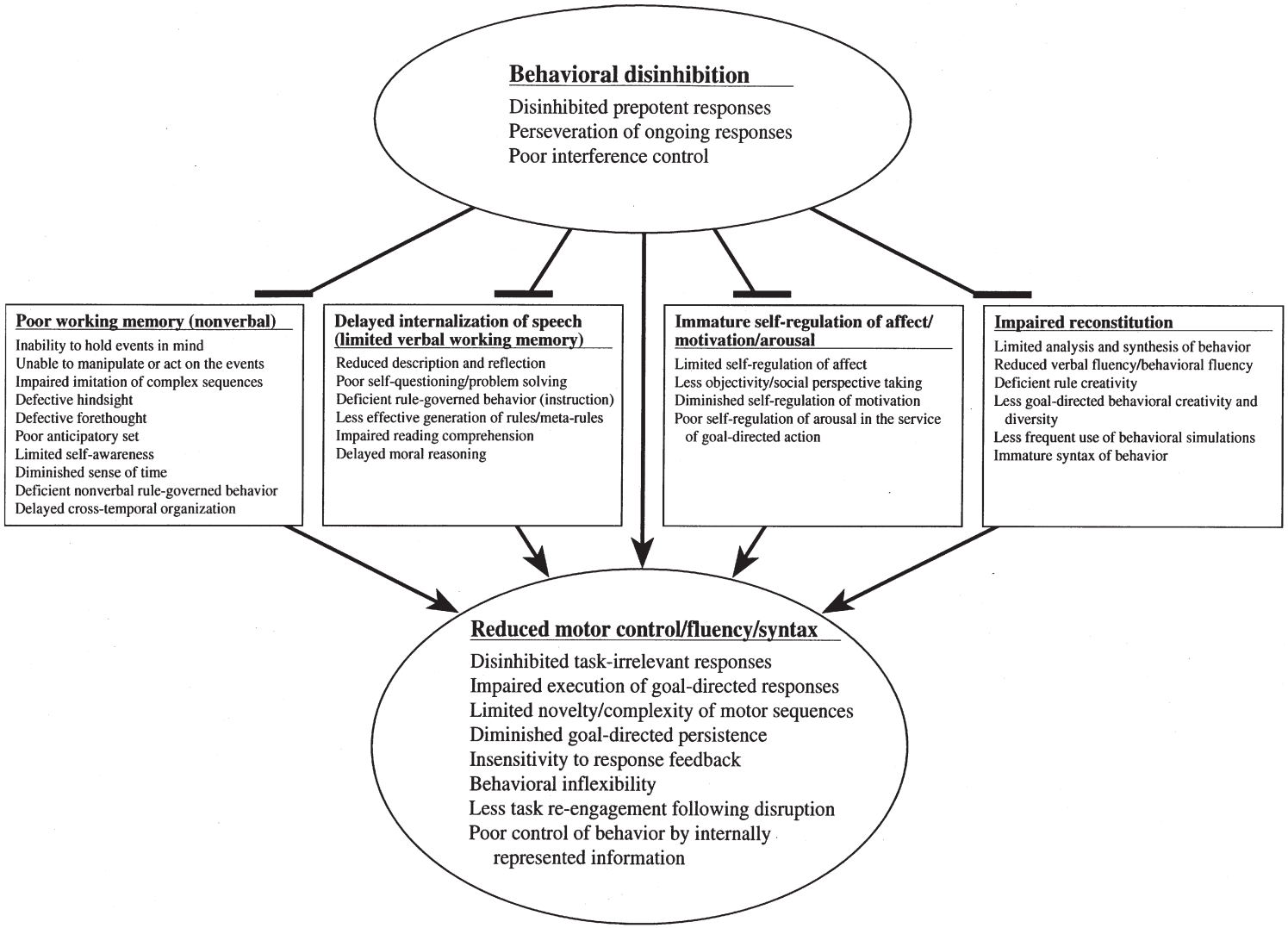

FIGURE 2.2. Diagram illustrating the original hybrid model of executive functions (boxes) and the relationship of these four functions to the behavioral inhibition and motor control systems. From Barkley (1997b). Copyright 1997 by The Guilford Press. Reprinted by permission.

the formation of friendships, social networks, and other reciprocal forms of social exchange with others to accomplish goals; and (4) strategic/cooperative, in which the lower levels of executive functioning now give rise to cooperative group ventures with like-minded others to accomplish joint goals no individual could attain alone or through trade (reciprocity). In this model, deficits at lower levels radiate upward to produce deficiencies in higher levels in daily life; if severe enough, these deficits may cause this hierarchical arrangement to collapse downward. Since ADHD is viewed as creating primary deficits at the first or instrumental level of executive functioning, it produces radiating effects upward (and outward) on these other zones of extended phenotypic effects.

The most recent theories of ADHD have almost all become explicitly "multiple-pathway" theories. That is, they all acknowledge that parallel developmental streams influence ADHD, that there are probably subgroups of ADHD with different causes, and that components of the syndrome may have distinct inputs. Thus Sonuga-Barke (2005) has argued that inattention is related to a breakdown in executive functioning and response inhibition (located in a neural circuit involving the dorsal striatum and dorsolateral prefrontal cortex), but that hyperactivity–impulsivity is related to a breakdown in motivational responding or reward gradient (located in a neural circuit involving the ventral striatum or nucleus accumbens and ventromedial prefrontal cortex). Although prior models all acknowledged the dialectical nature of top-down and bottom-up processes in self-regulation, this theory has the virtue of attempting to integrate the top-down and bottom-up aspects in a parallel model, rather than a sequential model with one component primary.

A novel proposal has also been offered by Nigg and Casey (2005). This theory also integrates multiple neural circuits, including prefrontal–striatal–thalamic circuits involved in cognitive control (which Nigg and Casey refer to as constituting the "what" circuit); frontal–cerebellar circuits involved in learning (which they refer to as composing the "when" circuit); and limbic–frontal circuits involved in emotion regulation and motivation. They have also integrated newer findings from cognitive neuroscience regading the important role of frontal–parietal–subcortical neural circuits in attentional capture and attentional suppression of competing information (the dorsal and ventral attention circuits). Their model, heavily neurobiological in nature, thus integrates several recent developments in the field. In particular, it provides a way to integrate the literature on emotional regulation with the literature on the cognitive neuroscience of attention, and shows how both may be involved in a coordinated way in ADHD. It has also opened the door to computational models of ADHD by specifying prediction functions for these circuits.

Castellanos and Tannock (2002) have offered yet another influential perspective, attempting to tie together the cognitive neuroscience of working memory and cognitive control with the literature on temporal information processing. That work has stimulated further study of working memory and of cerebellar-related time estimation functions in ADHD. It has also renewed interest in response variability in ADHD because these authors have emphasized newer research on response time profiles in ADHD on reaction time tests. Children with ADHD seem to have periodic extremely slow responses, which seem to occur at regular intervals. This is thought to be consistent with abnormal oscillations in the central nervous system. A key and very interesting premise of that model is that slow responses occur at a particular frequency. Karalunas, Huang-Pollock, and Nigg (2013) have recently shown that in fact children with ADHD have slow responses at multiple temporal frequencies, disproving that aspect of the theory. However, the theory will probably continue to stimulate work to understand the pattern of attentional variation over time in ADHD as a crucial bottom-up mechanism.

Nigg and colleagues (2005) have pointed out that no one psychological deficit can account for all cases of ADHD. Rather, different children with ADHD may have distinct underlying neuropsychological or neurobiological mechanisms that account for their problems. In this sense, each hypothesis or theory is capturing a piece of the picture. In support of that model, Nigg and colleagues (Fair, Bathula, Nikolas, & Nigg, 2012) recently conducted a sophisticated mathematical analysis called "community detection" on a large sample of children with ADHD who completed a neuropsychological battery. The model showed that one group of children had problems in response inhibition, another in arousal, and still another in excess response variability. Yet these groups had similar levels of ADHD symptoms.

Overall, the theoretical landscape for ADHD is increasingly rich and sophisticated. We still have very few true theories, but we have at least two that are comprehensive in their predictions (Barkley, 1997a, 2012c; Sagvolden et al., 2005), and many others that provide

strong starting points for understanding ADHD neurobiologically. Major themes in these theories include the importance of dopaminergic circuitry, as well as the effort to articulate an integration of top-down and bottom-up processes in self-regulation and to show how these may break down in ADHD.

IS ADHD A "REAL" DISORDER?

Social critics have been concerned for decades (Breggin, 1998; Kohn, 1989; Schrag & Divoky, 1975; Sroufe, 2012) that professionals may be too quick to label energetic and exuberant children as having a mental disorder. They also assert that educators may be using these labels as an excuse for poor home or educational environments. In other words, children who are diagnosed with hyperactivity or ADHD are actually typical children, but are being labeled as mentally disordered because of parent and teacher intolerance (Kohn, 1989), mismanagement, or lack of love at home (Breggin, 1998). While such instances no doubt sometimes occur, it is difficult to reconcile such claims with the array of biological correlates identified in ADHD: Children with ADHD have reliably reduced brain size (Castellanos et al., 2002) from age 4 on, slower maturation of the cortical mantle (Shaw, Greenstein, et al., 2006), elevated levels of lead in their blood (Nigg et al., 2008), more family members with ADHD (Stawicki et al., 2006), and differences in genotype (Banaschewski, Becker, Scherag, Franke, & Coghill, 2010).

The key problem, to which critics are perhaps alluding, is that the biological markers are not yet sufficient for clinical diagnosis. Diagnosis still relies on clinical judgment about behavioral symptoms. That judgment is only as good as the carefulness of clinical practitioners. The DSM diagnostic criteria are, in essence, not a polemic assertion but a clinical heuristic; they enable clinicians to reliably and validly identify children who are likely to get worse without treatment, who are probably impaired, who are at considerable risk for current and future impairment in multiple domains, and for whom treating is a lesser evil than not treating. The criteria work quite well for these purposes, when properly applied (for detailed support for that claim, see Willcutt et al., 2012).

The ontological status of ADHD as a "real" condition with a definable biological process that can be measured in every case of the disease (as we can do in, say, cancer or influenza) is still some distance off. It is likely that in the long run, if such biomarkers are identified, they will not apply to all individuals currently diagnosed with ADHD. Indeed, for all complex diseases (hypertension, obesity, diabetes, cancer, and psychiatric conditions), the ability to identify a single biological cause is likely to be possible only when we can differentiate subgroups. However, complex disease is inherently characterized by probabilistic prediction based on risk factors that predict morbidity and mortality. ADHD conveys considerable morbidity risk (see below), and thus examination of probabilistic diagnostic categories remains useful. This is likely to remain the state of affairs for the foreseeable future.

EPIDEMIOLOGY

Prevalence

In the past decade, systematic population-based national surveys of ADHD were conducted for the first time. Because of different methods, these did not yield identical results, but they still give a consistent picture of ADHD as a very common condition. In one national survey, the 1-year prevalence rate for children and adolescents was 8.5% (Muthen & Muthen, 2000). Among U.S. adults, the prevalence of ADHD is 4–5% (Barkley, 2012b; Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007). Practitioner surveys by the Centers for Disease Control and Prevention indicate a rising prevalence of ADHD in the United States from the late 1990s to the late 2000s (Boyle et al., 2011), but it is unclear whether this increase is due to true secular trends or to various changes affecting identification. Worldwide, or when data from different countries are pooled, meta-analytic reviews suggest a 1-year prevalence rate of ADHD in children and adolescents of about 5.3% (Polanczyk et al., 2007) and 2–3% in adults (Nylund, Bellmore, Nishina, & Graham, 2007).

However, even these estimates may be high. A sophisticated Baysian analysis that took into account variation in survey and assessment methods and anchored presence of ADHD to a conservative level of clear agreement across two informants estimated ADHD's true prevalence at only 2.2%, with some notable regional variation but no evidence of change in prevalence over the last decade (Erskine et al., 2014). Thus, it remains quite possible that if ADHD is defined conservatively, its prevalence is stable and rather lower than its rate of clinical identification. It is also possible

that this most recent paper defined ADHD too conservatively, and it is possible that over a longer period of several decades ADHD has increased. Furthermore, as those authors acknowledged, survey data are completely lacking in many nations. Thus, the question of true variation in prevalence remains in need of more data.

Although convergent, all of these figures probably represent high estimates of the individuals who have an impairing syndrome that could ultimately be related to a neurobiological injury or abnormality in development. For example, few studies have used *full* DSM-IV or DSM-5 criteria, obtained multiple informants, carefully assessed impairment, or ruled out the possibility that the observed symptoms were actually fully explainable by a co-occurring medical or psychiatric condition. Prevalence rates are much lower for ICD-10 criteria (typically about 1%; Döpfner et al., 2008), due largely to ICD-10's exclusion of children with comorbid mood or behavioral conditions. It is unknown what the prevalence will be for the revised definition in ICD-11.

Sex Differences

As with most psychiatric/developmental disorders of childhood onset, ADHD shows a male preponderance, on the order of 2:1 or higher (Polanczyk et al., 2007); this ratio drops somewhat, to only 1.6:1 or even 1:1 by adulthood (Nigg, Lewis, Edinger, & Falk, 2012), perhaps due in part to underidentification of girls in childhood. Boys are referred for treatment at much higher rates than girls, in part because of higher levels of aggression. In addition, the larger sex difference in childhood may be an artifact of criteria that were developed on the basis of predominantly male samples. Girls may be more likely to display inattentive behaviors, yet whether they show a greater number of comorbid internalizing problems is controversial. Studies of clinically referred girls and boys with ADHD indicate that they show comparable levels of impairment in academic and social functioning, but girls with the disorder may have greater intellectual deficits (Gaub & Carlson, 1997). In community samples, however, girls are less likely to have comorbid externalizing problems than boys, and they do not show greater intellectual impairment (Gaub & Carlson, 1997). With regard to cognitive and biological correlates, girls with ADHD show patterns of impairments in executive functioning and cognitive control similar to those of their male counterparts (Hinshaw, Carte, Sami, Treuting, & Zupan, 2002; Rucklidge & Tannock, 2001). In a major series of clinical cases, girls and boys with ADHD showed similar patterns of impairment on measures of set shifting and interference control, and both groups performed significantly worse than sex-matched controls (Seidman et al., 2005). Doyle and colleagues (2005) reported patterns of neuropsychological impairment in family members of girls with ADHD that were similar to those seen in the relatives of boys with the disorder. These types of results (along with longitudinal studies of symptom severity over development) suggest that important similarities exist between manifestations of ADHD in boys and girls, and that the same construct is being captured (Lahey et al., 2007; Monuteaux, Mick, Faraone, & Biederman, 2010).

Recent large longitudinal studies of girls with ADHD followed from childhood to early adulthood indicate many similarities in the elevation of risks for various impairments between girls and boys with the disorder (Hinshaw et al., 2012; Owens, Hinshaw, Lee, & Lahey, 2009), such as risks for academic performance problems, comorbidity for learning disorders, and peer problems or even rejection, among others. However, some important differences in risk may exist: Girls (especially those with a predominantly inattentive presentation) may have even more difficulties than boys with ADHD in academic performance and peer relationships (Elkins, Malone, Keyes, Iacono, & McGue, 2011). One also finds an increased likelihood of eating pathology (mainly binge eating and higher risk for bulimia), anxiety, and depression among girls and women with ADHD than among males with the disorder (Barkley et al., 2008; Lahey et al., 2007), and these difficulties may be more stable across development into adolescence in girls with ADHD than in boys (Monuteaux et al., 2010). However, both sexes are more prone to these disorders than are typically developing children or adults in the general population (Barkley et al., 2008; Lahey et al., 2007; Monuteaux et al., 2010). Males with ADHD are also more likely than females to engage in antisocial activities, certain forms of substance use disorders, and risky driving with associated adverse outcomes (Barkley et al., 2008; Nussbaum, 2012). Yet here again, both sexes demonstrate higher levels of these difficulties than do comparison groups of same-sex children (Barkley et al., 2008).

However, key issues remain. It is unclear whether sex-specific cutoffs should be considered when ADHD is diagnosed in girls (see Petty et al., 2009). Although girls are less active and disruptive than boys overall, the symptom counts used to diagnose ADHD are the

same for both sexes. Hence it is possible that some girls who have fewer than six symptoms on either DSM symptom dimension, yet who are impaired, are missed by current criteria. Second, girls may have greater resistance to the etiological factors that cause ADHD. In a twin study, Rhee, Waldman, Hay, and Levy (2008) found evidence consistent with this differential threshold model, suggesting that girls with ADHD need more risk genes before manifesting ADHD. Further studies that incorporate studies of hormonal and other sex-specific effects in early development will be important to a complete understanding of ADHD. Despite recent advances, ADHD in girls remains less well understood than in boys, and the apparent equalizing of prevalence in adolescence and adulthood is not well explained.

Socioeconomic Differences

Few studies have examined the relationship of ADHD to socioeconomic status (SES), and those that have are not especially consistent. Lambert, Sandoval, and Sassone (1978) found only slight differences in the prevalence of hyperactivity across SES when parents, teachers, and physicians all agreed on the diagnoses. However, SES differences in prevalence did arise when only two of these three sources had to agree; in this instance, there were generally more children with ADHD from lower- than from higher-SES backgrounds. For instance, when parent and teacher agreement (but not physician agreement) was required, 18% of those identified as hyperactive were from high-SES, 36% from middle-SES, and 45% from low-SES backgrounds. Where only teachers' opinions were used, the percentages were 17%, 41%, and 41%, respectively. Trites (1979), and later Szatmari (1992), both found that rates of ADHD tended to increase with lower SES; however, Szatmari, Offord, and Boyle (1989) found that low SES was no longer associated with rates of ADHD when other comorbid conditions, such as CD, were controlled for. For now, it is clear that ADHD occurs across all socioeconomic levels. Variations across SES may be artifacts of the source used to define the disorder, or of the comorbidity of ADHD with other disorders related to SES (such as ODD and CD).

Ethnic/Cultural/National Issues

Numerous considerations come into play when one considers cultural variation in a syndrome like ADHD, for which abnormality depends heavily on departure from culturally accepted standards of behavior. By way of mental experiment, how would ADHD be defined in an aboriginal culture or a nontechnological hunter–gatherer society? One can still imagine individuals who are very inattentive, impulsive, or severely lacking in self-control being unable to succeed in such a culture, but the behavioral manifestations and societal tolerance for such impairments would probably be quite different. The same caveat probably applies in subtler ways to our efforts to estimate differences in modern cultures.

We begin with prevalence. When using a DSM definition, we can appeal to numerous surveys around the world in the past 20 years. A pooled metaregression analysis by Polanczyk and colleagues (2007) included data from over 170,000 participants in 102 studies on all major populated regions (although the majority of studies have been conducted in North America and Europe). Although these authors found that prevalence varied with assessment method, their final pooled worldwide prevalence rate of 5.3% is quite a plausible one. Across major regions of the world, significant variation was found. Prevalence was highest in South America (11.8%) and Africa (8.5%), and lowest in the Middle East (2.4%), though these differences were nonsignificant after adjustment for ascertainment differences (i.e., differences in how ADHD was assessed). Furthermore, few studies were available in these three regions, so confidence intervals encompassed too wide a range to enable differentiation across them. Regions with enough data for narrow confidence intervals all had similar prevalences (North America, 6.3%; Europe, 4.7%; Oceania, 4.6%; Asia, 3.7%), although these might be significantly different with enough data points.

As noted earlier, a more extensive analysis was undertaken by Erskine and colleagues (2014). This statistically more powerful study did detect reliable regional variation. Rates were highest in North Africa/Middle East and in Oceania, and lowest in South Asia. Again, however, this analysis relied on substantial data imputation given the scarcity of data in many of these regions. Even so, the suggestion of regional variation in true prevalence could, if better pinpointed, provide important clues to etiology and to disease modifiers.

Pinpointing local variation will be crucial, however. Variation within regions or countries (e.g., urban–rural differences) might be extremely important and even more important than variation across countries or regions. But within-country data were not analyzed in any of these studies, due to the reduced sample size of

available studies. Thus additional prevalence data will be important to etiological theories. For example, if lead exposure, anemia, or malnutrition contributes to ADHD, then prevalence should be somewhat higher in regions, nations, or localities with higher exposures (e.g., South Africa), unless these effects are countered by alternative etiologies in developed nations (e.g., higher rates of surviving children with low birth weight). Even so, rates of stimulant treatment are up to twice as high or more in the United States as in many other nations, due to differences in historical approach, laws, and professional practice (Giles et al., 1997); other wealthy nations are on a similar use trajectory (Steckler, Goodman, & Alciati, 1997).

Beyond prevalence, however, several complexities are worthy of comment. First, ADHD-related behaviors may not have the same meaning in the eyes of teachers and parents across cultural groups. For example, Mann and colleagues (1992) found that clinicians of different cultures rated the same child actors at significantly different symptom levels even when faced with identical behaviors (independent of the race of each child). On the other hand, Epstein and colleagues (2008) found that teachers' ratings of excess ADHD symptoms in African American children were consistent with behavioral observations of the same classrooms. This main effect of race was partially due to the fact that African American children were more often in classrooms where the average child had more misbehavior. The paucity of research on these issues represents a gaping hole in our knowledge base.

Second, it is unclear to what extent the ADHD syndrome has similar internal validity across ethnic or cultural groups, or under what conditions this might change. Data suggest that the ADHD symptom factor structure is essentially the same across nations (Goodman, Steckler, & Alciati, 1997). Reid and associates (1998) examined the factor loadings of ADHD symptoms in African American and European American children in the United States. Although the general two-factor symptom structure was preserved across groups, the item loadings differed, suggesting that the syndrome might have a different meaning in the two groups. African American children are often identified at different rates than European American children, but the reasons for this are unclear (Miller, Nigg, & Miller, 2009). It is not difficult to imagine how the same behavior could have different meanings across U.S. racial groups (e.g., one might speculate that an African American child more often may be socialized to call out in groups, whereas a European American child may be socialized to remain quiet or wait his or her turn in large groups). Different meanings across nations are also plausible.

Still, countering such suppositions, the major review by Rohde and colleagues (1999) concluded that studies in developing nations yield factor structures, treatment responses, prevalences, and biological correlates similar to those of studies in developed nations—a conclusion supporting the cross-cultural validity of ADHD. Such evidence raises the question of when, if at all, racially or culturally specific norms should be included in the assessment of ADHD. Again, a paucity of research signifies ripe opportunities for future investigators in this area to clarify local variation or boundary conditions (if any) on the cross-cultural validity of ADHD, and thus to provide a more differentiated map of construct validity.

Third, treatment rates vary radically across nations (Forero, Arboleda, Vasquez, & Arboleda, 2009), and approaches to treatment may be different across cultural groups even within the United States (Kandziora et al., 2003). Data are lacking on the important issue of whether this discrepancy leads to an excess of poor outcomes among minority children. These differences in services may reflect reduced access to care, or they may reflect distinct attitudes toward the diagnostic and treatment infrastructure. Further empirical work is needed on such issues as costs, access to care, attitudes/beliefs, and differential outcomes.

In particular, we would be interested to see more work on the effects of race of child, race of informant, and race of provider on ratings of child behavior using standardized probes (e.g., child actors). Race entails cultural variation (in some cases) as well as stereotype effects, and disentangling these will be extremely valuable to improving culturally competent assessment in an increasingly diverse society.

DEVELOPMENTAL COURSE AND ADULT OUTCOME

Major follow-up studies into adulthood of clinically referred children with hyperactivity or ADHD have been ongoing during the last 40 years at many sites: (1) Montreal (Weiss & Hechtman, 1993); (2) New York City (Gittelman, Mannuzza, Shenker, & Bonagura, 1985; Klein et al., 2012; Mannuzza, Klein, Bessler, Malloy, & LaPadula, 1993); (3) Iowa City (Loney, Kramer, &

Milich, 1981); (4) Los Angeles (Satterfield, Hoppe, & Schell, 1982); (5) Milwaukee (Barkley et al., 2008); (6) San Francisco (Lee, Lahey, Owens, & Hinshaw, 2008); (7) Boston (Biederman, Faraone, Milberger, et al., 1996; Biederman, Petty, Evans, Small & Faraone, 2010); and (8) Rochester, Minnesota (Barbaresi et al., 2013). Follow-up studies of children identified as hyperactive from a general population have also been conducted in the United States (Lambert, 1988), New Zealand (McGee, Williams, & Silva, 1984; Moffitt, 1990), and England (Taylor, Sandberg, Thorley, & Giles, 1991), among others. Many other follow-up studies of shorter duration (such as from childhood to adolescence) have also been published in the last decade; these are too numerous to list here.

But before we proceed, some cautionary notes are in order. First, most of the long-term follow-up studies began prior to the current DSM-based definitions of ADHD, and so estimates may vary as to the degree of overlap with children defined by current criteria. Most of the earliest studies selected for children known at the time as "hyperactive." Such children are most likely representative of those diagnosed with ADHD, combined type/presentation, in the current DSM taxonomy. Even then, the degree of deviance of the samples on parent and teacher ratings of these symptoms was not established at the entry point in most of these studies. These studies also cannot be viewed as representing the predominantly inattentive type/presentation of ADHD or SCT, for which no follow-up information is currently available. The descriptions of clinic-referred children with ADHD who are of similar age groups to those in the follow-up studies, but who are not followed over time, may help us understand the risks associated with different points in development.

Second, to the extent that the context for children's development is rapidly changing and affecting attention and externalizing problems (e.g., screen media and violent video games; two- parent working households), studies of children recruited some decades ago may not be fully relevant to present-day children. Such cohort effects may be minor in some respects; at least in the past, for example, adolescents with ADHD referred to clinics seemed to have types and degrees of impairment similar to those of children with ADHD followed up to adolescence (cf. Barkley, Anastopoulos, Guevremont, & Fletcher, 1991; Barkley, Fischer, Edelbrock, & Smallish, 1990). This is also the case for the most part with clinic-referred adults versus children followed to adulthood (Barkley et al., 2008), but in this case the children followed to adulthood had more severe adverse outcomes in some areas (education, work) than did adults currently referred to clinics receiving a diagnosis.

Third, discontinuities of measurement that exist in these follow-up studies between their different points of assessments make straightforward conclusions about developmental course difficult. Fourth, the differing sources of children greatly affect the outcomes to be found, with children drawn from clinic-referred populations having two to three times the occurrence of some negative outcomes and more diverse negative outcomes as those drawn from population screens have had (e.g., cf. Barkley, Fischer, et al., 1990; Lambert, 1988), although in a more recent instance the results were similar (cf. Barkley et al., 2008; Barbaresi et al., 2013). Generalizing from the clinic-recruited samples to the general population is not straightfoward.

We concentrate here on the course of the disorder itself, returning to the comorbid disorders and associated conditions likely to arise in the course of ADHD in a later section of this chapter ("Comorbid Psychiatric Disorders").

The average onset of ADHD symptoms, as noted earlier, is often in the preschool years, typically at ages 3–4 (Applegate, Lahey, Hart, Waldman, Biederman et al., 1997; Loeber et al., 1992; Taylor et al., 1991) and more generally by entry into formal schooling. Yet onset is heavily dependent on the type of ADHD under study. First to arise is the pattern of hyperactive– impulsive behavior (and, in some cases, oppositional and aggressive conduct), giving that subtype the earliest age of onset. The combined type of ADHD has an onset within the first few grades of primary school (ages 5–8; Hart et al., 1995), most likely due to the requirement that both hyperactivity and inattention must be present for this subtype to be diagnosed. Predominantly inattentive ADHD appears to emerge a few years later (ages 8–12) than the other types (Applegate et al., 1997).

Preschool-age children who are perceived as difficult and resistant to control, or who have inattentive and hyperactive behavior that persists for at least a year or more, are highly likely to have ADHD and to remain so into elementary school years (Beitchman et al., 1987; Campbell, 2006; Palfrey et al., 1985) and even adolescence (Olson, Bates, Sandy, & Lanthier, 2000). Persistent cases seem especially likely to occur where parent–child conflict, greater maternal directiveness and negativity, and greater child defiant behavior or frank ODD exist (Campbell, March, Pierce, Ewing, &

Szumowski, 1991; Olson et al., 2000; Richman, Stevenson, & Graham, 1982). More negative temperament and greater emotional reactivity to events are also more common in preschool children with ADHD (Barkley, DuPaul, & McMurray, 1990; Campbell, 2006). It is little wonder that greater parenting stress is associated with having preschool children with ADHD, and such stress seems to be at its highest with preschoolers relative to later age groups (Mash & Johnston, 1983a, 1983b). Within the preschool setting, children with ADHD will be found to be more often out of their seats, wandering the classroom, being excessively talkative and vocally noisy, and disruptive of other children's activities (Campbell, Schleifer, & Weiss, 1978; Schleifer et al., 1975).

By the time children with ADHD move into the elementary-school-age range of 6–12 years, the problems with hyperactive–impulsive behavior are likely to continue and to be joined now by difficulties with attention (executive functioning and goal-directed persistence). Difficulties with work completion and productivity; distraction; forgetfulness related to what needs doing; lack of planning; poor organization of work activities; and trouble meeting time deadlines associated with home chores, school assignments, and social promises/commitments to peers are now combined with the impulsive, heedless, and disinhibited behavior typifying these children since preschool age. Problems with oppositional and socially aggressive behavior may emerge at this age in at least 40–70% of children with ADHD (Loeber, Burke, Lahey, Winters, & Zera, 2000; Loeber, Burke, & Pardini, 2009; Loeber et al., 1992; Taylor et al., 1991).

By ages 8–12 years, these early forms of defiant and hostile behavior or outright ODD may evolve further into symptoms of CD in 25–45% or more of all children with ADHD, if CD was not present already (Barkley, Fischer, et al., 1990; Gittelman et al., 1985; Loeber et al., 1992; Mannuzza et al., 1993; Taylor et al., 1991). Certainly by late childhood, most or all of the deficits in the executive functions related to inhibition in the model presented earlier are likely to be arising and interfering with adequate self-regulation (Barkley, 1997a). Not surprisingly, the overall adaptive functioning (self-sufficiency) of many children with ADHD (Stein, Szumowski, Blondis, & Roizen, 1995) is significantly below their intellectual ability. This is also true of preschoolers with high levels of these externalizing symptoms (Barkley, Shelton, et al., 2002). The disparity between adaptive functioning and age-appropriate expectations (or IQ) may itself be a predictor of greater severity of ADHD, as well as risk for oppositional and conduct problems in later childhood (Shelton et al., 1998). The disorder takes its toll on self-care, personal responsibility, chore performance, trustworthiness, independence, and appropriate social skills, as well as on doing tasks on time specifically and moral conduct generally (Barkley, 2006; Hinshaw et al., 1993).

If ADHD is present in clinic-referred children, the likelihood is that 50–80% will continue to have their disorder into adolescence, with most studies supporting the higher figure (August, Stewart, & Holmes, 1983; Claude & Firestone, 1995; Barkley, Fischer, et al., 1990; Gittelman et al., 1985; Lee et al., 2008; Mannuzza et al., 1993). Using the same parent rating scales at both the childhood and adolescent evaluation points, Fischer and colleagues (1993b) were able to show that inattention, hyperactive–impulsive behavior, and home conflicts declined by adolescence. The hyperactive group showed far more marked declines than the control group, mainly because the former were so far from the mean of the normative group to begin with in childhood. Nevertheless, even at adolescence the groups remained significantly different in each domain, with the mean for the hyperactive group remaining two standard deviations or more above the mean for the controls. This emphasizes a point made earlier: Simply because severity levels of symptoms are declining over development, this does not mean that children with ADHD are necessarily outgrowing their disorder relative to normal children. Like intellectual disabilities, ADHD may need to be defined as a developmentally relative deficiency rather than an absolute one, and a deficiency that persists in most children over time.

The persistence of ADHD symptoms across childhood as well as into early adolescence appears, again, to be associated with initial degree of hyperactive–impulsive behavior in childhood; the coexistence of conduct problems or oppositional hostile behavior; poor family relations (specifically, conflict in parent–child interactions); and maternal depression, as well as duration of maternal mental health interventions (Fischer et al., 1993a; Taylor et al., 1991). These predictors have also been associated with the development and persistence of ODD and CD into this age range (12–17 years; Barkley et al., 2008; Fischer et al., 1993a; Loeber, 1990; Mannuzza & Klein, 1992; Taylor et al., 1991).

Studies following large samples of clinic-referred children with hyperactivity or ADHD into adulthood

are few in number. Only seven follow-up studies have retained 50% or more of their original samples from childhood into adulthood and reported on the persistence of symptoms to that time. These are the Montreal study by Weiss, Hechtman, and their colleagues (see Weiss & Hechtman, 1993); the New York City study by Mannuzza, Klein, and colleagues (see Klein et al., 2012; Mannuzza et al., 1993; Mannuzza, Klein, Bessler, Malloy, & LaPadula, 1998); the Swedish study by Rasmussen and Gillberg (2001); Barkley's research with Mariellen Fischer in Milwaukee (Barkley et al., 2008); the Rochester, Minnesota study (Barbaresi et al., 2013); and the Boston study (Biederman et al., 2010). Results regarding the persistence of disorder into young adulthood (middle 20s) are mixed, but can be understood as being a function of reporting source and the diagnostic criteria used (Barkley, Fischer, Smallish, & Fletcher, 2002).

The Montreal study (n = 103) found that two-thirds of the original sample (n = 64; mean age = 25 years) claimed to be troubled as adults by at least one or more disabling core symptoms of their original disorder (restlessness, impulsivity, or inattention), and that 34% had at least moderate to severe levels of hyperactive, impulsive, and inattentive symptoms (Weiss & Hechtman, 1993). In Sweden (n = 50), Rasmussen and Gillberg (2001) obtained similar results, with 49% of probands reporting marked symptoms of ADHD at age 22 years compared to 9% of controls. Formal diagnostic criteria for ADHD, such as those in DSM-III or later editions, were not employed at any of the outcome points in either study, however. In contrast, the New York study has followed two separate cohorts of hyperactive children, using DSM criteria to assess persistence of disorder. That study found that 31% of the initial cohort (n = 101) and 43% of the second cohort (n = 94) met DSM-III criteria for ADHD by ages 16–23 (mean age = 18.5 years) (Gittelman et al., 1985; Mannuzza et al., 1991). Eight years later (mean age = 26 years), however, these figures fell to 8% and 4%, respectively (with DSM-III-R criteria now being used) (Mannuzza et al., 1993, 1998). These authors reported the prevalence of ADHD by age 40 to be 22% vs. 5% in the control group (Klein et al., 2012). If more adult-sensitive diagnostic thresholds are used (say, four instead of six symptoms, as discussed above), then persistence of full disorder was 32%. The uptick in prevalence from the last follow-up to this one is due in part to relying on self-reported symptoms, which are often underreported in early adulthood but increase with age (Barkley et al., 2008). The recent follow-up study in Rochester, Minnesota (Barbaresi et al., 2013), like the Milwaukee study, followed the children to age 27 or older. It reported a 29% persistence of disorder to young adulthood. These results might imply that the vast majority of hyperactive children no longer qualify for the diagnosis of ADHD by adulthood.

The interpretation of the relatively low rate of persistence of ADHD into adulthood is clouded by at least two issues, apart from differences in selection criteria. One is that the source of information about the disorder changed in all of these studies from that used at the childhood and adolescent evaluations to that used at the adult outcome. At study entry and at adolescence, all studies used the reports of others (parents and typically teachers); all found that the majority of hyperactive participants (50–80%) continued to manifest significant levels of the disorder by midadolescence (see above). In young adulthood (approximately age 26 years), however, most studies switched to self-reports of disorder. Changing sources of reporting in longitudinal studies on behavioral disorders can be expected to lead to marked differences in estimates of persistence of those disorders (Barkley, Fischer, et al., 2002; Barkley et al., 2008).

The question obviously arises: Whose assessment of the probands is more accurate? This would depend on the purpose of the assessment, but the prediction of impairment in major life activities would seem to be an important one in research on psychiatric disorders. The Milwaukee study examined these issues by interviewing both the participants and their parents about ADHD symptoms at the young adult follow-up (age 21 years). It then examined the relationship of each source's reports to significant outcomes in major life activities (education, occupation, social, etc.), after controlling for the contribution made by the other source. As noted earlier, another limitation in the earlier studies may reside in the DSM criteria, in that these grow less sensitive to the disorder with age. Using a developmentally referenced criterion (age comparison) to determine diagnosis might identify more cases than would the DSM approach. As discussed earlier, the Milwaukee study found that the persistence of ADHD into adulthood was heavily dependent on the source of the information (self or parent) and the diagnostic criteria (DSM or developmentally referenced). Self-report identified just 5–12% of probands as currently having ADHD (DSM-III-R), whereas parent reports placed this figure at 46–66%. Using the DSM resulted in lower rates of persistence (5% for proband reports and 46% for par-

ents), whereas using a developmentally referenced cutoff (98th percentile) yielded higher rates of persistence (12% by self-reports and 66% by parent reports). The parent reports appeared to have greater validity, in view of their greater contribution to impairment and to more domains of current impairment, than did self-reported information (Barkley, Fischer, et al., 2002). We have concluded that past follow-up studies underestimated the persistence of ADHD into adulthood by relying solely on the self-reports of the probands, especially in young adulthood, while not obtaining corroborative information from others who know the cases well.

COMORBID PSYCHIATRIC DISORDERS

Individuals diagnosed with ADHD often have other disorders besides their ADHD. What is known about comorbidity is largely confined to the combined type/presentation of ADHD. In community-derived samples, up to 44% of children with ADHD have at least one other disorder, and 43% have at least two or more additional disorders (Willcutt et al., 2012). The figure is higher, of course, for children seen in clinics, where as many as 80–87% may have at least one other disorder (Kadesjo & Gillberg, 2001). This is also true for clinic-referred adults with ADHD (Barkley et al., 2008). The disorders likely to co-occur with ADHD are briefly described below.

Conduct Problems and Antisocial Disorders

Disruptive or externalizing behavior problems are the most common co-occuring domain for ADHD. In this group, the most common disorder is ODD, with CD following some distance behind in a subset. The presence of ADHD increases the odds of ODD/CD by 10.7-fold (95% confidence interval [CI] = 7.7–14.8) in general population studies (Angold, Costello, & Erkanli, 1999). Studies of clinic-referred children with ADHD find that between 54 and 67% will meet criteria for a diagnosis of ODD by 7 years of age or later. One possible reason for this heightened comorbidity has been proposed by Barkley (2010) as a causal one, given that ODD is bi- or tridimensional in nature (see Kimonis, Frick, & McMahon, Chapter 3, this volume) and that one of those dimensions involves emotional dysregulation (anger, temper, irritability, etc.). Barkley has made the case that ADHD involves a significant deficit in the self-regulation of emotion, and that it is through this pathway that ADHD heightens risk for the emotional dysregulation element of ODD.

ODD is a frequent precursor to or co-occurring disorder with CD, a more severe and often (though not always) later-occurring stage of ODD (Loeber et al., 2000, 2009). The co-occurrence of CD with ADHD may be 20–50% in children and 44–50% in adolescents with ADHD (Barkley, 2006; Barkley, Fischer, et al., 1990; Biederman, Faraone, & Lapey, 1992; Lahey, McBurnett, & Loeber, 2000). By adulthood, up to 26% may continue to have CD, while 12–21% will qualify for a diagnosis of antisocial personality disorder (ASPD) (Barbaresi et al., 2013; Barkley et al., 2008; Biederman et al., 1992; Klein et al., 2012; Mannuzza & Klein, 1992; Rasmussen & Gillberg, 2001; Weiss & Hechtman, 1993). Similar or only slightly lower degrees of overlap are noted in studies using epidemiologically identified samples rather than those referred to clinics.

ADHD therefore has a strong association with ODD, CD, and ASPD, and is one of the most reliable early predictors of these disorders (Fischer et al., 1993a; Kimonis et al., Chapter 3, this volume; Lahey et al., 2000). Indeed, at least in boys, it is almost invariably the case that when CD is observed, ADHD has preceded it. Recent longitudinal research suggests that severity of early ADHD is actually a contributing factor to risk for later ODD, regardless of severity of early ODD (Burns & Walsh, 2002; Loeber et al., 2009), perhaps due to the problems with poor emotion (anger) regulation in ADHD noted above (Barkley, 2010). Familial associations among the disorders have also been consistently found, whether across boys and girls with ADHD or across European American and African American samples (Biederman et al., 1995; Faraone et al., 2000; Samuel et al., 1999). This suggests some underlying causal connection among these disorders.

Evidence from twin studies indicates a shared or common genetic contribution to ADHD, ODD, and CD, particularly between ADHD and ODD (Coolidge, Thede, & Young, 2000; Silberg et al., 1996; Tuvblad, Zheng, Raine, & Baker, 2009). When CD occurs in conjunction with ADHD, it may represent simply a more severe form of ADHD having a greater family genetic loading for ADHD (Thapar, Harrington, & McGuffin, 2001). Other research, however, suggests that a shared environmental risk factor may also account for the overlap of ODD and CD with ADHD beyond their shared genetics (Burt, Krueger, McGue, & Iacono, 2001); this risk factor is likely to be family adversity

generally and impaired parenting specifically (Patterson, Degarmo, & Knutson, 2000). To summarize, ODD and CD have a substantial likelihood of co-occurring with ADHD, and the risk for ODD/CD seems to be mediated in large part by severity of ADHD and its family genetic loading and in part by adversity in the familial environment.

Substance Use Disorders

ADHD is a powerful risk factor for future substance use disorders (SUDs) (Charach, Yeung, Climans, & Lillie, 2011; Lee, Humphreys, Flory, Liu, & Glass, 2011). One of the strongest predictors of risk for SUDs among children with ADHD upon reaching adolescence and adulthood is prior or coexisting CD or ASPD (Burke, Loeber, & Lahey, 2001; Charach et al., 2011; Chilcoat & Breslau, 1999; Molina & Pelham, 1999; White, Xie, Thompson, Loeber, & Stouthamer-Loeber, 2001). Given the heightened risk for ODD/CD/ASPD in children with ADHD as they mature, one would naturally expect a greater risk for SUDs as well. Although an elevated risk for alcohol abuse has not been documented in all follow-up studies, it has been seen in many (Barkley et al., 2008). The risk for other SUDs among hyperactive children followed to adulthood ranges from 12 to 24% (Barbaresi et al., 2013; Barkley et al., 2008; Gittelman et al., 1985; Klein et al., 2012; Mannuzza et al., 1993, 1998; Rasmussen & Gillberg, 2001). One longitudinal study of hyperactive children suggested that childhood treatment with stimulant medication may predispose youth to develop SUDs (Lambert & Hartsough, 1998). All other longitudinal studies, however, find no such elevated risk, and in some cases even a protective effect if stimulant treatment is continued for a year or more or into adolescence (Barkley, Fischer, Smallish, & Fletcher, 2003). The basis for the conflicting findings in the Lambert and Hartsough (1998) study was probably not examining or statistically controlling for severity of ADHD and CD at adolescence and young adulthood (Barkley et al., 2003).

Anxiety and Mood Disorders

The overlap of anxiety disorders with ADHD has been found to range from 10 to 40% in clinic-referred children, averaging about 25% (for reviews, see Jarrett & Ollendick, 2008; Shatz & Rostain, 2006; Tannock, 2000). In longitudinal studies of children with ADHD, however, the risk of anxiety disorders is no greater than in control groups at either adolescence or young adulthood (Barkley et al., 2008; Mannuzza et al., 1993, 1998; Russo & Beidel, 1994; Weiss & Hechtman, 1993). In some follow-up studies the rate increases with age (Barkley et al., 2008); in others, especially in midlife, it is not different from that of controls (Klein et al., 2012). The disparity in findings is puzzling. Perhaps some of the overlap of ADHD with anxiety disorders in children is due to referral bias (Biederman et al., 1992; Tannock, 2000). General population studies of children, however, do suggest an elevated odds ratio of having an anxiety disorder in the presence of ADHD of 3.0 (95% CI = 2.1–4.3), with this relationship being significant even after researchers control for comorbid ODD/CD (Angold et al., 1999). This implies that the two disorders may have some association apart from referral bias, at least in childhood. The co-occurrence of anxiety disorders with ADHD has been shown to reduce the degree of impulsiveness, relative to ADHD without comorbid anxiety disorders (Pliszka, 1992). Some research suggests that the disorders are transmitted independently in families and so are not linked to each other in any genetic way (Biederman, Newcorn, & Sprich, 1991; Last, Hersen, Kazdin, Orvaschel, & Perrin, 1991). This may not be the case for predominantly inattentive ADHD or especially for SCT. Higher rates of anxiety disorders have been noted in some studies of these children (see Milich et al., 2001), and in their first- and second-degree relatives (Barkley, DuPaul, & McMurray, 1990; Biederman et al., 1992), though again not always (Lahey & Carlson, 1992; Milich et al., 2001). Regrettably, research on the overlap of anxiety disorders with ADHD has generally chosen to consider the various anxiety disorders as a single group in evaluating this issue. Greater clarity and clinical utility from these findings might occur if the types of anxiety disorders present were to be examined separately.

The evidence for the co-occurrence of mood disorders as defined in earlier editions of DSM (i.e., depressive disorders; we omit discussion of bipolar disorder in this paragraph) with ADHD is now fairly substantial (Biederman et al., 2008; Faraone & Biederman, 1997; Jensen, Martin, & Cantwell, 1997; Jensen, Shervette, Xenakis, & Richters, 1993; Spencer, Wilens, Biederman, Wozniak, & Harding-Crawford, 2000), although such comorbidity only exists in a minority of individuals with ADHD. Most studies place the association for depression with ADHD between 20 and 30% of ADHD cases (Barkley et al., 2008; Biederman et al., 1992; Cuffe et al., 2001) with risk possibly increasing into

adolescence and early adulthood (Barkley et al., 2008). The odds ratio of having depression, given the presence of ADHD in general population samples, is 5.5 (95% CI = 3.5–8.4) (Angold et al., 1999). As discussed above under "Sex Differences," the risk for depression appears to be higher in girls than in boys with ADHD, although both experience higher risk than do typically developing children. It is possible that some of the overlap between ADHD and depression is mediated by the increased deficits in emotion regulation associated with ADHD (especially for irritability, as discussed above, which is also a symptom of depression but can also be seen in ADHD and other disorders).

Some evidence also suggests that these disorders may be genetically related to each other (Cole, Ball, Martin, Scourfield, & McGuffin, 2009), with familial risk for one disorder substantially increasing the risk for the other (Biederman, Faraone, Keenan, & Tsuang, 1991; Biederman, Newcorn, & Sprich, 1991; Faraone & Biederman, 1997), particularly in cases where ADHD is comorbid with CD. Supportive of this mediational role of CD, one follow-up study (Barkley et al., 2008) found a 26% risk of major depression among children with ADHD by young adulthood, but this risk was largely mediated by the co-occurrence of CD. Likewise, a meta-analysis of general population studies indicated that the link between ADHD and depression was entirely mediated by the linkage of both disorders to CD (Angold et al., 1999). In the absence of CD, ADHD was not more likely to be associated with depression. This has also been shown in some follow-up studies of ADHD children into adolescence (Bagwell, Molina, Kashdan, Pelham, & Hoza, 2006).

The comorbidity of ADHD with bipolar (manic–depressive) disorders has been controversial over the past 25 years (Carlson, 1990; Geller & Luby, 1997; Skirrow, Hosang, Farmer, & Asherson, 2012). Some studies of children with ADHD indicate that 10–20% may have a bipolar disorder (Spencer et al., 2000; Wozniak et al., 1995)—a figure substantially higher than the 1% risk for the general population (Lewinsohn, Klein, & Seeley, 1995). However, this has not held up when examined by others; for instance, Hassan, Agha, Langley, and Thapar (2011) found less than 1% of their ADHD sample would meet criteria for mania. Follow-up studies have not documented any significant increase in risk of bipolar disorders in children with ADHD followed into adulthood (Barbaresi et al., 2013; Barkley et al., 2008; Klein et al., 2012; Mannuzza et al., 1993, 1998; Skirrow et al., 2012; Weiss & Hechtman, 1993); however, given small sample sizes that risk would have to exceed 7% for these studies to have sufficient power to detect any comorbidity. Children with ADHD may therefore have slightly elevated risks for bipolar disorders (Skirrow et al., 2012; Youngstrom, Arnold, & Frazier, 2010). A 4-year follow-up of children with ADHD reported that 12% met criteria for a bipolar disorder in adolescence (Biederman, Faraone, Mick, et al., 1996). Children with ADHD but without bipolar disorder do not always have an increased prevalence of bipolar disorders among their biological relatives (Biederman et al., 1992; Faraone, Biederman, & Monuteaux, 2001; Lahey et al., 1988) but other reviews have shown such a familial presence of each disorder among relatives of children with the other disorder (Faraone, Biederman, & Wozniak, 2012; Skirrow et al., 2012; Youngstrom et al., 2010). Regardless, children with both ADHD and bipolar disorder do have such an elevated incidence of both disorders among family members (Faraone et al., 1997, 2001). This suggests that where the overlap occurs, it may represent a familially distinct subset of ADHD. Children and adolescents diagnosed with childhood bipolar disorder often have a substantially higher lifetime prevalence of ADHD, particularly in their earlier childhood years (Skirrow et al., 2012; Youngstrom et al., 2010). Where the two disorders coexist, the onset of bipolar disorder may be earlier than in bipolar disorder alone (Faraone et al., 1997, 2001; Sachs, Baldassano, Truman, & Guille, 2000). Some of this overlap with ADHD may be partly an artifact of similar symptoms in the symptom lists used for both diagnoses (hyperactivity, distractibility, poor judgment, etc.) (Geller & Luby, 1997; Youngstrom et al., 2010). In any case, the overlap of ADHD with bipolar disorder appears to be mostly unidirectional: A diagnosis of ADHD seems not to increase the risk for bipolar disorder or does so only slightly, whereas a diagnosis of childhood bipolar disorder seems to dramatically elevate the risk of a prior or concurrent diagnosis of ADHD (Geller & Luby, 1997; Skirrow et al, 2012; Spencer et al., 2000; Youngstrom et al., 2010).

Tourette's Disorder and Other Tic Disorders

Up to 18% of children may develop a motor tic in childhood, but this declines to a base rate of about 2% by midadolescence and less than 1% by adulthood (Peterson, Pine, Cohen, & Brook, 2001). Tourette's disorder, a more severe disorder involving multiple motor and vocal tics, occurs in less than 0.4% of the population

(Peterson et al., 2001). A diagnosis of ADHD may elevate somewhat the risk for tic disorders or Tourette's disorder (Simpson, Jung, & Murphy, 2011), but the point is arguable (Peterson et al., 2001). Among clinic-referred adults diagnosed with ADHD, there may be a slightly greater occurrence of tic disorders (12%; Spencer et al., 2001). In contrast, individuals with obsessive–compulsive disorder or Tourette's disorder have a marked elevation in risk for ADHD—up to 55% (Freeman, 2007), and averaging 48% or more (range = 35–71%; Comings, 2000; Simpson et al., 2011). Complicating matters is the fact that the onset of ADHD often seems to precede that of Tourette's disorder in cases of comorbidity (Comings, 2000; Freeman, 2007), and it may result in earlier onset of Tourette's disorder as well as in substantial comorbidity for other disorders (Freeman, 2007).

Autism Spectrum Disorder

DSM-5 now allows codiagnosis of ADHD and autism spectrum disorder (ASD). This is sensible because as many as half of children with ASD may have co-occuring inattention and/or hyperactivity meeting clinical thresholds (van der Meer et al., 2012). A growing literature points to some overlaps in neuropsychological, neuroimaging, and genetic loci associated with these two disorders (Nijmeijer et al., 2010; Rommelse, Franke, Geurts, Hartman, & Buitelaar, 2010; Rommelse et al., 2011).

ASSOCIATED HEALTH OUTCOMES

Health outcomes related to ADHD have recently been reviewed in detail by Nigg (2013). Here we follow that review substantially, while adding other recent findings.

Accident-Proneness and Injury

In one of the first studies of the issue, Stewart, Pitts, Craig, and Dieruf (1966) found that four times as many hyperactive children as control children (43% vs. 11%) were described by parents as accident-prone. Later studies have also identified such risks; up to 57% of children with hyperactivity or ADHD are said to be accident-prone by parents, relative to 11% or fewer of control children (Mitchell, Aman, Turbott, & Manku, 1987). Interestingly, knowledge about safety does not appear to be lower in overactive, impulsive children than in control children. And so simply teaching more information about safety may not suffice to reduce the accident risks of hyperactive children (Mori & Peterson, 1995).

Over a 20-year period, several studies of small, local, or convenience samples found that children with ADHD experienced more injuries of various sorts than control children. For example, one group reported that 16% of the hyperactive sample had at least four or more serious accidental injuries (broken bones, lacerations, head injuries, severe bruises, lost teeth, etc.), compared to just 5% of control children (Hartsough & Lambert, 1985). Jensen, Shervette, Xenakis, and Bain (1988) found that 68% of children with DSM-III ADD, compared to 39% of control children, had experienced physical trauma sufficient to warrant sutures, hospitalization, or extensive/painful procedures. Several other small studies of convenience or local samples likewise found a greater frequency of accidental injuries than among control children (Shelton et al., 1998; Taylor et al., 1991).

More accurate estimates have recently been provided by large-scale population surveys, taking advantage of insurance databases. Common physical traumas among individuals with ADHD include superficial injuries and contusions, open wounds, dislocations, strains, sprains, and fractures of the upper limbs (Marcus, Wan, Zhang, & Olfson, 2008; Merrill, Lyon, Baker, & Gren, 2009). Many studies examining the association between ADHD and unintentional injury rely on medical records, and are therefore limited to those diagnoses that have received medical attention. However, using data from the National Health Interview Survey among more than 50,000 children ages 6–17 years, Pastor and Reuben (2006) examined parent-reported injuries (excluding poisoning) that required consultation with a medical professional. The annualized injury rate in the general population was 115/1,000 (11.5%), but among those ever diagnosed with ADHD, this rate was 204/1000 (20.4%; adjusted odds ratio = 1.83; 95% CI = 1.48–2.26).

Not surprisingly, the types of injuries associated with ADHD appear to vary with individuals' stage of development. In very young children, ADHD and hyperactivity in general are associated with an increased risk of nasal and aural foreign body insertions (Perera, Fernando, Yasawardena, & Karunaratne, 2009). Pediatric patients with ADHD are at increased risk for burns (Badger, Anderson, & Kagan, 2008; Fritz &

Butz, 2007; Perera et al., 2009), and adolescents and adults with ADHD are at risk of auto accidents (Barkley & Cox, 2007) and related injuries (Barkley & Cox, 2007; Barkley, Murphy, DuPaul, & Bush, 2002; Barkley, Murphy, & Kwasnik, 1996a), as discussed next, due to poorer driving including more traffic violations and license suspensions (Barkley & Cox, 2007; Barkley, Guevremont, Anastopoulos, DuPaul, & Shelton, 1993; Jerome, Segal, & Habinski, 2006).

Driving Risks and Auto Accidents

The most extensively studied form of accidents occurring among those with hyperactivity or ADHD is motor vehicle crashes. Evidence emerged years ago that hyperactive teens as drivers had a higher frequency of vehicular crashes than control teens (1.3 vs. 0.07; $p < .05$) (Weiss & Hechtman, 1993). Also noteworthy in their driving histories was a significantly greater frequency of citations for speeding. Subsequently, Barkley and colleagues (1993) found that teens with ADHD had more crashes as drivers (1.5 vs. 0.4) than did control teens over their first few years of driving. Forty percent of the group with ADHD had experienced at least two or more such crashes, relative to just 6% of the control group. Four times more teens with ADHD were deemed to have been at fault in their crashes as drivers than controls (48.6% vs. 11.1%), and these teens were at fault more frequently than the controls (0.8 vs. 0.4). In keeping with the Weiss and Hechtman (1993) initial report, teens with ADHD were more likely to get speeding tickets (65.7% vs. 33.3%) and got them more often (means = 2.4 vs. 0.6). Two studies in New Zealand using community samples suggest a similarly strong relationship between ADHD and vehicular accident risk (Nada-Raja et al., 1997; Woodward, Fergusson, & Horwood, 2000). Adults diagnosed with ADHD also manifest more unsafe motor vehicle operation and crashes. Six times more adults with ADHD in one study had their licenses suspended (24% vs. 4.0%) than in the control group, and reported having received four times more speeding tickets (means = 4.9 vs. 1.1) than control adults (Murphy & Barkley, 1996). The difference in the frequency of vehicular crashes between the groups was only marginally significant (means = 2.8 vs. 1.8; $p < .06$), however.

Later, in a more thorough examination of driving, Barkley and colleagues (1996a) reported that the group with ADHD reported having had more vehicular crashes than the control group (means = 2.7 vs. 1.6), and that a larger proportion of this group had been involved in more severe crashes (resulting in injuries) than the control participants (60% vs. 17%). Again, speeding citations were overrepresented in these self-reported outcomes of those with ADHD (100% vs. 56%) and occurred more frequently in this group than in the control group (means = 4.9 vs. 1.3).

The most thorough study to date of driving performance among young adults with ADHD (Barkley, Murphy, et al., 2002) used a multimethod, multisource battery of measures. More than twice as many young adults with ADHD as members of the control group (26% vs. 9%) had been involved in three or more vehicular crashes as drivers, and more had been held at fault in three or more such crashes (7% vs. 3%). The group with ADHD had also been involved in more vehicular crashes overall than the control group (means = 1.9 vs. 1.2) and had been held to be at fault in more crashes (means = 1.8 vs. 0.9). The dollar damage caused in their first accidents was estimated to be more than twice as high in the group with ADHD as in the control group (means = $4,221 vs. $1,665). As in the earlier studies, the group with ADHD reported a greater frequency of speeding citations (3.9 vs. 2.4), and a higher percentage had had their licenses suspended than in the control group (22% vs. 5%). The greater frequencies of both speeding citations and license suspensions were corroborated through the official state driving records for these young adults.

A key question concerns the mechanisms that would account for an association of ADHD with driving accidents or proximal behaviors like dangerous driving. The possible mechanisms seem obvious enough: Either distractibility (Farmer & Peterson, 1995; Merrill et al., 2009) or impulsive risk taking (Badger et al., 2008; Garzon, Huang, & Todd, 2008) easily comes to mind. However, with regard to driving problems, Oliver, Nigg, Cassavaugh, and Backs (2012) conducted a small experimental simulation study suggesting that driving errors and accidents in individuals with ADHD were related not to inattention, but to negative emotionality and poor frustration tolerance. This finding was also suggested in another study (Barkley & Fischer, 2010) examining the importance of impulsive emotions as a predictor of various risks and impairments in children with ADHD followed to adulthood.

In any event, these studies leave little doubt that ADHD, or its symptoms of inattention and hyperactive–impulsive behavior (and possibly emotional dysregulation), are associated with a higher risk

for unsafe driving and motor vehicle accidents than in the population without ADHD. This seems to be the case even independently of comorbid CD (Barkley & Cox, 2007), though the potential role of that confounding disorder requires further investigation. In view of the substantial costs that must be associated with such a higher rate of adverse driving outcomes, prevention and intervention efforts to reduce the driving risks among those with ADHD certainly seem needed. Some evidence suggests that ADHD medications may improve driving performance in teens and adults with ADHD (Barkley & Cox, 2007); no research has yet reported on the value of psychsocial treatments for this domain of risk.

Sleep Problems

Many studies over the past four decades or more have suggested an association between ADHD and sleep disturbances (Ball, Tiernan, Janusz, & Furr, 1997; Gruber, Sadeh, & Raviv, 2000; Kaplan, McNichol, Conte, & Moghadam, 1987; Stewart et al., 1966; Trommer, Hoeppner, Rosenberg, Armstrong, & Rothstein, 1988; Wilens, Biederman, & Spencer, 1994). The relationship between sleep and ADHD is quite complex and likely bidirectional, due to the extensive interplay of sleep and diurnal rhythm with basic functions of arousal and attention that are also relevant to ADHD; the numerous shared neurotransmitter systems; and the interplay of behavior and context with sleep readiness and quality. The observational clinical data on ADHD and sleep problems have been reviewed in many places, and interested students can consult Cortese, Faraone, Konofal, and Lecendreux (2009) and other sources (Corkum, Tannock, & Moldofsky, 1998; Spruyt & Gozal, 2011; Yoon, Jain, & Shapiro, 2012). An accessible yet detailed outline of basic mechanisms and research hypotheses and questions that might productively be pursued in ADHD and sleep was recently summarized by a special review panel and published by Owens and colleagues (2013).

In general, those clinical reviews concluded that (1) studies of intrinsic sleep disorder in ADHD (e.g., sleep apnea, parasomnias, restless legs syndrome, circadian rhythm disorder) yield numerous but inconsistent findings; and (2) parent ratings data and actigraphy studies provide fairly convincing evidence that ADHD is often (in perhaps 50% of cases) related to impairments in sleep quality due to sleep-related behavior problems, such as bedtime resistance, sleep-onset difficulties, and trouble with waking in the morning—all of which in turn may exacerbate daytime inattention and overactivity, at least in children (Dahl, 1996; Spruyt & Gozal, 2011) Adults with ADHD are also at substantially higher risk for experiencing disturbed sleep than are control populations; this finding is independent of other psychiatric comorbidities and is not accounted for by ADHD pharmacotherapy (Surman et al., 2009).

More specifically, the sleep-related behavior problems include a longer time to fall asleep, instability of sleep duration, tiredness at awakening, or frequent night waking. For instance, Stein (1999) compared 125 psychiatrically diagnosed children with 83 pediatric outpatient children and found moderate to severe sleep problems in 19% of those with ADHD, 13% of the psychiatric controls, and 6% of pediatric outpatients. These problems could be reduced to three general factors: (1) dyssomnias (bedtime resistance, sleep-onset problems, or difficulty arising); (2) sleep-related involuntary movements (teeth grinding, sleep talking, restless sleep, etc.); and (3) parasomnias (sleepwalking, night wakings, sleep terrors). Dyssomnias were primarily related to comorbid ODD or treatment with stimulant medication, whereas parasomnias were not significantly different from those in the control group. However, involuntary movements were significantly elevated in children with ADHD, combined type.

Within nondisabled populations, quantity of sleep is inversely associated with an increased risk for school behavioral problems (Aronen, Paavonen, Fjallberg, Soinen, & Torronen, 2000), particularly daytime sleepiness and inattention rather than hyperactive–impulsive behavior (Fallone, Acebo, Arnedt, Seifer, & Carskadon, 2001). The direction of effect, then, between ADHD and sleep problems is unclear. It is possible that sleep difficulties increase ADHD symptoms during the daytime, especially for inattention, as the research on typical children implies. Yet some research finds that the sleep problems of children with ADHD are not associated with the severity of their symptoms; this suggests that the disorder, not the impaired sleeping, is what contributes to impaired daytime alertness, inattention, and behavioral problems (Lecendreux, Konofal, Bouvard, Falissard, & Mouren-Simeoni, 2000). Overall, while it is clear that poor sleep can cause inattention, primary sleep disorders do not account for most cases of ADHD. Rather, behavior-related sleep problems may compound problems with ADHD, especially inattention, and in some cases may provide an avenue for intervention.

ASSOCIATED FUNCTIONAL PROBLEMS

Apart from an increased risk for various psychiatric disorders, children and teens with ADHD are also more likely to experience a substantial array of developmental, social, and health risks; these are discussed in this and the next section. Far less is known about the extent to which these correlated problems are evident in those with predominantly inattentive ADHD, particularly the putative subgroup of children who are underactive or sluggish.

Motor Coordination Problems

Problems with motor development have long been associated with ADHD. As a group, as many as 60% of children with ADHD, compared to up to 35% of typical children, may have poor motor coordination or developmental coordination disorder (Barkley, DuPaul, & McMurray, 1990; Hartsough & Lambert, 1985; Kadesjo & Gillberg, 2001; Stewart et al., 1966; Szatmari et al., 1989). Neurological examinations for "soft" signs related to motor coordination and motor overflow movements find children with ADHD to demonstrate more such signs (as well as generally sluggish gross motor movements) than control children, including those with "pure" learning disabilities (Carte et al., 1996; Denckla & Rudel, 1978; Denckla, Rudel, Chapman, & Krieger, 1985; McMahon & Greenberg, 1977). These overflow movements have been interpreted as indicators of delayed development of motor inhibition (Denckla et al., 1985).

Studies using tests of fine motor coordination, such as balance assessment, tests of fine motor gestures, electronic or paper-and-pencil mazes, and pursuit tracking, often find children with ADHD to be less coordinated in these actions (Hoy, Weiss, Minde, & Cohen, 1978; Mariani & Barkley, 1997; McMahon & Greenberg, 1977; Moffitt, 1990; Ullman, Barkley, & Brown, 1978). Simple motor speed, as measured by finger-tapping rate or grooved pegboard tests, does not seem to be as affected in ADHD as is the execution of complex, coordinated sequences of motor movements (Barkley, Murphy, & Kwasnik, 1996b; Breen, 1989; Grodzinsky & Diamond, 1992; Marcotte & Stern, 1997; Mariani & Barkley, 1997; Seidman, Benedict, et al., 1995; Seidman, Biederman, et al., 1995). The bulk of the available evidence therefore supports the existence of deficits in motor control (Harvey et al., 2007), particularly when motor sequences must be performed, in those with ADHD. Such motor difficulties may be part of the family phenotype of ADHD, since they are evident in unaffected siblings as well (Fliers et al., 2010).

Academic Functioning

The vast majority of clinic-referred children with ADHD have difficulties with school performance, most often underproductivity. Such children frequently score lower than typical or control groups of children on standardized achievement tests (Barkley et al., 1990a, 1990b; Fischer, Barkley, Edelbrock, & Smallish, 1990; Hinshaw, 1992, 1994). These differences are likely to be found even in preschool-age children with ADHD (Barkley, Shelton, et al., 2002; Mariani & Barkley, 1997), suggesting that the disorder may take a toll on the acquisition of academic skills and knowledge even before entry into first grade. Indeed, in general population samples, prospective data indicate that early childhood attention problems (defined by Child Behavior Checklist scale scores) prospectively predict adolescent academic failure, even after controlling for intervening IQ and disruptive behavior problems, although ADHD was not formally assessed (Breslau et al., 2010). All of this makes sense, given that some of the executive functions believed to be disrupted by ADHD are also likely to be involved in some forms of academic achievement (e.g., working memory in mental arithmetic or spelling; internalized speech in reading comprehension; verbal fluency in oral narratives and written reports).

A recent review found that 45% of children with ADHD qualified for a diagnosis of a learning disability (DuPaul, Gormley, & Laracy, 2013). Between 19 and 26% of children with ADHD are likely to have any single type of learning disability, conservatively defined as a significant delay in reading, arithmetic, or spelling relative to intelligence and achievement in one of these three areas at or below the 7th percentile (Barkley, 1990). If a learning disability is defined as simply a significant discrepancy between intelligence and achievement, then up to 53% of hyperactive children could be said to have such a disability (Lambert & Sandoval, 1980). Or, if the simple criterion of performance two grades below grade level is used, then as many as 80% of children with ADHD in late childhood (age 11 years) may have learning disorders (Cantwell & Baker, 1992). Studies suggest that the risk for reading disorders among children with ADHD is 16–39%, while that for spelling disorders is 24–27% and for math disorders

is 13–33% (August & Garfinkel, 1990; Barkley, 1990; Capano, Minden, Chen, Schachar, & Ickowicz, 2008; Casey, Rourke, & Del Dotto, 1996; Frick et al., 1991; Semrud-Clikeman et al., 1992).

Although the finding that children with ADHD are more likely to have learning disabilities (Gross-Tsur, Shalev, & Amir, 1991; Tannock & Brown, 2000) might imply a possible genetic link between the two disorders, other research (Doyle, Faraone, DuPre, & Biederman, 2001; Faraone et al., 1993; Gilger, Pennington, & DeFries, 1992) shows that the two sets of disorders are transmitted independently in families. Some subtypes of reading disorders associated with ADHD may have a common genetic etiology (Gilger et al., 1992; Paloyelis, Rijsdijk, Wood, Asherson, & Kuntsi, 2010). This may arise from the finding that early ADHD inattention may predispose children toward certain types of reading problems, whereas early reading problems do not generally give rise to later symptoms of ADHD or are much less likely to do so (Chadwick, Taylor, Taylor, Heptinstall, & Danckaerts, 1999; Grevens, Rijsdijk, Asherson, & Plomin, 2012; Rabiner, Coie, & The Conduct Problems Prevention Research Group, 2000; Velting & Whitehurst, 1997; Wood & Felton, 1994). The picture is less clear for spelling disorders; a common or shared genetic etiology for ADHD and spelling disorder has been shown in a joint analysis of twin samples from London and Colorado (Stevenson, Pennington, Gilger, DeFries, & Gillis, 1993). This may result from the fact that early spelling ability seems to be linked to the integrity of working memory (Mariani & Barkley, 1997; Levy & Hobbes, 1989), which may be impaired in those with ADHD (see the discussion of the theoretical model, above). Writing disorders have not received as much attention in research on ADHD, though handwriting deficits are often found among children with ADHD, particularly those with the combined type (Marcotte & Stern, 1997). Re, Pedron, and Cornoldi (2007) reported three studies that explored the prevalence and nature of these writing problems. It concluded that children with ADHD symptoms scored lower than controls on four qualitative parameters (adequacy, structure, grammar, and lexicon), produced shorter texts, and made more errors. Whether these are distinct from or related to motor or other learning problems is a fruitful area for future study.

Rapport, Scanlan, and Denney (1999) provided some early evidence for a dual-pathway model of the link between ADHD and academic underachievement. Briefly, ADHD may predispose to academic underachievement through its contribution to a greater risk for ODD/CD and conduct problems in the classroom more generally, the net effect of which is an adverse impact on productivity and general school performance. But ADHD is associated with cognitive deficits not only in attention, but in general intelligence (see below) and working memory (see above), all of which may have a direct and adverse impact on academic achievement. Supportive of this view as well are findings that the inattention dimension of ADHD is more closely associated with academic achievement problems than is the hyperactive–impulsive dimension (Faraone, Biederman, Weber, & Russell, 1998; Hynd et al., 1991; Marshall, Hynd, Handwerk, & Hall, 1997; Paloyelis et al., 2010). According to this dual-pathway model, both pathways will require interventions if the marked association of ADHD with school underachievement is to be addressed.

A higher prevalence of speech and language disorders has also been documented in many studies of children with ADHD, typically ranging from 30 to 64% of the samples (Bellani, Moretti, Perlini, & Brambilla, 2011; Gross-Tsur et al., 1991; Hartsough & Lambert, 1985; Szatmari et al., 1989; Taylor et al., 1991). The converse is also true: Children with speech and language disorders have a higher than expected prevalence of ADHD (approximately 30–58%), among other psychiatric disorders (McGrath et al., 2008; see Tannock & Brown, 2000, for a review of comorbidity with ADHD). In children with ADHD, the pragmatic aspects of speeh along with impaired verbal working memory and discourse analysis are the primary difficulties (Bellani et al., 2011).

Reduced Intelligence

For decades, it has been observed that clinic-referred children with ADHD often have lower scores on intelligence tests than control groups used in these same studies, particularly in verbal intelligence (Barkley, Karlsson, & Pollard, 1985; Mariani & Barkley, 1997; McGee, Williams, & Feehan, 1992; Moffitt, 1990; Werry, Elkind, & Reeves, 1987). Deficiencies in both fluid and crystallized intelligence have been noted (Tillman, Bohlin, Sorensen, & Lundervold, 2009). Differences in IQ have also been found between hyperactive boys and their normal siblings (Halperin & Gittelman, 1982; Tarver-Behring, Barkley, & Karlsson, 1985; Welner, Welner, Stewart, Palkes, & Wish, 1977). The differences found in these studies often

range from 7 to 10 standard score points. Studies using both community samples (Hinshaw, Morrison, Carte, & Cornsweet, 1987; McGee et al., 1984; Peterson et al., 2001) and samples of children with behavior problems (Sonuga-Barke, Lamparelli, Stevenson, Thompson, & Henry, 1994) also have found significant negative associations between degree of ADHD and intelligence (r's = –.25–.35). In contrast, associations between ratings of conduct problems and intelligence in children are often much smaller or even nonsignificant, particularly when hyperactive–impulsive behavior is partialed out of the relationship (Hinshaw et al., 1987; Lynam, Moffitt, & Stouthamer-Loeber, 1993; Sonuga-Barke et al., 1994). This implies that the relationship between IQ and ADHD is not likely to be a function of comorbid conduct problems (see Hinshaw, 1992, for a review). Although a portion of the IQ disparity may be attributable to the impact of ADHD on executive functioning (which is also related to IQ), studies suggest that some IQ disparity remains even after statistical controls for executive functioning deficits and may be due to executive attentional deficits (Tillman et al., 2009).

Social Problems

With regard to social impairment, the association between ADHD and peer rejection and neglect is perhaps the most notable. Inattention is more closely associated with peer neglect, and hyperactivity–impulsivity with peer rejection (due to either the intrusiveness or the emotionality and especially aggressiveness linked with the latter dimension of ADHD). The overall association of ADHD with disrupted peer relations was first noted decades ago (Cunningham & Siegel, 1987; Whalen, Henker, Collins, McAuliffe, & Vaux, 1979), but it is becoming increasingly well described (Hoza, 2007; Hoza et al., 2005). This literature highlights the importance of peer effects in overall outcome for ADHD (Hoza et al., 2005; Mikami & Lorenzi, 2011; Mrug et al., 2012), as well as of the interplay across psychosocial domains (e.g., parenting and peer relations; see Hurt, Hoza, & Pelham, 2007; Mikami, Jack, Emeh, & Stephens, 2010). These effects are present in both boys and girls, but girls are understudied, and some indications suggest potential unique patterns of risk and protection in girls (Blachman & Hinshaw, 2002; Mikami & Lorenzi, 2011).

Children with ADHD are less liked by other children, have fewer friends, and are overwhelmingly rejected as a consequence, particularly if they have comorbid conduct problems (Gresham, MacMillan, Bocian, Ward, & Forness, 1998; Hinshaw & Melnick, 1995; Hoza, 2007). Indeed, among children with such comorbidity, up to 70% may be rejected by peers and have no reciprocated friendships by fourth grade (Gresham et al., 1998). These peer relationship problems are the result not only of these children's more active, talkative, and impulsive actions, but also of their greater emotional, facial, tonal, and bodily expressiveness (particularly anger); more limited reciprocity in interactions; use of fewer positive social statements; more limited knowledge of social skills; and more negative physical behavior (Barkley, 2010; Grenell, Glass, & Katz, 1987; Madan-Swain & Zentall, 1990). Those with ODD/CD also prefer more sensation-seeking, fun-seeking, and trouble-seeking activities, which further serve to alienate their nondisabled peers (Hinshaw & Melnick, 1995; Melnick & Hinshaw, 1996). While comorbid ODD or CD is most often associated with even greater peer problems, comorbidity alone does not account for the peer social problems evident in ADHD (Becker, Luebbe, & Langberg, 2012). Furthermore, children with ADHD seem to process social and emotional cues from others in a more limited and error-prone fashion, as if they were not paying as much attention to emotional information provided by othrs. Yet they do not differ in their capacity to understand the emotional expressions of other children (Casey, 1996). However, in those with comorbid ODD/CD, there may be a greater misperception of anger and a greater likelihood of responding with anger and aggression to peers than in typical children (Cadesky, Mota, & Schachar, 2000; Casey, 1996; Matthys, Cuperus, & van Engeland, 1999). Little wonder, then, that children with ADHD perceive themselves as receiving less social support from peers (and teachers) than do typical children (Demaray & Elliot, 2001). The problems with aggression and poor emotion regulation are also evident in the sports behavior of these children with their peers (Johnson & Rosen, 2000). Once more, stimulant medication has been observed to decrease these negative and disruptive behaviors toward teachers (Whalen, Henker, & Dotemoto, 1980) and peers (Cunningham, Siegel, & Offord, 1985; Wallander, Schroeder, Michelli, & Gualtieri, 1987; Whalen et al., 1987), but it may not result in any increase in more prosocial or positive initiatives toward peers (Wallander et al., 1987).

ADHD in children can also have a direct negative influence on familial relationships (Johnston & Mash, 2001; Mash & Johnston, 1990) and on other family

members (Barkley, 2006; Harpin, 2005). These effects may reflect either gene–environment correlations (the parents and children share genes that predispose the children to ADHD and the parents to depression or substance use), or they may also reflect parents' inability to cope with the burden of caring for children with ADHD. This burden may be perceived differently by mothers and fathers, but both appear to experience elevated stress that is only partly attributable to comorbid child defiant/oppositional behavior (Podolski & Nigg, 2001; Theule, Wiener, Rogers, & Marton, 2011).

Parent–child conflict is well appreciated as a complication in ADHD and is an important target for behavioral intervention, as it may contribute to continuing ADHD symptoms (Wells et al., 2000). However, children with ADHD have also reported witnessing more interparental conflict than children without ADHD, which was associated with teacher ratings of ADHD severity (Counts, Nigg, Stawicki, Rappley, & von Eye, 2005)—an effect that may be modulated by child genotype (Martel et al., 2011; Nikolas, Friderici, Waldman, Jernigan, & Nigg, 2010). Still, data from twin studies using behavioral genetic methods indicate that these child reports do not merely reflect child genotype (e.g., temperament), but also environmental effects, such as conflict in the home (Nikolas & Nigg, 2013). These reports indicate that a recursive loop may occur in which ADHD provokes interparental conflict, which in turn exacerbates emotional load and ADHD symptoms in the child. This possibility, and the potential that a subset of children with ADHD are particularly vulnerable, suggests both avenues for intervention and avenues for understanding the underlying etiological process.

ADHD affects the interactions of children with their parents, and hence the manner in which parents may respond to these children (Johnston & Mash, 2001). Those with ADHD are more talkative, negative, and defiant; less compliant and cooperative; more demanding of assistance from others; and less able to play and work independently of their mothers (Danforth et al., 1991; Gomez & Sanson, 1994; Johnston, 1996; Johnston & Mash, 2001). Their mothers are less responsive to the questions of their children, more negative and directive, and less rewarding of their children's behavior (Danforth et al., 1991; Johnston & Mash, 2001). Mothers of children with ADHD have been shown to give both more commands and more rewards to sons with ADHD than to daughters with the disorder (Barkley, 1989a; Befera & Barkley, 1984), but also to be more emotional and acrimonious in their interactions with sons (Buhrmester, Camparo, Christensen, Gonzalez, & Hinshaw, 1992; Taylor et al., 1991). Children and teens with ADHD seem to be nearly as problematic for their fathers as their mothers (Buhrmester et al., 1992; Edwards et al., 2001; Johnston, 1996; Tallmadge & Barkley, 1983). Contrary to what may be seen in typical mother–child interactions, the conflicts between children and teens with ADHD (especially boys) and their mothers may actually increase when fathers join the interactions (Buhrmester et al., 1992; Edwards et al., 2001). Such increased maternal negativity and acrimony toward sons in these interactions has been shown to predict greater noncompliance in classroom and play settings, as well as greater covert stealing away from home, even when the level of the sons' own negativity and parental psychopathology are statistically controlled for in the analyses (Anderson et al., 1994). The negative parent–child interaction patterns also occur in the preschool age group (Cohen, Sullivan, Minde, Novak, & Keens, 1983; DuPaul, McGoey, Eckert, & VanBrakle, 2001), and may be even more negative and stressful (to the parents) in this age range (Mash & Johnston, 1982, 1990) than in later age groups. With increasing age, the degree of conflict in these interactions lessens, but remains deviant from normative levels into later childhood (Barkley, Karlsson, & Pollard, 1985; Mash & Johnston, 1982) and adolescence (Barkley, Anastopoulos, Guevremont, & Fletcher, 1992; Barkley, Fischer, Edelbrock, & Smallish, 1991; Edwards et al., 2001). In families of children with ADHD, negative parent–child interactions in childhood have been observed to be significantly predictive of continuing parent–teen conflicts 8–10 years later in adolescence (Barkley, Fischer, et al., 1991). Few differences are noted between mothers' interactions with their children who have ADHD and their interactions with the siblings of these children (Tarver-Behring et al., 1985).

The presence of comorbid ODD is associated with the highest levels of interaction conflicts between parents and their children and adolescents with ADHD (Barkley, Anastopoulos, et al., 1992; Barkley, Fischer, et al., 1991; Edwards et al., 2001; Johnston, 1996). In a sequential analysis of these parent–teen interaction sequences, investigators have noted that the immediate or first lag in the sequence is most important in determining the behavior of the other member of the dyad (Fletcher, Fischer, Barkley, & Smallish, 1996). That is, the behavior of each member is determined mainly by the immediately preceding behavior of the other member, and not by earlier behaviors of either member in

the chain of interactions. The interactions between the teens with comorbid ADHD/ODD and their parents reflected a strategy best characterized as "tit for tat," in that the type of behavior (positive, neutral, or negative) of each member was most influenced by the same type of behavior emitted immediately preceding it. Mothers of teens with ADHD only and of nondisabled teens were more likely to utilize positive and neutral behaviors regardless of the immediately preceding behavior of their teens; this has been characterized as a "be nice and forgive" strategy, which is thought to be more mature and more socially successful for both parties in the long run (Fletcher et al., 1996). Even so, those with ADHD alone are still found to be deviant from the norm in these interaction patterns, though less so than those with comorbid ADHD/ODD. The presence of comorbid ODD has also been shown to be associated with greater maternal stress and psychopathology, as well as parental marital/couple difficulties (Barkley, Anastopoulos, et al., 1992; Barkley, Fischer, et al., 1991; Johnston & Mash, 2001; Theule et al., 2011).

These interaction conflicts in families of children with ADHD are not limited to parent–child interactions. Increased conflicts have been observed between children with ADHD and their siblings, relative to typical child–sibling dyads (Mash & Johnston, 1983b; Taylor et al., 1991). Research on the larger domain of family functioning has shown that families of children with ADHD experience more parenting stress and decreased sense of parenting competence (Johnston & Mash, 2001; Mash & Johnston, 1990; Theule et al., 2011); increased alcohol consumption in parents (Cunningham, Benness, & Siegel, 1988; Pelham & Lang, 1993); decreased extended family contacts (Cunningham et al., 1988); and increased marital/couple conflict, separations, and divorce, as well as maternal depression (Barkley, Fischer, et al., 1990; Befera & Barkley, 1984; Cunningham et al., 1988; Johnston & Mash, 2001; Lahey et al., 1988; Taylor et al., 1991). Again, the comorbid association of ADHD with ODD or CD is linked to even greater degrees of parental psychopathology, marital/couple discord, and divorce than is ADHD only (Barkley, Fischer, et al., 1990, 1991; Lahey et al., 1988; Taylor et al., 1991). Interestingly, Pelham and Lang (1993) have shown that the increased alcohol consumption in these parents is in part a direct function of their stressful interactions with their children with ADHD. Those findings were recently replicated and extended in a larger study by showing that the increase in alcohol consumption was partly mediated by parental stress reactivity (Kashdan, Adams, Kleiman, Pelham, & Lang, 2013).

Research has demonstrated that the primary direction of effects within these interactions is from child to parent (Danforth et al., 1991; Johnston & Mash, 2001; Mash & Johnston, 1990), rather than the reverse. That is, much of the disturbance in the interaction seems to stem from the effects of the child's excessive, impulsive, unruly, noncompliant, and emotional behavior on the parent, rather than from the effects of the parent's behavior on the child. This was documented primarily through studies that evaluated the effects of stimulant medication on the behavior of such children and their interaction patterns with their mothers. Such research found that medication improves the compliance of those with ADHD and reduces their negative, talkative, and generally excessive behavior, so that their parents reduce their levels of directive and negative behavior as well (Barkley & Cunningham, 1979a; Barkley, Karlsson, Pollard, & Murphy, 1985; Danforth et al., 1991; Humphries, Kinsbourne, & Swanson, 1978). These effects of medication are noted even in preschool-age children with ADHD (Barkley, 1988), but also in those in late childhood (Barkley, Karlsson, Pollard, & Murphy, 1985), as well as in children of both sexes (Barkley, 1989a).

Nonetheless, parental ADHD may have difficult-to-predict effects in relation to child adjustment in children with ADHD. Because ADHD is familial, many children with ADHD have at least one parent who also has ADHD. ADHD in a parent may contribute to breakdowns in parenting effectiveness that may make it more difficult for that parent to handle that particularly challenging child (Johnston, Mash, Miller, & Ninowski, 2012). Alternatively, the parent with ADHD may more easily empathize with the child who has ADHD, reducing conflict between them. More research in this regard will be of interest.

Besides a general reduction in the negative, disruptive, and conflictual interaction patterns between children with ADHD and their parents as a result of stimulant medication, general family functioning also seems to improve when these children are treated with stimulant medication (Schachar, Taylor, Weiselberg, Thorley, & Rutter, 1987). None of this is meant to suggest that parental reactions to disruptive child behavior; parental skill and competence in child management and daily rearing; and parental psychological impairment are unimportant influences on children with ADHD. Evidence certainly shows that parental man-

agement, child monitoring, parental antisocial activity, maternal depression, father absence, and other parent and family factors are exceptionally important in the development of ODD, CD, major depression, and other disorders likely to be comorbid with ADHD (Johnson, Cohen, Kasen, Smailes, & Brook, 2001; Johnston & Mash, 2001; Patterson et al., 2000; Pfiffner, McBurnett, & Rathouz, 2001). But it must be emphasized, as the behavioral genetic studies described below strongly attest, that these are not the origins of the impulsive, hyperactive, and inattentive behaviors or the related deficits in executive functioning and self-regulation.

ETIOLOGY AND PATHOPHYSIOLOGY

ADHD falls into a group of disorders known as "complex disease," meaning that etiology is multifactorial and probabilistic. An important goal is to identify particular etiologies that may function as risk factors and thus may be used to predict clinical outcome, as well as to open the door for prevention. Etiological factors can include the interplay of genetic liability and environmental potentiators. Pathophysiology then concerns the particular neurobiological processes that may be involved in development and enable us to eventually place more precise biological markers on ADHD. We thus consider first neurobiological factors, then genetic factors.

Neurobiological Factors

Various neurological etiologies have been proposed for ADHD. Brain damage was initially proposed as a chief cause of ADHD symptoms (see "Historical Context," above), whether it occurred as a result of known brain infections, trauma, or other injuries or complications occurring during pregnancy or at the time of delivery. Several studies show that brain damage, particularly hypoxic/anoxic types of insults, is associated with greater attention deficits and hyperactivity (Cruickshank, Eliason, & Merrifield, 1988; O'Dougherty, Nuechterlein, & Drew, 1984). ADHD symptoms also occur more often in children with seizure disorders (Holdsworth & Whitmore, 1974) that are clearly related to underlying neurological malfunction. However, most children with ADHD have no history of significant brain injuries or seizure disorders, and so brain damage is unlikely to account for the majority of children with ADHD (Rutter, 1977).

Throughout the past 100 years, investigators have repeatedly noted the similarities between symptoms of ADHD and those produced by lesions or injuries to the frontal lobes more generally and the prefrontal cortex specifically (Barkley, 1997a; Benton, 1991; Heilman, Voeller, & Nadeau, 1991; Levin, 1938; Mattes, 1980). Both children and adults suffering injuries to the prefrontal region demonstrate deficits in sustained attention, inhibition, regulation of emotion and motivation, and the capacity to organize behavior across time (Fuster, 1997; Stuss & Benson, 1986). In the past 20 years, this discussion has been transformed by dramatic advances both in neuroimaging technology and in appreciation of the complex, interdependent, and nonlinear nature of neural development.

Early research in the 1960s and 1970s focused on psychophysiological measures of nervous system (central and autonomic) electrical activity, variously measured (electroencephalograms [EEGs], galvanic skin responses, heart rate deceleration, etc.). These studies were inconsistent in demonstrating group differences between children with ADHD and control children in resting arousal. But where differences from typical children were found, they were consistently in the direction of diminished reactivity to stimulation, or arousability, in those with ADHD (see Hastings & Barkley, 1978, for a review). Later research continued to demonstrate differences in skin conductance and heart rate parameters in response to stimulation in those with ADHD (Borger & van der Meere, 2000), which may distinguish them from children with CD or those with comorbid ADHD and CD (Beauchaine, Katkin, Strassberg, & Snarr, 2001; Herpertz et al., 2001).

Far more consistent have been the results of quantitative EEG (qEEG) and event-related potential (ERP) measures, sometimes taken in conjunction with vigilance tests (Frank, Lazar, & Seiden, 1992; Klorman, 1992; Klorman, Salzman, & Borgstedt, 1988). Although results have varied substantially across these studies (see Loo & Makieg, 2012, for a review), the most consistent pattern for qEEG research is increased slow-wave or theta activity (particularly in the frontal lobe) and excess beta activity, all potentially indicative of a pattern of underarousal and underreactivity in ADHD (Loo & Makieg, 2012; Monastra, Lubar, & Linden, 2001). Some of these qEEG differences may be linked to the DRD4 gene polymorphisms known to increase risk for the disorder (Loo et al., 2010). Children with ADHD also have been found to have smaller amplitudes in the late positive and negative components

of their ERPs. These late components are believed to be functions of the prefrontal regions of the brain, are related to poorer performances on inhibition and vigilance tests, and are improved by stimulant medication and motivational manipulations (Groom et al., 2010; Johnstone, Barry, & Anderson, 2001; Johnstone, Barry, Markovska, Dimoska, & Clarke, 2009; Kuperman, Johnson, Arndt, Lindgren, & Wolraich, 1996; Pliszka, Liotti, & Woldorff, 2000). Thus psychophysiological abnormalities related to sustained attention and inhibition demonstrate an underresponsiveness of children with ADHD to stimulation that is improved or even corrected by stimulant medication.

Several studies have also examined cerebral blood flow using single-photon emission computed tomography (SPECT) in children with ADHD and typical children (for reviews, see Hendren, De Backer, & Pandina, 2000; Tannock, 1998). They have consistently shown decreased blood flow to the prefrontal regions (most recently in the right frontal area), and to pathways connecting these regions with the limbic system via the striatum and specifically its anterior region known as the caudate, and with the cerebellum (Gustafsson, Thernlund, Ryding, Rosen, & Cederblad, 2000; Yeh et al., 2012). Degree of blood flow in the right frontal region has been correlated with behavioral severity of the disorder, while that in more posterior regions and the cerebellum seems related to degree of motor impairment (Gustafsson et al., 2000).

More than a decade ago, a radioactive chemical ligand known as [I^{123}]Altropane was developed that binds specifically to the dopamine transporter protein in the striatum of the brain, and thus can be used to indicate level of dopamine transporter activity within this region. Following intravenous injection of the ligand, SPECT is used to detect the binding activity of Altropane in the striatum. The dopamine transporter is responsible for the reuptake of extracellular dopamine from the synaptic cleft after neuronal release. Several pilot studies found that adults with ADHD had significantly increased binding potential of Altropane and thus greater dopamine transporter activity (Dougherty et al., 1999; Krause, Dresel, Krause, Kung, & Tatsch, 2000). These findings are interesting because research suggests that the drug methylphenidate, which is often used to treat ADHD, has a substantial effect on activity in this brain region and may produce its therapeutic effect by slowing down this dopamine transporter activity (Krause et al., 2000; Volkow et al., 2001).

Studies using positron emission tomography (PET) to assess cerebral glucose metabolism have found diminished metabolism in adults with ADHD, particularly in the frontal region (Schweitzer et al., 2000; Zametkin et al., 1990), and in adolescent females with ADHD (Ernst et al., 1994), but have proven negative in adolescent males with ADHD (Zametkin et al., 1993). An attempt to replicate the finding in adolescent females with ADHD in younger female children with ADHD failed to find such diminished metabolism (Ernst, Cohen, Liebenauer, Jons, & Zametkin, 1997). Such studies are plagued by their exceptionally small sample sizes, which result in very low power to detect group differences and considerable unreliability in replicating previous findings. However, significant correlations have been noted between diminished metabolic activity in the anterior frontal region and severity of ADHD symptoms in adolescents with ADHD (Zametkin et al., 1993). Also, using a radioactive tracer that indicates dopamine activity, Ernst and colleagues (1999) found abnormal dopamine activity in the right midbrain region of children with ADHD, and discovered that severity of symptoms was correlated with the degree of this abnormality. These demonstrations of an association between the metabolic activity of certain brain regions on the one hand, and symptoms of ADHD and associated executive deficits on the other, are critical to proving a connection between the findings pertaining to brain activation and the behaviors constituting ADHD.

MRI (both functional and structural) of ADHD, however, now constitutes the primary avenue of study. This research has been reviewed in detail in meta-analyses, most recently by Cortese and colleagues (2012). By the late 1990s, the basic outlines of circuitry in ADHD were becoming clear. Functional MRI activity in various brain regions revealed that children with ADHD had altered patterns of activation during attention and inhibition tasks, particularly in the right prefrontal region, the basal ganglia (striatum and putamen), and the cerebellum (Cortese et al., 2012; Rubia et al., 1999; Teicher et al., 2000).

Significant progress has been reported by a longitudinal brain imaging study established at the intramural child psychiatry branch at the National Institutes of Health in the 1990s, which has yielded several interesting reports and reviews in the past decade (Castellanos et al., 2002; Giedd, Blumenthal, Molloy, & Castellanos, 2001; Krain & Castellanos, 2006; Shaw et al., 2007; Shaw, Lerch, et al., 2006). This research,

which has focused only on brain structure, initially revealed that alterations in structural volume in ADHD were present early in life, were not explained by medication treatment, and appeared to be nonprogressive. These findings suggested that early life insult or genetic influences were primarly responsible for observed alterations in brain structure in ADHD. More recently, a series of papers from this study (see Shaw, Lerch, et al., 2006) has examined cortical thickness measures. These appear to show a more dynamic pattern, with altered or delayed trajectory of cortical mantle thickening and then normative thinning during adolescent development. This finding highlights that despite some early alterations, the trajectory of development of the brain and the timing of developmental events will be extremely important to clarify in the coming decade of research on ADHD.

That specific regulatory brain systems are involved in ADHD is now supported by dozens of studies (Casey et al., 2007; Cubillo et al., 2010; Epstein et al., 2009; Gatzke-Kopp et al., 2009; Rubia, 2011; Rubia et al., 2010; Stanley et al., 2008) and, decisively, by comprehensive meta-analyses (Bush, 2010; Dickstein, Bannon, Castellanos, & Milham, 2006). First, ADHD involves frontal–subcortical (frontal–limbic/frontal–striatal) circuits, important for behavioral and emotional regulation and impulse control (including dorsolateral and ventromedial prefrontal cortex, dorsal anterior cingulate cortex, amygdala, and regions of striatum, as well as thalamus; Dickstein et al., 2006; Nigg & Casey, 2005). These findings are supported by diffusion tensor imaging studies as well, where meta-analysis shows widespread alterations in white matter (van Ewijk, Heslenfeld, Zwiers, Buitelaar, & Oosterlaan, 2012) but also anterior corona radiata/longitudinal fasciculus and internal capsule, consistent with our circuit model.

Second, as shown in two separate meta-analyses (Cortese et al., 2012), ADHD involves abnormality in nodes in frontal–parietal–subcortical circuits (the canonical ventral attention stream but also the dorsal stream, including dorsolateral prefrontal cortex and inferior parietal lobule). Third, a circuit that was little discussed until recently, called the "default mode network," appears to operate abnormally in ADHD. The default mode circuit is a network of structures that tends to be active at rest (e.g., when the mind is wandering or not engaged in a task). This circuit tends to shut off during task engagement—but not as well in ADHD. It includes medial and lateral parietal cortex, medial prefrontal cortex, and precuneus/ posterior cingulate cortex (or retrosplenial cortex) (Cortese et al., 2012). The method used to assess these circuits—resting-state functional connectivity—assesses spontaneous correlations of activity throughout the brain during rest, when the brain is actually very active. While many methodological questions remain about this newer method of brain assessment, the findings are intriguing and likely to continue to inform brain development in ADHD.

These brain alterations involve both structure and function—and, increasingly, connectivity among regions. The various brain regions and circuits often implicated in ADHD are illustrated in Figure 2.3. It illustrates three fundamental types of circuits that are relevant. The prefrontal cortex is important for behavioral control and regulation, but as outlined by Casey, Nigg, and Durston (2007) and Nigg and Casey (2005), subcortical and posterior brain regions are important in signaling the control systems to engage. Frontal–parietal circuits are involved in attentional capture, including a dorsal and a ventral attention circuit involved in attentional allocation and in attentional capture by new information, respectively. The frontal–thalamic–basal ganglia loop actually implicates multiple parallel neural circuits that are differentially involved in regulating motor response and emotional response. Cerebellar–frontal loops are involved in helping to learn temporal associations of events and their consequences.

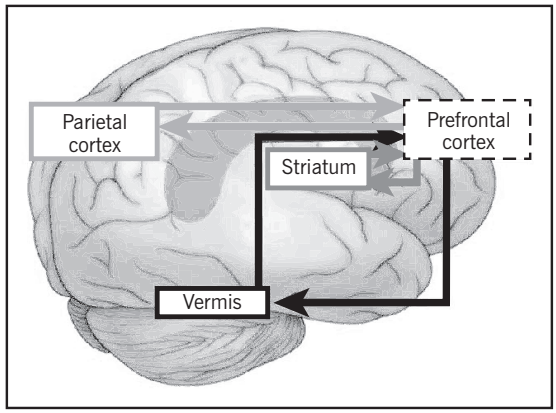

FIGURE 2.3. Conceptual brain circuits involved in ADHD. From Casey, Nigg, and Durston (2007). Copyright 2007 by Lippincott Williams & Wilkins. Reprinted by permission.

Again, the demonstrated linkage of brain structure and function with psychological measures of ADHD symptoms and executive deficits is exceptionally important in such research, to permit causal inferences to be made about the role of these brain abnormalities in the cognitive and behavioral abnormalities constituting ADHD. However, the effects are still not large or specific enough to permit the identification of individual cases. Much work remains to be done to render this work clinically applicable in terms of selecting individual children with particular brain alterations related to their individual cases of ADHD.

Neurotransmitter Associations with ADHD

Possible neurotransmitter dysfunction or imbalances, especially in dopamine pathways (Tripp & Wickens, 2008) have been proposed in ADHD for quite some time. (See Pliszka, McCracken, & Maas, 1996, for an early review; for an alternative view, see Arnsten, 2001; more recent formulations have been discussed in the "Theoretical Considerations" section of this chapter.) Initially, these ideas rested chiefly on the responses of children with ADHD to differing drugs.

Children with ADHD tend to respond dramatically to stimulants, most of which act by changing availability of dopamine at the synapse via various mechanisms, and by producing some effects on the noradrenergic pathways as well (Connor, 2006). The mechanism of action in ADHD is dynamic in that there is acute increase of dopamine availability at the synapse, but this is accompanied by changes over time in receptor density in some brain areas. Nonetheless, it is clear that increased dopamine availability at the synapse, particularly in circuitry related to motivation and incentive response, is one part of the effect (for recent findings and expert discussions, see Swanson, Baler, & Volkow, 2011; Volkow et al., 2012). These children also respond well to noradrenergic agonists, providing further support for a possible noradrenergic basis to ADHD (Arnsten, 2001). Consequently, it seemed sensible to hypothesize that these two neurotransmitters might be involved in the disorder. The finding that nondisabled children show a positive (albeit lesser) response to stimulants (Rapoport et al., 1978), however, partially undermines this logic. Other, more direct evidence comes from studies of cerebrospinal fluid in children with ADHD and typical children, which indicate decreased brain dopamine in the children with ADHD (Raskin, Shaywitz, Shaywitz, Anderson & Cohen, 1984). Similarly, other studies have used blood and urinary metabolites of brain neurotransmitters to infer deficiencies in ADHD, largely related to dopamine regulation. Early studies of this sort proved conflicting in their results (Shaywitz, Shaywitz, Cohen, & Young, 1983; Shaywitz et al., 1986; Zametkin & Rapoport, 1986). A subsequent study continued to find support for reduced noradrenergic activity in ADHD, as inferred from significantly lower levels of a metabolite of this neurotransmitter (Halperin et al., 1997).

Environmental and Genetic Factors

Genetic Factors

Family studies established long ago that ADHD runs in families, with at least a two- to fourfold increased risk among first-degree relatives (Mick & Faraone, 2009). How much of this familial similarity is due to genes versus common family experiences? Over a dozen behavioral genetic (twin and/or adoption) studies of ADHD have established that in parent ratings, substantial portions of liability are carried by genetic variation; the heritability coefficient, averaged across many studies, exceeds .80 (Boomsma, Cacioppo, Muthen, Asparouhov, & Clark, 2007; Grant et al., 2007). Heritability estimates are somewhat lower, however, when teacher ratings are examined, although the heritability of a latent variable for shared parent and teacher agreement was .78 in a large Dutch sample (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Relatively few studies have examined twin concordance of ADHD diagnoses derived from full clinical evaluation or from the combination of parent and teacher input on symptoms and impairment.

The variation in results for teacher versus parent ratings raises questions of rater bias (also known as "contrast bias") as an influence on heritability estimates. Contrast bias (i.e., parents' emphasizing differences more in dizygotic than in monozygotic twins) is known to inflate heritability estimates of activity level in preschoolers. Such effects in ADHD ratings appear to depend on what rating scale is used. Rietveld, Hudziak, Bartels, van Beijsterveldt, and Boomsma (2004) reported on a longitudinal study of a large sample of twins in Europe, with maternal Child Behavior Checklist ratings at four age points (3, 7, 10, and 12 years). Even with rater contrast effects controlled, heritability

was above .70 at each age. Simonoff and colleagues (1998) confirmed maternal contrast effects but also noted biases in teacher ratings due to twin confusion (also known as "correlated errors"), especially for monozygotic twins. In other words, many twins have the same teacher, and teachers have more difficulty keeping monozygotic twins straight in their minds. When these effects are accounted for, heritability was in the range of .60–.70.

In sum, the heritability of ADHD is likely to be about .70, which is substantial for a psychological trait and greater than that for many other traits or disorders. Nonshared environmental effects account for the remainder of variance in ADHD liability. In response to these findings, researchers aggressively pursued molecular genetic studies during the period from 2000 to 2010.

The most common approach to studying molecular correlates in ADHD initially was to look at candidate genes—that is, selected markers on genes believed for theoretical reasons to be of interest, such as dopamine receptor genes. A meta-analysis of that literature indicated that six genes have common markers that had been reliably associated with ADHD to that point: dopamine transporter (DAT1), dopamine D4 and D5 receptors (DRD4, DRD5), serotonin transporter (5-HTTPLR), serotonin 1B receptor gene (HTR1B), and synaptosomal-associated protein of molecular weight 25 kDa (SNAP25) (Gizer et al., 2008). However, ongoing larger studies will likely identify new associations.

A second approach is to conduct genome-wide scans. With this approach, searches are conducted across hundreds of thousands of common markers (called single-nucleotide repeats or polymorphisms). Somewhat to the surprise and disappointment of many scientists, genome-wide scans have failed to identify important new genes in ADHD (Maliakkal et al., 1992). In part, such failures have occurred because a very large number of statistical tests are required (hundreds of thousands), resulting in low statistical power. Yet pending studies appear likely to identify genome-wide significant markers in psychiatric illness. Furthermore, the studies have identified additional candidates that warrant follow-up, including one that is under a genome-wide significant linkage peak in a meta-analysis, the cadhedrin coding gene known as cadhedrin 13 (CDH13) (Lasky-Su et al., 2008). This gene is expressed in nicotinic receptors and neurite outgrowth (Canino & Alegria, 2008).

A third approach is to organize common gene variants into their chemical and physiological groupings, called "pathways." This approach tests for significant association with an over- or underexpressed pathway and thus has more power than searches for individual markers have. To date, only two studies have attempted this approach with ADHD, and both used a limited approach of examining enrichment of a subset of only already known pathways (the existing catalogues of biological gene pathways as well as gene sets are notably varied as well as incomplete). Still, results were intriguing. Poelmans, Pauls, Buitelaar, and Franke (2011) identified a coherent network related to nicotinic receptors (already one of the biochemical theories of ADHD) and related to neural growth (relevant to newer theories of neurodevelopmental delay). Stergiakouli and colleagues (2012) also identified relevant biological pathways, most interestingly in those metabolic systems related to central nervous system development and choleresterol metabolism (essential for neural development). Once again, the findings, although representing only a first look at this type of approach and likely to be updated in coming years, provoke new ideas about pathophysiology. It is likely that more gene-pathway-based approaches will be fruitful in the future.

A fourth approach, which has been somewhat successful in research on schizophrenia and ASD, is to examine rare structural variants, many of which are copy number variants (meaning that the only difference in such a variant is that a given nucleotide sequence is repeated too many times). This can be accomplished by reanalyzing data from genome-wide scans. For example, one of the first attempts at this method found evidence of a rare copy number variation at a locus related to ADHD on chromosome 15 at q13.3 occurring in a little under 1% of the population, which doubles the risk of ADHD (Williams et al., 2012). Another study using a similar approach concluded that the PARK2 gene (a gene associated with Alzheimer disease) has a rare variant occurring in < 1% of the population that is overrepresented in ADHD (Jarick et al., 2014). More studies of this type are likely to emerge.

New variants can be discovered by sequencing exomal regions of the genome (nonsynonymous variants) or by sequencing the entire genome. These types of studies are now underway in ADHD on a large scale and are likely to yield new discoveries in the coming decade. At this writing, an international consortium has assembled 15,000 samples of children with ADHD

and control children for an analysis of nonsynonymous (functional) variants, most of which are relatively rare in the population; the researchers are using a chip array, but not yet doing sequencing. Sequencing is just getting underway, but is expected to identify some rare causal variants, similar to what is already occurring in ASD research.

In short, the molecular genetics of ADHD remains a vibrant, exciting area of research, despite some surprising and disappointingly small results to date. The problem of the "missing heritability" in ADHD, as in all of psychiatry, remains an interesting problem. Recent work suggests that when we consider polygenetic effects, that there is not so much missing heritability after all. However, a key issue is likely to remain gene × environment interaction (G×E) and/or epigenetic effects.

Gene × Environment Interaction

]In the past decade, studies of G×E have become the norm in psychiatric research. Most of these studies examine one or two selected genetic markers (candidates) in relation to selected measures of the environment. The hazards in such studies are many. In particular, (1) the environmental measure may itself be influenced by variation in unmeasured genes; and (2) if variables are not properly scaled, artifactual or false-positive effects are easily found. Nonetheless, initial efforts in this area have been interesting. A recent meta-analysis (Nigg, Nikolas, & Burt, 2010) indicated reliable and consistent interactions of psychosocial distress measures and genotype, particularly for DAT1 and 5-HTTLPR, in predicting ADHD. Although these effects remain reliant on a few small studies and could still be overturned, more work on G×E in ADHD is likely to be of considerable interest in coming years.

Furthermore, recent years have seen exciting developments in "epigenetics"—that is, the ways in which experience can alter the genome and thus the phenotype, sometimes dramatically. This occurs through multiple mechanisms; the most commonly studied to date is DNA methylation (modification of chromatin, the material in which DNA is "housed"), which can alter gene expression in an ongoing manner. That is, the expression of much of human variation may not depend only on DNA structure, but on the regulatory markings that control whether and how a gene is expressed.

These two insights (the importance of G×E and the importance of epigenetic effects) have sparked a renaissance in studies of environmental contributions to ADHD (as well as several other psychiatric conditions).

Environmental Risks and Triggers

When G×E and epigenetic mechanisms are recognized, many possible environmental contributors to the etiology of ADHD emerge as potentially important. A fruitful way to think about the etiology of ADHD is to consider structural DNA (the part that, as far as we know, cannot be changed except by mutations) as conveying liability or susceptibility to ADHD. Experiences then activate the condition, either by causing direct changes in the brain or physiology, or via epigenetic markings that change gene expression. This model suggests that a given environmental risk will not affect all children; some are "immune" to the effect, but other children will be susceptible and develop ADHD in the presence of this risk.

G×E empirical studies tend to support such possibilities. For example, it is known that (1) neurotoxic pesticide clearance rates from the body depend on genotype (Engel et al., 2011); (2) blood lead levels are modulated by iron uptake, which in turn is controlled by genotype; and (3) responses to dietary additives may be modulated by genotype (Stevenson et al., 2010). It also appears from neuroimaging studies of discordant identical twins (i.e., cases in which one twin has ADHD and one does not) that major changes in the brain associated with ADHD are not accounted for genetically (Castellanos et al., 2002). Thus it appears likely that a susceptibility–plasticity model will ultimately work best for ADHD (and probably for other kinds of psychopathology and complex disease generally), rather than a genetic main-effect model.

As for specific environments, several are notable. First, commentators have suggested that inadequate schooling, rapid societal tempo, and family stress are contributing to an alleged increase in ADHD incidence. Many of these sociological ideas are interesting but untested (or untestable), and some proposed factors (e.g., schooling) occur too late in development to account for ADHD onset.

Regarding other potential environmental potentiates of genetic liability, both pre- and postnatal biological context may be especially important. For example, low birth weight (< 2,500 grams) is a specific risk factor for inattention, hyperactivity, and certain learning and motor problems, but not other behavioral or emotional problems at age 6 (Willcutt, 2012). However, low birth

weight is itself multiply determined by factors such as maternal health and nutrition, maternal smoking, maternal weight, low SES, stress, and other factors, making identification of specific biological mechanisms difficult.

Some studies have not found a greater incidence of pregnancy or birth complications in children with ADHD compared to normal children (Barkley, DuPaul, & McMurray, 1990), whereas others have found a slightly higher prevalence of unusually short or long labor, fetal distress, low forceps delivery, and toxemia or eclampsia (Hartsough & Lambert, 1985; Minde, Webb, & Sykes, 1968). Nevertheless, though children with ADHD may not experience greater pregnancy complications, prematurity, or lower birth weight as a group, children who are born prematurely or who have markedly lower birth weights are at high risk for later hyperactivity or ADHD (Breslau et al., 1996; Schothorst & van Engeland, 1996; Sykes et al., 1997; Szatmari, Saigal, Rosenbaum, & Campbell, 1993). It is not merely low birth weight that seems to pose the risk for symptoms of ADHD or the disorder itself (among other psychiatric disorders), but the extent of white matter abnormalities due to birth injuries, such as parenchymal lesions and/or ventricular enlargement (Whittaker et al., 1997). These findings suggest that although certain pregnancy complications may not be the cause of most cases of ADHD, some cases may arise from such complications, especially prematurity associated with minor bleeding in the brain.

Several studies suggest that mothers of children with ADHD are younger when they conceive these children than are mothers of control children, and that such pregnancies may have a greater risk of adversity (Denson, Nanson, & McWatters, 1975; Hartsough & Lambert, 1985; Minde et al., 1968). Since pregnancy complications are more likely to occur among young mothers, mothers of children with ADHD may have a higher risk for such complications, which may act neurologically to predispose their children toward ADHD. However, the complications that have been noted to date are rather mild and hardly represent compelling evidence of pre- or perinatal brain damage as a cause of ADHD. Some epidemiological studies have generally found a significant association between pre- or perinatal adversity (apart from prematurity as noted above) and symptoms of ADHD (Froehlich et al., 2011; Pineda et al., 2007). But some of these associations dissipate once other factors are taken into account, such as maternal smoking (see below) and socioeconomic disadvantage, both of which may predispose offspring to perinatal adversity and hyperactivity (Goodman & Stevenson, 1989; Werner et al., 1971).

One study found that the season of a child's birth was significantly associated with risk for ADHD, at least among those subgroups of children who either also had a learning disability or did not have any psychiatric comorbidity (Mick, Biederman, & Faraone, 1996). Birth in September was overrepresented in this subgroup of children with ADHD. The authors conjecture that the season of birth may serve as a proxy for the timing of seasonally mediated viral infections to which these mothers and their fetuses may have been exposed, and that such infections may account for approximately 10% of cases of ADHD.

On the other hand, an extensive literature indicates that some prenatal teratogens increase risk of ADHD. For example, alcohol exposure, at least for women in the United States at moderate levels of drinking (Huo et al., 1992), seems to increase risk of offspring ADHD in some studies; however, other researchers suggest that the link is due to confounding by co-occurring social adversity and smoking (Rodriguez et al., 2009). Fetal alcohol exposure may result in a somewhat distinct neuropsychological profile from that of typical ADHD, with particular problems in visual attention and mathematics. Prospective population studies implicate household and outdoor pesticide exposures during critical periods in pregnancy as predictive of ADHD (Goldman et al., 1997; Sagiv et al., 2010). A crucial challenge is to determine whether such correlates, even though they emerge in prospective population based studies, are causal. Although G×E as well as gene–environment correlation can mask environmental effects, they can also mask genetic effects. Teratogens and toxins could be proxies for genetic risk because of gene–environment correlation.

Although experimental proof among humans is difficult to obtain, it is not impossible particularly through the avenue of clinical trials. A meta-analysis of randomized experimental data concluded that dietary factors provide a clinically meaningful causal influence on ADHD (Nigg, Lewis, Edinger, & Falk, 2012). In contrast, two clever family designs—one using surrogate mothers who were related and unrelated to their offspring, and one using siblings who differed in whether their mother smoked during pregnancy—both concluded that causal effects of prenatal smoking on ADHD were likely to be far smaller than previously believed (D'Onofrio et al., 2008; Thapar et al., 2009).

It is also possible that prenatal nicotine exposure is linked more specifically with conduct problems than with ADHD (e.g., Gatzke-Kopp et al., 2009).

It is unclear into which category neurotoxicants will fall. However, because they are fairly universally distributed in the population, exposure to them, unlike maternal smoking, is unlikely to be a proxy for genetic risk. In addition to early household pesticide exposure, particularly well studied are effects of lead exposure. It has been known for centuries that lead is neurotoxic, and for decades that lead at sufficiently high exposures can cause hyperactivity and other health problems. However, more unexpected in the past decade has been the discovery that even at background-level exposure—which is near-universal in the U.S. population (about 1 ug/dL of blood)—blood lead level is correlated with ADHD symptoms (Nigg et al., 2008; Nigg, Nikolas, Knottnerus, Cavanagh, & Friderici, 2010; Roa et al., 1994; Willcutt et al., 2012). The link between lead levels and ADHD appears to be as reliable as, and of a similar magnitude to, that shown between lead and reduced intelligence (Goodlad, Marcus, & Fulton, 2013). It will be extremely difficult to prove causal effects, but from a precautionary point of view these findings are of significant public health concern because the levels of lead being studied remain common in the United States and are epidemic in many nations around the world.

Many other experiential factors have been hypothesized to influence ADHD, from general sociological claims such as "faster pace of life" to more testable effects of early electronic media exposure on brain development. Although no conclusive evidence has been reported for those various ideas, it remains possible that important discoveries will emerge regarding experiential triggers.

Summary

It should be evident from the research reviewed here that ADHD arises from multiple factors, and that neurological and genetic factors are substantial contributors. Like Taylor (1999), Nigg and Casey (2005), Sonuga-Barke (2005), and others, we envision ADHD as having a heterogeneous etiology, with various developmental pathways leading to this behavioral syndrome. These various pathways, however, may give rise to the disorder through disturbances in a final common pathway in the nervous system. That pathway appears to be the integrity of the prefrontal cortical–striatal–cerebellar network. It now appears that hereditary factors play the largest role in the occurrence of ADHD symptoms in children. It may be that what is transmitted genetically is a tendency toward a smaller and less active prefrontal–striatal–cerebellar network. The condition can also be caused or exacerbated by pregnancy complications, exposure to toxins, or neurological disease. Social factors alone cannot be supported as causal of this disorder, but such factors may exacerbate or attenuate the condition, contribute to its persistence, increase the degree of impairment in major life activities, and (most likely) contribute to the forms of comorbid disorders associated with ADHD. Cases of ADHD can also arise without a genetic predisposition to the disorder, provided that children are exposed to significant disruption of or injury to this final common neurological pathway, but this would seem to account for only a small minority of children with ADHD.

In general, then, research conducted since the second edition of this text was published has further strengthened the evidence for genetic and developmental neurological factors as likely causes of this disorder, while greatly reducing the support for purely genetic or purely environmental factors as having a role in most instances of ADHD. Instead, it is likely that a small percentage of cases will be attributable to rare genetic mutations; another small percentage to severe environmental deprivation; and the main group of cases to various combinations of genetic susceptibility and early environmental challenge or insult, perhaps mediated by epigenetic mechanisms.

FUTURE DIRECTIONS

A number of the issues raised in this chapter point the way to potentially fruitful research. The theoretical models discussed above suggest the continued need to examine multiple mechanistic models in conjunction (e.g., temporal information processing and cognition); to expand the routine investigation of ADHD phenomonology to study of emotion and emotion regulation; to consider developmental theory; and to be constrained by what is known about neural development and neurobiology. Furthermore, there is clearly much to learn about G×E effects and the epigenetics of ADHD.

Certainly, the diagnostic criteria developed to date, even though the most rigorous and empirical ever provided, still have important limitations. The fact that such criteria are not theory-driven and developmentally referenced, despite being empirically derived, risks cre-

ating several difficulties for understanding the disorder and clinically applying these criteria. The criteria probably do not map cleanly onto neurobiology, but rather constitute several co-occurring neurobiological dimensions that still need further sorting. Heterogeneity has not been adequately captured, and breakthroughs in characterizing mechanistic subtypes, if they exist, are sorely needed.

It seems increasingly clear that ADHD is best conceived, at least in the main, as a disorder of self-control and self-regulation, with the regulation of attention as just one component of this fundamental issue. In this way, the conception is related to a wide range of life outcomes and problems that do not rise to the level of frank ADHD; it also helps explain why nearly all self-control related outcomes can be traced to ADHD as a risk factor, from drug abuse to underemployment.

Although molecular genetic research in ADHD both has increased hugely and to some extent has disappointed observers in the past decade, it is likely that findings in molecular genetics will continue to transform understanding of behavior, development, and ADHD. The movement toward epigenetic analysis is likely to be even more transformative, even if it is slow because of the need to develop appropriate methods for study of human brain function from this perspective.

Neuroimaging is likely to continue to be informative with regard to pathophysiology, but will face the challenge of how the pathophysiology may be translated into clinical utility. The most likely benefit will be in clarifying pathophysiology so that ideas for treatment not yet imagined can be identified.

Key to understanding ADHD may be the notion that it is actually a disorder of performance, rather than skill; of how intelligence is applied in everyday effective adaptive functioning, rather than intelligence itself; of "doing what you know," rather than "knowing what to do"; and of when, rather than how, to perform behavior generally. The concept of time, how it is sensed, and particularly how one uses it in self-regulation are coming to be critical elements in our understanding of ADHD (Barkley, 2012c), as they have already been in our understanding of the unique role of the prefrontal cortex more generally (Fuster, 1997). Likewise, the study of how events are mentally represented and prolonged in working memory, and of how private thought arises out of initially public behavior through the developmental process of internalization, are likely to hold important pieces of information for the understanding of ADHD itself. And as the evolutionary (adaptive) purposes of the prefrontal lobes and the executive functions they mediate come to be better understood (Barkley, 2012c), it is highly likely that these findings will yield a rich vein of insights into the sorts of adaptive deficits caused by ADHD.

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NOTES

1. Confirmatory factor analyses of the DSM-IV and DSM-5 item sets do show a slightly better fit for a model with three factors (impulsivity, hyperactivity, inattention) than two, but the fit is also very good with a two-factor solution. Therefore, the expert committees for DSM-IV and DSM-5 opted for the simpler model.

2. DSM-5 has changed the age of onset from 7 years to 12 years, reduced the cutoff point for diagnosing ADHD in adults from six symptoms to five symptoms, and allowed concurrent diagnosis of ADHD and autism spectrum disorder. These changes are expected to have minimal effects on epidemiology or clinical practice, but make the criteria more congruent with empirical findings.

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CHAPTER 3

Conduct and Oppositional Defiant Disorders

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Oppositional defiant disorder (ODD) and conduct disorder (CD), often collectively termed "conduct problems," are among the most common disorders for which children and adolescents are referred for mental health treatment. For example, 40% of children referred for mental health treatment by a primary care provider were diagnosed with a conduct problem; this percentage was surpassed only by the 50% for attention-deficit/hyperactivity disorder (ADHD) (Rushton, Bruckman, & Kelleher, 2002). This high rate may be attributed to the significant disruption and distress these children's behavior causes to family members, peers, and school personnel. Societal consequences and costs associated with the antisocial and criminal behaviors of youth with conduct problems are substantial, and even more so when these problems develop at younger ages. One estimate suggests that the potential value of saving a single high-risk youth from a criminal career ranges from $3.2 to $5.5 million (Cohen & Piquero, 2009).

ODD and CD are typically first diagnosed in childhood or adolescence, and fall into the broader dimension of mental disorders characterized by disinhibition or externalizing behaviors (American Psychiatric Association [APA], 2013). Factor-analytic research supports the distinction between the angry and defiant behaviors forming the diagnostic criteria for ODD and the antisocial and aggressive behaviors forming the criteria for CD (Frick et al., 1992; Lahey et al., 2008). However, all disorders within the externalizing domain appear to share substantial genetic influences, suggesting at least some common causal factors between them (Lahey, Van Hulle, Singh, Waldman, & Rathouz, 2011; Markon & Krueger, 2005). This externalizing dimension contrasts with a second broad dimension that conceptually organizes overcontrolled or internalizing symptoms of common child and adolescent mental disorders. Internalizing symptoms include social withdrawal, anxiety, and depression (see Hammen, Rudolph, & Abaied, Chapter 5, and Higa-McMillan, Francis, & Chorpita, Chapter 8, this volume). A number of factor-analytic studies support the distinction of these symptoms from those captured by the externalizing domain (Achenbach, 1995; Lahey et al., 2008).

BRIEF HISTORICAL CONTEXT AND CONTROVERSIES

CD first appeared as a psychiatric diagnosis in the second edition of APA's (1968) *Diagnostic and Statistical Manual of Mental Disorders* (DSM-II). The diagnosis involved antisocial, aggressive, and delinquent behavior that was believed to be a reaction to pathological environmental factors, but, like most diagnostic criteria in this early DSM, the criteria for CD were poorly defined. The DSM-II definition also distinguished among

children and adolescents who showed specific types of conduct problems (i.e., runaway reaction, unsocialized aggressive reaction, and group delinquent reaction), highlighting the important issue of subtyping that continues to influence diagnostic classification of CD today.

The current distinction between ODD and CD was first introduced in DSM-III (APA, 1980). Since this time, the predictive validity of CD has been well established (Moffitt et al., 2008). CD is associated with a variety of adjustment problems across the lifespan, including mental health problems (e.g., substance abuse), legal problems (e.g., risk for arrest), educational problems (e.g., school dropout), social problems (e.g., poor marital adjustment), occupational problems (e.g., poor job performance) and physical health problems (e.g., poor respiratory function) (Odgers et al., 2007, 2008). Even among young children (ages 4 and 5), CD predicted significant behavioral and educational difficulties 5 years later (Kim-Cohen et al., 2009).

In contrast, since it was first included in formal classification systems, significant concerns have been raised about the diagnosis of ODD. These concerns largely focus on two issues (Moffitt et al., 2008). The first issue is that the oppositional and argumentative behaviors that form the criteria for ODD are commonly displayed in normally developing children. The second issue is that ODD frequently co-occurs with a host of other adjustment problems. These issues have led some to suggest that the diagnosis overpathologizes normative behavior and, unless accompanied by another disorder, is transient and benign, not warranting consideration as a separate disorder. However, in their review, Frick and Nigg (2012) report on substantial evidence indicating that ODD predicts problems in adjustment (e.g., later antisocial behavior, substance use, and emotional disorders)—even after research controls for the presence of the most common co-occurring childhood disorders (i.e., ADHD and CD)—and that it has predictive power in children as young as 3–5 years of age (e.g., Gadow & Nolan, 2002). This evidence suggests that ODD has important clinical utility and that abandoning its diagnosis is not warranted.

DESCRIPTION OF THE DISORDERS

Core Symptoms

In DSM-5 (APA, 2013), ODD and CD are subsumed under the rubric of the disruptive, impulse-control, and conduct disorders, along with intermittent explosive disorder, pyromania, and kleptomania. Disorders in this category involve problems in the self-control of emotions and behaviors. Whereas many other psychiatric disorders may also involve problems in emotional and/or behavioral regulation, these disruptive disorders are unique in that the problems associated with them are manifested in behaviors that violate the rights of others (e.g., aggression, destruction of property) and/or that bring the individual into significant conflict with societal norms or authority figures (APA, 2013).

The specific diagnostic criteria for ODD include a recurrent pattern of angry, irritable, argumentative, defiant, or vindictive behavior that persists for at least 6 months (see Table 3.1). Factor-analytic studies converge on a three-dimensional conceptualization of the criteria (Burke, 2012; Burke, Hipwell, & Loeber, 2010; Rowe, Costello, Angold, Copeland, & Maughan, 2010). Although item loadings vary somewhat across samples, these studies are consistent in suggesting that the angry–irritable mood dimension (e.g., loses temper, angry/resentful) forms a separate factor from the defiant–headstrong behavior dimension (e.g., argues with adults, defiant/noncompliant). What is less clear from these analyses is the appropriate placement of the symptom given in DSM-IV as "is often spiteful and vindictive" (APA, 2000, p. 102). This symptom has been included on its own to comprise the hurtful dimension, since it does not consistently load with the other two symptom dimensions (Burke, Hipwell, & Loeber, 2010; Rowe et al., 2010) and may be more related to the severe conduct problems of CD (Stingaris & Goodman, 2009). Also, the three dimensions are highly correlated, with *r*'s ranging from .62 to .78 (Stingaris & Goodman, 2009). This suggests that a large number of youth scoring high on one dimension would also show elevated scores on another. This research has influenced DSM-5, which organizes ODD symptoms into these three clusters: angry/irritable mood, argumentative/defiant behavior, and vindictiveness (Table 3.1).

CD is defined as a repetitive and persistent pattern of behavior that violates the rights of others or in which major age-appropriate societal norms or rules are violated (APA, 2013). CD symptoms fall into four dimensions, which have remained unchanged from DSM-IV to DSM-5 (see Table 3.2):

- Aggression to people and animals
- Destruction of property
- Deceitfulness or theft
- Serious violations of rules

TABLE 3.1. DSM-5 Diagnostic Criteria for Oppositional Defiant Disorder

A. A pattern of angry/irritable mood, argumentative/defiant behavior, or vindictiveness lasting at least 6 months as evidenced by at least four symptoms from any of the following categories, and exhibited during interaction with at least one individual who is not a sibling.

Angry/Irritable Mood

1. Often loses temper.
2. Is often touchy or easily annoyed.
3. Is often angry and resentful.

Argumentative/Defiant Behavior

4. Often argues with authority figures or, for children and adolescents, with adults.
5. Often actively defies or refuses to comply with requests from authority figures or with rules.
6. Often deliberately annoys others.
7. Often blames others for his or her mistakes or misbehavior.

Vindictiveness

8. Has been spiteful or vindictive at least twice within the past 6 months.

Note: The persistence and frequency of these behaviors should be used to distinguish a behavior that is within normal limits from a behavior that is symptomatic. For children younger than 5 years, the behavior should occur on most days for a period of at least 6 months unless otherwise noted (Criterion A8). For individuals 5 years or older, the behavior should occur at least once per week for at least 6 months, unless otherwise noted (Criterion A8). While these frequency criteria provide guidance on a minimal level of frequency to define symptoms, other factors should also be considered, such as whether the frequency and intensity of the behaviors are outside a range that is normative for the individual's developmental level, gender, and culture.

B. The disturbance in behavior is associated with distress in the individual or others in his or her immediate social context (e.g., family, peer group, work colleagues), or it impacts negatively on social, educational, occupational, or other important areas of functioning

C. The behaviors do not occur exclusively during the course of a psychotic, substance use, depressive, or bipolar disorder. Also, the criteria are not met for disruptive mood dysregulation disorder.

Specify current severity:

Mild: Symptoms are confined to only one setting (e.g., at home, at school, at work, with peers).

Moderate: Some symptoms are present in at least two settings.

Severe: Some symptoms are present in three or more settings.

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Subtypes

Youth with conduct problems are quite heterogeneous with regard to their behavioral manifestations, causal influences, developmental courses, associated risk factors, and responses to intervention (McMahon & Frick, 2007; McMahon, Wells, & Kotler, 2006). Therefore, understanding this heterogeneity is critical for both causal research and effective intervention. A number of different methods for classifying youth with conduct problems into more homogeneous subgroups have been proposed—starting with the distinction between ODD and CD, but also considering other dimensions (such as the age at which the serious behaviors emerge) or considering the presence of comorbid conditions, the presence of aggression, or the presence of a callous and unemotional interpersonal style.

Childhood- and Adolescent-Onset Subtypes

Within the diagnosis of CD, perhaps the most commonly used method for subtyping is based on the age at which antisocial behavior first emerges. This subtyping method focuses on whether a child's CD symptoms emerge prior to adolescence (i.e., childhood onset) or coincide with the onset of adolescence (i.e., late onset or adolescent onset)—a distinction that is well supported by research (for reviews, see Frick & Viding, 2009; Moffitt, 2006). The childhood-onset group is more

TABLE 3.2. DSM-5 Diagnostic Criteria for Conduct Disorder

A. A repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated, as manifested by the presence of at least three of the following 15 criteria in the past 12 months from any of the categories below, with at least one criterion present in the past 6 months:

Aggression to People and Animals

1. Often bullies, threatens, or intimidates others.
2. Often initiates physical fights.
3. Has used a weapon that can cause serious physical harm to others (e.g., a bat, brick, broken bottle, knife, gun).
4. Has been physically cruel to people
5. Has been physically cruel to animals.
6. Has stolen while confronting a victim (e.g., mugging, purse snatching, extortion, armed robbery).
7. Has forced someone into sexual activity.

Destruction of Property

8. Has deliberately engaged in fire setting with the intention of causing serious damage.
9. Has deliberately destroyed others' property (other than by fire setting).

Deceitfulness or Theft

10. Has broken into someone else's house, building, or car.
11. Often lies to obtain goods or favors or to avoid obligations (i.e., "cons" others).
12. Has stolen items of nontrivial value without confronting a victim (e.g., shoplifting, but without breaking and entering; forgery).

Serious Violations of Rules

13. Often stays out at night despite parental prohibitions, beginning before age 13 years.
14. Has run away from home overnight at least twice while living in the parental or parental surrogate home, or once without returning for a lengthy period.
15. Is often truant from school, beginning before age 13 years.

B. The disturbance in behavior causes clinically significant impairment in social, academic, or occupational functioning.

C. If the individual is age 18 years or older, criteria are not met for antisocial personality disorder.

Specify whether:

312.81 (F91.1) Childhood-onset type: Individuals show at least one symptom characteristic of conduct disorder prior to age 10 years.

312.82 (F91.2) Adolescent-onset type: Individuals show no symptom characteristic of conduct disorder prior to age 10 years.

312.89 (F91.9) Unspecified onset: Criteria for a diagnosis of conduct disorder are met, but there is not enough information available to determine whether the onset of the first symptom was before or after age 10 years.

Specify if:

With limited prosocial emotions: To qualify for this specifier, an individual must have displayed at least two of the following characteristics persistently over at least 12 months and in multiple relationships and settings. These characteristics reflect the individual's typical pattern of interpersonal and emotional functioning over this period and not just occasional occurrences in some situations. Thus, to assess the criteria for the specifier, multiple information sources are necessary. In addition to the individual's self-report, it is necessary to consider reports by others who have known the individual for extended periods of time (e.g., parents, teachers, co-workers, extended family members, peers).

Lack of remorse or guilt: Does not feel bad or guilty when he or she does something wrong (exclude remorse when expressed only when caught and/or facing punishment). The individual shows a general lack of concern about the negative consequences of his or her actions. For example, the individual is not remorseful after hurting someone or does not care about the consequences of breaking rules.

Callous—lack of empathy: Disregards and is unconcerned about the feelings of others. The individual is described as cold and uncaring. The person appears more concerned about the effects of his or her actions on himself or herself, rather than their effects on others, even when they result in substantial harm to others.

(continued)

TABLE 3.2. *(continued)*

Unconcerned about performance: Does not show concern about poor/problematic performance at school, at work, or in other important activities. The individual does not put forth the effort necessary to perform well, even when expectations are clear, and typically blames others for his or her poor performance.

Shallow or deficient affect: Does not express feelings or show emotions to others, except in ways that seem shallow, insincere, or superficial (e.g., actions contradict the emotion displayed; can turn emotions "on" or "off" quickly) or when emotional expressions are used for gain (e.g., emotions displayed to manipulate or intimidate others).

Specify current severity:

Mild: Few if any conduct problems in excess of those required to make the diagnosis are present, and conduct problems cause relatively minor harm to others (e.g., lying, truancy, staying out after dark without permission, other rule breaking).

Moderate: The number of conduct problems and the effect on others are intermediate between those specified in "mild" and those in "severe" (e.g., stealing without confronting a victim, vandalism).

Severe: Many conduct problems in excess of those required to make the diagnosis are present, or conduct problems cause considerable harm to others (e.g., forced sex, physical cruelty, use of a weapon, stealing while confronting a victim, breaking and entering).

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likely to show aggressive behaviors in childhood and adolescence (Moffitt, Caspi, Dickson, Silva, & Stanton, 1996) and to continue antisocial behavior into adulthood, compared with the adolescent-onset group (Odgers et al., 2007). Childhood-onset conduct problems are also more strongly associated with a host of neuropsychological, cognitive, temperamental, familial, and psychosocial risk factors than is the adolescent-onset type (Frick & Viding, 2009; Moffitt, 2006). Youth with adolescent-onset CD show fewer risk factors, although they tend to score higher on measures of rebelliousness and rejection of conventional values than those in the childhood-onset group (Dandreaux & Frick, 2009; Moffitt et al., 1996).

Although it was long thought that adolescent-onset CD reflected an exaggeration of normative adolescent behavior and was limited to the adolescent period, the picture now appears far less optimistic. According to the Dunedin data that initially led Moffitt (1993) to propose the taxonomy, individuals with adolescent-onset CD continue to show significant levels of antisocial activity into their mid-20s and early 30s, as well as various other problems in life adjustment (e.g., impulsivity, substance-related problems, financial difficulties, physical health problems); these findings have led to abandonment of the once-used term "adolescence-limited" (Moffitt, Caspi, Harrington, & Milne, 2002; Odgers et al., 2008). Furthermore, access to opportunities (e.g., gainful employment, higher education) may be limited for these individuals through their encounter of "snares" related to early delinquent involvement, such as substance use disorders, a criminal record, or teen parenthood.

Despite the strong support for this method of subtyping youth with antisocial behaviors, there are also several important limitations to this approach. First, the exact age at which to differentiate childhood- from adolescent-onset CD is not firmly established. In an early test of the differential predictive utility of various age cutoffs, Robins (1966) found that youth who were 11 years of age or younger at the onset of their serious conduct problems were over twice as likely as those over 11 to be diagnosed with antisocial personality disorder as adults. Since that time, age cutoffs for defining the childhood-onset group have ranged from 10 years (APA, 2000, 2013) to 14 years (Patterson & Yoerger, 1997; Tibbetts & Piquero, 1999) for the onset of the first serious conduct problem or first arrest. This difficulty in defining a clear cutoff point for the age of onset has led some researchers to suggest that this distinction should be more dimensional than categorical (Lahey, Waldman, & McBurnett, 1999b). However, a cutoff age of 10 years has been maintained in DSM-5 for distinguishing between the childhood- and adolescent-onset subtypes (APA, 2013).

Accurately pinpointing the age at which a child first showed severe conduct problems is often challenging because of difficulties in the retrospective recall of past behaviors, especially for older adolescents (Moffitt et al., 2008). The typical method for establishing age of onset in research is to collect information from multiple sources (e.g., youth self-report, parent report, official

records) and to use the youngest age reported across those sources (Dandreaux & Frick, 2009). The use of both parent and child reports to determine the earliest age of the first serious conduct problem is supported by research showing that parent report and adolescent self-report showed similar median age of onset for antisocial behaviors, and that both were independently correlated with external criteria (e.g. severity of impairment; Lahey, Miller, Gordon, & Riley, 1999). In addition, Farrington, Barnes, and Lambert (1996) reported that self-report may tap behaviors that may not have come to the attention of authorities or parents. Alternatively, parental report and record reviews may capture behaviors to which youth may be unwilling to admit.

Another issue with this broad subtyping approach is that there appear to be important distinctions that can be made *within* the childhood-onset group. First, not all youth with childhood-onset CD continue to show problems into adulthood; at least some show problems that are limited to childhood (Odgers et al., 2007; Tremblay, 2003). For example, those on such a "childhood-limited" pathway, who constituted 24.3% of the Dunedin sample, were found to experience few physical or mental health problems as adults, with the possible exception of internalizing problems among men in middle adulthood (Odgers et al., 2008). Second, although the childhood-onset group generally tends to show more dispositional risk factors than the adolescent-onset group, the type of dispositional risk factors may vary for subgroups of children and adolescents *within* the childhood-onset group (Frick & Viding, 2009). This latter finding has led to research exploring other methods for distinguishing subgroups within the broader category of childhood-onset CD.

Subtypes Based on Co-Occurring Conditions

Other attempts to separate unique subgroups within the childhood-onset type focus on the presence of co-occurring conditions, such as ADHD (Lynam, 1996). Children with comorbid ADHD and conduct problems show a more severe and aggressive pattern of antisocial behavior than do children with conduct problems alone (Lilienfeld & Waldman, 1990; Waschbusch, 2002). In addition, the combination of ADHD and conduct problems predicts poorer outcomes, including higher rates of adolescent delinquency and adult arrests (Babinski, Hartsough, & Lambert, 1999; Loeber, Brinthaupt, & Green, 1990). This approach to subtyping is also limited, however, as the vast majority of children with childhood-onset CD show comorbid ADHD, especially those referred for treatment (Abikoff & Klein, 1992). As a result, this method of subtyping often fails to designate a group of youth that is very distinct from the larger group defined by an early age of onset.

Subtypes Based on Aggression

Another approach to subtyping children within childhood-onset CD is to distinguish between those with aggressive and those with nonaggressive behavior problems (APA, 1980; Frick et al., 1993). More recent extensions of this approach focus on the two distinct types of aggressive behavior exhibited by children or adolescents with aggressive conduct problems (Poulin & Boivin, 2002). Specifically, "reactive" aggression is characterized by impulsive, defensive responses to a real or perceived provocation or threat. In contrast, "proactive" or "instrumental" aggression is not associated with provocation, but is defined as aggression in pursuit of an instrumental goal (i.e., for gain) and is usually premeditated and planned (Dodge & Pettit, 2003).

Reactive and proactive aggression show different correlates. For example, proactive aggression is more highly correlated with delinquency and alcohol abuse in adolescence, as well as criminality in adulthood (Pulkkinen, 1996; Vitaro, Brendgen, & Tremblay, 2002), whereas reactive aggression is more highly correlated with school adjustment problems and peer rejection (Poulin & Boivin, 2000; Waschbusch, Willoughby, & Pelham, 1998). The two types of aggression are also associated with different social-cognitive and emotional characteristics. Specifically, proactive aggression is associated with a tendency to overestimate the possible positive consequences of aggressive behavior and to underestimate the probability of getting punished for bad behavior (Price & Dodge, 1989; Schwartz et al., 1998), whereas reactive aggression is associated with a tendency to attribute hostile intent to ambiguous provocations by peers and to difficulties with developing nonaggressive solutions to problems in social encounters (Crick & Dodge, 1996; Hubbard, Dodge, Cillessen, Coie, & Schwartz, 2001). Also, heightened physiological reactivity to perceived provocation often accompanies reactive aggression, but not proactive aggression (Hubbard et al., 2002; Muñoz, 2009; Pitts, 1997).

The utility of the proactive–reactive aggression distinction is hotly debated, despite evidence supporting their distinct correlates (Bushman & Anderson, 2001;

Walters, 2005). A primary concern is the high correlation between the two types of aggression. Two meta-analyses suggest that reactive and proactive types of aggression are correlated in the .64 to .68 range in samples of children and adolescents (Card & Little, 2006; Polman, Orobio de Castro, Koops, van Boxtel, & Merk, 2007). In studies that have explored this relationship, a distinct pattern of overlap between the two types of aggression has emerged. There appear to be two groups of aggressive children: The first shows both proactive and reactive aggressive behavior, and the second group is less aggressive overall and shows only the reactive type of aggression (Crapanzano, Frick, & Terranova, 2010; Dodge & Coie, 1987; Frick, Cornell, Barry, Bodin, & Dane, 2003; Muñoz, 2009; Pitts, 1997). Thus it is possible that differences between the two types of aggression are largely due to more severe aggression in the proactive group.

Callous–Unemotional Traits

Another attempt to define meaningful subgroups of children and adolescents within childhood-onset conduct problems is based on a long history of clinical research showing that psychopathic traits designate an important subgroup of antisocial adults (Cleckley, 1941; Hare, 1993; Lykken, 1995). Historically, the study of psychopathic traits has not focused solely on these individuals' antisocial behavior, but instead emphasizes their affective (e.g., lack of empathy, lack of guilt, shallow emotions) and interpersonal (e.g., egocentricity, callous use of others for own gain) style. Importantly, antisocial adults who also manifest the affective and interpersonal facets of psychopathy show a much more severe, violent, and chronic pattern of antisocial behavior than those who do not (Hare & Neumann, 2008). They also show very different affective, cognitive, and neurological characteristics from those of antisocial individuals without these traits (Blair, Mitchell, & Blair, 2005; Newman & Lorenz, 2003; Patrick, 2007).

Over the past several decades, there have been various attempts to use the affective and interpersonal traits of psychopathy to designate a distinct group of children and adolescents with conduct problems (Forth, Hart, & Hare, 1990; Frick, 2009; McCord & McCord, 1964; Quay, 1964). For example, this approach was the basis for the distinction between "socialized" and "undersocialized" forms of CD that was made in DSM-III (APA, 1980). The following quotation from DSM-III describes the characteristics of the undersocialized type of CD, illustrating its link to the adult construct of psychopathy:

> The Undersocialized types [of CD] are characterized by a failure to establish a normal degree of affection, empathy, or bond with others. Peer relationships are generally lacking, although the youngster may have superficial relationships with other youngsters. Characteristically, the child does not extend himself or herself for others unless there is an obvious immediate advantage. Egocentrism is shown by readiness to manipulate others for favors without any effort to reciprocate. There is generally a lack of concern for the feelings, wishes, and well-being of others, as shown by callous behavior. Appropriate feelings of remorse are generally absent. Such a child may readily inform on his or her companions and try to place blame on them. (APA, 1980, p. 45)

Research on the undersocialized subtype of CD supported its validity, in that adolescents who were classified as such tended to have poorer adjustment in juvenile institutions and were more likely to continue to show antisocial behavior into adulthood compared to other adolescents with CD (Frick & Loney, 1999; Quay, 1987). The undersocialized group was also more likely to show several neurophysiological correlates to their antisocial behavior, such as low serotonin levels and autonomic irregularities (Lahey, Hart, Pliszka, Applegate, & McBurnett, 1993; Quay, 1993; Raine, 1993).

Despite the promising research findings for this subtyping approach, in practice there was considerable confusion over the core features that should define the undersocialized subgroup and differentiate it from other groups of antisocial youth. This confusion was due to two issues. First, in an attempt to avoid using the pejorative term "psychopathy," the term "undersocialized" was used. Unfortunately, this term did not clearly describe the affective or interpersonal features of psychopathy and led to other connotations (e.g., that such a child was not well socialized by parents or was unable to form relationships with peers). Second, the operational definition for the undersocialized subgroup that was provided in the DSM-III listed several indicators, of which no more than one could be present. This list included only one symptom specific to the affective and interpersonal dimensions of psychopathy (i.e., "apparently feels guilt or remorse when such a reaction is appropriate (not just when caught or in difficulty)"; APA, 1980, p. 48). The other four symptoms focused on indicators of social attachment (e.g., " has one or

more peer group friendships that have lasted over six months," "avoids blaming or informing on companions") that have not proven to be reliable indicators of the affective and interpersonal features of psychopathy (Frick, 2009).

This method for classifying subgroups of children with CD was not continued in later editions of the DSM, due to these definitional problems. However, a significant body of contemporary research has emerged refining how the key features associated with psychopathy may be expressed in children and adolescents, and demonstrating the clinical and etiological importance of using these features to designate a distinct subgroup of antisocial youth. Specifically, there appears to be a subgroup of antisocial children and adolescents who show a "callous" (e.g., lack of empathy, absence of guilt, uncaring attitudes) and "unemotional" (e.g., shallow or deficient emotional responses) interpersonal style (Kahn, Frick, Youngstrom, Findling, & Youngstrom, 2012). Youth with childhood-onset CD show higher levels of these callous–unemotional (CU) traits than youth in the adolescent-onset group do (Dandreaux & Frick, 2009; Silverthorn, Frick, & Reynolds, 2001). However, CU traits designate an important subgroup *within* the childhood-onset group (see Figure 3.1). For example, CU traits predict a more severe, stable, and aggressive pattern of behavior within youth who show severe early conduct problems (Kahn et al., 2012; McMahon, Witkiewitz, Kotler, & Conduct Problems Prevention Research Group, 2010; Rowe et al., 2009). Children and adolescents with CU traits also show a more severe and pervasive pattern of aggressive behavior that is more proactive in nature (Flight & Forth, 2007; Frick et al., 2003; Kruh, Frick, & Clements, 2005). Frick, Ray, Thornton, and Kahn (2014) have provided a comprehensive review of research documenting several other emotional, cognitive, personality, and social differences between antisocial youth with and without CU traits. This research is discussed in more detail later in this chapter.

The subtyping of youth with CD on the basis of the presence–absence of CU traits may help to integrate and advance many of the previous subtyping methods. First, although CU traits are more likely to be present in the childhood-onset type, there is also significant support for their predictive utility, even after researchers have controlled for the age of onset of serious antisocial behavior (Loeber et al., 2005; McMahon et al., 2010; Stickle, Kirkpatrick, & Brush, 2009; Vitacco, Caldwell, Van Rybroek, & Gabel, 2007). For example,

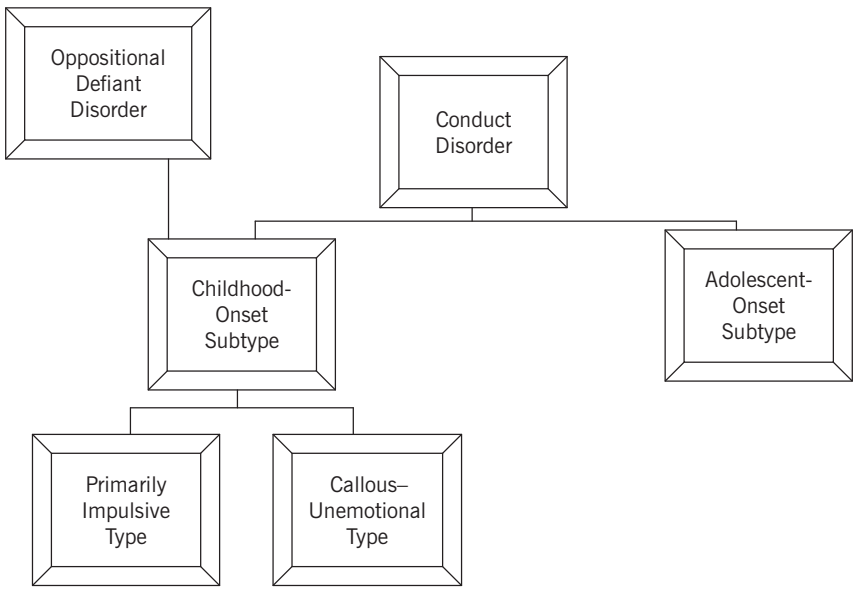

FIGURE 3.1. Developmental pathways to conduct problems.

in a large high-risk community sample ($N = 754$), McMahon and colleagues (2010) reported that CU traits assessed in seventh grade significantly predicted adult antisocial outcomes (e.g., arrests, antisocial personality symptoms), even after controls for diagnoses of ADHD, ODD, CD, and a childhood onset to CD. Second, CU traits seem to be important for designating a subgroup of youth with both CD and ADHD. For example, Barry and colleagues (2000) found that clinic-referred children with ADHD, conduct problems, and CU traits differed from those with ADHD and conduct problems without CU traits by showing a distinct temperamental style characterized by low fearfulness and high reward dominance. Finally, as noted above, children and adolescents with CU traits are more likely to show the combination of reactive and proactive aggression that has also been used to designate an important subgroup of youth with conduct problems. Unfortunately, it is not clear whether the poor outcomes for children with this severe pattern of aggressive behavior are better predicted by the aggressive behavior itself or by the presence of CU traits. However, some of the social-cognitive deficits (e.g., a tendency to emphasize the rewarding aspects of aggressive behavior and ignore the punishments) and some of the emotional characteristics (e.g., lack of emotional responsiveness to provocation) that are associated with proactive aggression may be more specifically associated with CU traits (Muñoz, Frick, Kimonis, & Aucoin, 2008; Pardini, Lochman, & Frick, 2003).

COMMON COMORBIDITIES

In addition to the comorbidity with ADHD mentioned above, children with ODD or CD often have other types of emotional and behavioral problems. ODD in particular is frequently comorbid with a host of other disorders, including emotional disorders (Biederman, Petty, Dolan, et al., 2008; Biederman, Petty, Monuteaux, et al., 2008; Burke, Waldman, & Lahey, 2010; Garland & Garland, 2001; Harpold et al., 2007; Nock, Kazdin, Hiripi, & Kessler, 2007). For example, 10–20% of children with ODD develop internalizing disorders as preschoolers, with somewhat higher rates for older youth (among community samples, 15–46% present with comorbid major depression and 7–14% present with a comorbid anxiety disorder), particularly those with persistent ODD (Boylan, Vaillancourt, Boyle, & Szatmari, 2007). Importantly, the different symptom dimensions that form the criteria for ODD may differentially account for these common comorbid conditions (Frick & Nigg, 2012). To illustrate, a cross-sectional study of 18,415 participants in a national mental health survey in the United Kingdom (ages 5–16) reported that all three dimensions of ODD were related to CD (Stingaris & Goodman, 2009). However, the angry–irritable dimension was also related to emotional disorders; the defiant–headstrong dimension was also related to ADHD; and the spiteful–vindictive symptom was also related to indicators of CU traits (see also Drabick & Gadow, 2012; Ezpeleta, de la Osa, Granero, Penelo, & Domenech, 2012). Similar divergent predictions from the different ODD dimensions have been found longitudinally, with most studies reporting that all three dimensions predict risk for later CD, but that only the angry–irritable dimension also predicts risk for later emotional disorders (Burke, Hipwell, & Loeber, 2010; Rowe et al., 2010; Stingaris & Goodman, 2009).

As noted previously, CD (especially the childhood-onset type) shows considerable comorbidity with ADHD, with up to 41% of community children and adolescents with ODD/CD presenting with comorbid ADHD (Angold, Costello, & Erkanli. 1999). Children with comorbid CD/ODD and ADHD in childhood are at heightened risk for tobacco, alcohol, and illicit drug use in adolescence compared with controls, particularly when CD symptoms are persistent (Molina & Pelham, 2003; Wilens et al., 2011). Moreover, results from a national survey conducted in the Netherlands found that conduct problems fully explained the relationship between ADHD and alcohol use disorder (Tuithof, ten Have, van den Brink, Vollebergh, & de Graaf, 2012). CD also often co-occurs with anxiety and mood disorders (Boylan et al., 2007). It is estimated that one-third of children in the community and three-quarters of those who are clinic-referred with CD meet diagnostic criteria for a comorbid depressive and/or anxiety disorder (Russo & Beidel, 1994; Zoccolillo, 1993). The development of internalizing problems, particularly depression, among youth with conduct problems has been attributed to their frequent interpersonal conflicts (e.g., with parents, peers, teachers, and police) and to other stressors (e.g., family dysfunction, school failure) that often result from the youth's problematic behavior (Capaldi, 1991; Frick, Lilienfeld, Ellis, Loney, & Silverthorn, 1999). Much of the overlap between CD and internalizing problems may be attributed to co-occurring ODD (Loeber, Burke, & Pardini, 2009). Specifically,

the presence of the angry and irritable ODD symptoms may help to designate a group of children with CD who have problems with emotional regulation (Frick & Morris, 2004; Lahey & Waldman, 2003), which may place them at particular risk for developing emotional disorders (Burke, Hipwell, & Loeber, 2010; Drabick & Gadow, 2012; Ezpeleta et al., 2013; Rowe et al., 2010).

DEFINITIONAL AND DIAGNOSTIC ISSUES

As discussed in the "Core Symptoms" section above, there is support for recognizing three important symptom domains within ODD, as reflected in the DSM-5 criteria (see Table 3.1): angry/irritable mood, argumentative/defiant behavior, and vindictiveness. Another important indicator of the severity of ODD appears to be how pervasive the behaviors are across situations (i.e., at home, at school, with peers). Youngstrom (2011) conducted secondary data analyses on 292 clinic-referred youth diagnosed with ODD. Of those meeting criteria for ODD, 11% showed impairment only at home, 27% in two settings, and 62% in all three settings. Most importantly, the minority who reportedly had impairments only at home still showed significant problems in adjustment, albeit not as significant as the problems shown by those with impairments in two or more settings. Furthermore, those impaired in two settings showed fewer problems in adjustment than those impaired in all three settings. Similarly, ODD reported by parents alone has been associated with significant problems in adjustment, albeit not as severe as when it was reported by multiple informants (Drabick, Gadow, & Loney, 2007). Finally, Wakschlag and colleagues (2007) found that it was not unusual for preschool children with ODD to show problems in only one of three interactional contexts (i.e., two with a parent and one with an experimenter); however, those who showed problems in more than one setting had more severe behavioral disturbance.

With respect to CD, the importance of recognizing the utility of CU traits for distinguishing a distinct subgroup of youth is reflected by the incorporation of these traits into the diagnosis of CD in DSM-5. DSM-5 includes a specifier to CD for children "with limited prosocial emotions" (see Table 3.2). Specifically, for children who meet criteria for CD, the specifier would be given if the child persistently shows two or more of the following characteristics over at least 12 months and in multiple relationships and settings:

- Lack of remorse or guilt
- Callous—lack of empathy
- Lack of concern about performance (at school, at work, or in other important activities)
- Shallow or deficient affect

One of the driving concerns that led to referring to this constellation of traits as "with limited prosocial emotions" was the pejorative connotation associated with the term "callous–unemotional" (see Frick & Nigg, 2012). Although there is no research directly testing the effects of the label "CU traits," there is an empirical literature studying the negative effects of the use of the term "psychopathy" when applied to children and adolescents (for a review, see Murrie, Boccaccini, McCoy, & Cornell, 2007). To summarize, the findings indicate that the term "psychopathy" does affect the decisions made by professionals (e.g., clinicians' estimation of treatability), but it does not have any more negative effects than using the term "conduct disorder" itself. Thus it appears that any term used to describe individuals with antisocial behavior or traits will acquire negative connotations. Also, as noted above, previous attempts to capture CU traits in DSM used the term "undersocialized" to minimize the potentially stigmatizing effects of the label. It is not clear, however, that this term has any fewer negative connotations than the others; moreover, its lack of clarity led to considerable variability in how the construct was conceptualized and assessed by researchers and clinicians. Finally, there is a danger in using terms that appear to connote a less severe disturbance (e.g., "uncaring") for the specifier, in an effort to decrease the potential for stigmatization. Such definitions could actually be more harmful by leading clinicians to assign formal diagnoses to children and adolescents who are less impaired. These considerations led to the choice of "with limited prosocial emotions" for the specifier for CD in DSM-5; this label reflects the focus of the criteria on the absence of guilt, a callous lack of empathy, and the lack of interest in living up to others' expectations, which are characteristics whose primary function is to promote prosocial behavior (Eisenberg & Miller, 1987).

DEVELOPMENTAL COURSE AND PROGNOSIS

The development of ODD and CD can vary greatly across subgroups of youth with these disorders. Many investigators consider ODD to be a developmental pre-

cursor to CD, especially for those with a childhood onset (Burke, Waldman, & Lahey, 2010; Moffitt et al., 2008). In many children with childhood-onset CD, ODD emerges first, followed by the onset of mild CD symptoms as early as preschool or early elementary school. Over the course of childhood and into adolescence, these behaviors gradually escalate into patterns of increasingly frequent and severe conduct problems (Kim-Cohen et al., 2009; Loeber, Lahey, & Thomas, 1991; Shaw, Gilliom, Ingoldsby, & Nagin, 2003). Beauchaine, Hinshaw, and Pang (2010) further explain that the typical developmental course for delinquent behavior in boys begins with severe hyperactive–impulsive behaviors in early childhood, followed by ODD at preschool age, childhood-onset CD at elementary school age, substance-related disorders in adolescence, and antisocial personality disorder in adulthood. However, a large proportion of children with ODD do not go on to develop CD (Maughan, Rowe, Messer, Goodman, & Meltzer, 2004; Rowe, Maughan, Pickles, Costello, & Angold, 2002). To illustrate, in the Developmental Trends longitudinal study, approximately three-quarters of children diagnosed with ODD did not exhibit CD within 3 years (Hinshaw, Lahey, & Hart, 1993).

Extensive research supports divergent life course trajectories for childhood- versus adolescent-onset CD. Specifically, beyond adolescence the antisocial and criminal behavior of individuals with childhood-onset CD tends to be more severe than that of persons with adolescent-onset CD (Odgers et al., 2007). For example, in a prospective study of the adult outcomes of a birth cohort in New Zealand (i.e., Dunedin Study), Odgers and colleagues (2008) compared two groups of adults (age 32) who had severe conduct problems as youth. The childhood-onset group (those who began showing serious problems prior to puberty) made up only 10.5% of the male and 7.5% of the female birth cohort. Compared with the adolescent-onset group, which made up 19.6% of the male and 17.4% of the female birth cohort, childhood-onset men were over four times more likely to be convicted of a violent offense between the ages of 26 and 32, and women were almost four times more likely to engage in informant-reported violence (official convictions not available) and six times more likely to engage in intimate-partner violence. A prior follow-up of the men in this cohort demonstrated that at age 26 the childhood-onset group accounted for 43% of violent convictions, 40% of drug convictions, and 62% of convictions for violence against women in the sample. In contrast, the adolescent-onset group was 50–60% less likely to be convicted of an adult offense, and their offenses tended to be less serious (e.g., minor theft, public drunkenness) and less violent (e.g., accounting for 50% of the convictions for property offenses) (Moffitt et al., 2002). As noted previously, youth with conduct problems emerging in adolescence continue to show antisocial behavior and impairments in adjustment (e.g., financial problems) that persist into adulthood, but that are less related to enduring psychosocial vulnerabilities (e.g., neuropsychological impairments, deficits in social skills) and are usually direct consequences of their antisocial behaviors (e.g., poor educational attainment, criminal records) (Moffitt & Caspi, 2001; Moffitt et al., 2002).

The subgroup of children with CU features seems to exhibit a particularly stable pattern of antisocial behavior. For example, Byrd, Loeber, and Pardini (2012) reported that parent and teacher-rated CU traits at age 7 predicted criminal behavior at age 25 among a sample of boys (N = 503), even after the researchers controlled for childhood ODD, CD, and ADHD. Similarly, two studies report that CU traits in childhood are significantly associated with measures of psychopathy in adulthood, after controls for childhood conduct problems and other risk factors for antisocial behavior (Burke, Loeber, & Lahey, 2007; Lynam, Caspi, Moffitt, Loeber, & Stouthamer-Loeber, 2007).

EPIDEMIOLOGY

Prevalence

It is estimated that between 2 and 16% of youth in community settings present with significant conduct problems (i.e., ODD and/or CD), with higher estimates within clinic settings (Boylan et al., 2007; Loeber, Burke, Lahey, Winters, & Zera, 2000). A recent meta-analysis of the worldwide prevalence of both ODD and CD among children and adolescents ages 6–18 years reported overall pooled prevalence estimates of 3.3% for ODD and 3.2% for CD, based on epidemiological surveys (Canino, Polanczyk, Bauermeister, Rohde, & Frick, 2010). These estimates did not vary significantly across countries, but did vary depending on the restrictiveness of the criteria used to make the diagnosis. As would be expected, definitions that did not require substantial impairment to be associated with the conduct problems resulted in higher prevalence estimates.

Sex Differences

Most studies find that boys are more likely to show conduct problems than girls. However, gender differences in the prevalence of conduct problems vary somewhat across development. At preschool age, gender differences are small and sometimes nonexistent. Prevalence estimates indicate that ODD is diagnosed at an equivalent rate between boys and girls (Keenan & Shaw, 1997; Maughan et al., 2004). This changes at school age, when ODD and CD are both two to three times more likely to be diagnosed in boys than in girls (Lavigne, Lebailly, Hopkins, Gouze, & Binns, 2009; Moffitt, Caspi, Rutter, & Silva, 2001). This gap closes to about 2:1 by adolescence, when both boys and girls show a dramatic increase in the rates of ODD and CD (Loeber et al., 2000).

It is unclear whether developmental changes in prevalence rates are real differences or are artifacts of diagnostic criteria that are insensitive to sex differences in the expression of conduct problems. An important topic of debate is whether or not there should be gender-specific criteria for CD. Two specific potential sources of bias in the existing CD criteria have been considered (Frick & Nigg, 2012). First, some question whether the threshold for the diagnosis of CD (i.e., three symptoms) is too high for girls. This has led some to propose that gender-specific thresholds should be used (Zoccolillo, Tremblay, & Vitaro, 1996). Girls with one or two CD symptoms show impairments in their functioning both concurrently (Keenan, Wroblewski, Hipwell, Loeber, & Stouthamer-Loeber, 2010) and predictively (Messer, Goodman, Rowe, Meltzer, & Maughan, 2006). Although girls with subclinical levels of CD are at risk for current and future impairment, the three-symptom threshold still designates a substantially more impaired group than those with either one or two symptoms (Keenan et al., 2010).

A second consideration is whether the symptoms that form the CD criteria should be broadened to include the types of conduct problems that are more likely to be exhibited by girls. Namely, when girls behave aggressively, they exhibit indirect or relational forms of aggression (e.g., spreading rumors, attempts to harm one person's relationships with others) more often than physical forms of aggression (e.g., attempts to physically harm others) (Crapanzano et al., 2010; Underwood, 2003). In support of this proposition, a significant number of girls who show relational, but not physical, aggression present with impaired social functioning (i.e., bullying) and display a number of other risk factors often associated with CD (e.g., anger dysregulation, impulsivity; Crapanzano et al., 2010). In one of the few studies directly testing the incremental utility of relational aggression to the criteria for ODD and CD in girls, girls scoring high on relational aggression also exhibited higher rates of ODD and CD symptoms (Keenan, Coyne, & Lahey, 2008). However, those girls scoring high on relational aggression but without either diagnosis were not significantly more impaired than those who were not high on relational aggression. Thus the research basis does not appear strong enough at present to warrant developing gender-specific criteria for CD (Frick & Nigg, 2012; Moffitt et al., 2008).

One additional issue related to the cross-gender diagnosis of CD relates to the relevance of the current subtypes. A robust finding is that childhood-onset CD occurs less frequently in girls than in boys (Moffitt & Caspi, 2001; White & Piquero, 2004). For example, in an entire birth cohort of New Zealand children, only six girls with childhood-onset CD were identified, in contrast to larger groups of adolescent-onset girls (n = 78), childhood-onset boys (n = 47), and adolescent-onset boys (n = 122; Moffitt & Caspi, 2001). Similarly, in an adjudicated sample of adolescent boys and girls, an almost equal number of boys had a childhood onset (46%) or adolescent onset (54%) to their severe antisocial behavior, whereas 94% of girls had an adolescent onset to their antisocial behavior (Silverthorn et al., 2001). Despite the predominance of adolescent-onset CD in girls, there is evidence that these girls present with a large number of the dispositional and contextual risk factors associated with childhood-onset CD in boys (Frick & Dickens, 2006). For example, girls with CD often show poor outcomes in adulthood, such as high rates of criminality, violence, antisocial personality disorder, and other psychiatric disorders (Zoccolillo, 1993).

To reconcile these findings, Silverthorn and Frick (1999) have proposed that a small number of girls may show a childhood onset to their conduct problem behavior and may present similarly to boys with childhood-onset CD. However, despite having early risk factors similar to those of childhood-onset boys, girls with CD are more likely to show an adolescent onset to their conduct problems, which Silverthorn and Frick have described as a "delayed-onset pathway" to CD. They propose that among girls with predisposing vulnerabilities (e.g., CU traits, problems in emotional regulation), severe conduct problem behavior is often

delayed until adolescence, coinciding with biological (e.g., hormonal changes associated with puberty) and psychosocial (e.g., less parental monitoring and supervision, greater contact with deviant peers) changes that encourage these behaviors. In an initial test of this theory, adjudicated adolescent girls who largely showed an adolescent onset to their conduct problems also showed high levels of CU traits, problems with impulse control, and several other social and temperamental vulnerabilities that were more similar to those of childhood-onset boys than to those of adolescent-onset boys (Silverthorn et al., 2001). Despite this initial positive finding, additional tests of this model have been mixed (Moffitt & Caspi, 2001; Odgers et al., 2008; White & Piquero, 2004). Thus the possibility of a delayed-onset trajectory in girls does not appear to currently have the support necessary for integration into diagnostic classification systems for CD.

Cultural Variations

The evidence for cultural variations in ODD and CD is mixed. A review of 25 epidemiological studies conducted in 16 different countries found highly consistent prevalence rates for ODD and CD across countries that differed in their cultural composition (Canino et al., 2010). However, within the United States, higher rates of conduct problems in African American youth have been found in some samples (Fabrega, Ulrich, & Mezzich, 1993) but not others (McCoy, Frick, Loney, & Ellis, 2000). Also, lower rates of CD have been reported for Americans of Asian descent than for European Americans and African Americans (Compton, Conway, Stinson, Colliver, & Grant, 2005). More importantly, it is unclear whether any association between minority status and conduct problems is independent of the fact that some ethnic minorities are more likely to experience economic hardships and live in urban neighborhoods with higher concentrations of crime than nonminority individuals (Lahey, Waldman, & McBurnett, 1999). With the growing immigrant populations in the United States, risk for CD appears to vary according to migration status and level of exposure to American culture. For example, a study found that risk for CD was highest among Mexican American children of U.S.-born parents (odds ratio = 7.64), compared with Mexican-born immigrants raised in the United States (odds ratio = 4.12) and the general population of Mexico (odds ratio = 0.54; Breslau, Saito, Tancredi, Nock, & Gilman, 2012).

RISK AND PROTECTIVE FACTORS

A significant amount of research focuses on understanding the causes of childhood and adolescent conduct problems. This is not surprising, given the associated levels of current and future impairment, as well as the significant costs to society incurred by the criminal and violent behavior that often accompanies conduct problems (for reviews, see Dodge & Pettit, 2003; Frick & Viding, 2009; Moffitt, 2006). This research has resulted in a long list of factors that have been identified as placing a child at risk for acting in an antisocial or aggressive manner (see Table 3.3). They include such dispositional risk factors as genetic predispositions; neurochemical (e.g., low serotonin) and autonomic (e.g. low resting heart rate) irregularities; neurocognitive deficits (e.g., deficits in executive functioning); deficits in the processing of social information (e.g., cognitive biases); temperamental vulnerabilities (e.g., poor emotional regulation); and personality predispositions (e.g., impulsivity). In addition, there are multiple contextual risk factors, including prenatal factors (e.g., exposure to toxins); characteristics of the early environment (e.g., poor-quality child care); family variables (e.g., ineffective discipline, poor attachment); peer variables (e.g., association with deviant peers); and neighborhood characteristics (e.g., high levels of violence exposure). Importantly, ODD and CD typically show the same dispositional and environmental risk factors (Boden, Fergusson, & Horwood, 2010; Rowe et al., 2002).

Although research has been very successful in documenting risk factors for ODD and CD, their number and diversity have led to great debate over the best way to integrate them into a coherent, yet comprehensive, causal model for the development of severe conduct problems. This debate has arisen both because the sheer number of factors is so large and because they involve so many different types of causal processes. There are a few points of agreement, however. First, to adequately explain the development of aggressive and antisocial behaviors associated with conduct problems, causal models must consider the potential role of multiple risk factors. Second, risk factors are also typically not independent of each other and are likely to operate in a transactional fashion (e.g., with one risk factor having an influence on another risk factor) or a multiplicative fashion (as in the case of gene–environment interactions) (Dodge & Pettit, 2003). For example, Jaffee and colleagues (2005) found that childhood-onset conduct problems were more common among chil-

TABLE 3.3. Summary of Risk Factors by Conduct Problem Subtype

Risk factor	ODD	Childhood-onset CD	Adolescent-onset CD	CU traits
Biological				
• Genetic	✓	✓	> ✓	< ✓
• Anterior and posterior cingulate cortex development				✓
• Abnormal prefrontal cortex response				✓
• Reduced amygdala activity				✓
Psychophysiological/neuroendocrine				
• Blunted emotional reactivity				✓
• Blunted cortisol reactivity				✓
Temperamental				
• Emotion dysregulation	✓	✓		
• Insensitivity to distress				✓
• Fearlessness/low anxiety				✓
• Impulsivity	✓	✓		✓
Cognitive/neurocognitive				
• Executive functioning deficit		✓		
• Low verbal IQ		✓		
• Hostile attribution bias		✓		
• Positive outcome expectancies				✓
• Impaired moral reasoning				✓
• Blame externalization				✓
• Response modulation deficit/reversal learning deficit				✓
• Less traditionalism/greater rebellion			✓	
Prenatal				
• Toxin exposure	✓	✓		
Familial				
• Low socioeconomic status	✓	✓	✓	
• Family stress/conflict/instability	✓	✓	✓	
• Maternal depression	✓	✓		
• Parental separation	✓	✓		
• Dysfunctional parenting (e.g., harsh, inconsistent)	✓	✓	✓	
• Poor supervision/monitoring/low involvement	✓	✓	✓	
• Low parental warmth				✓
• Disorganized attachment		✓		✓
Peer				
• Deviant peer affiliation		✓	✓	< ✓
• Peer rejection	✓	✓		
• Bullying	✓	✓	✓	< ✓
Neighborhood				
• Violence exposure	✓	✓		
• Poor neighborhood quality/disorder	✓	✓		

Note. Checkmarks are used to indicate risk factors that have been identified as being associated with the specific conduct problem subtype.

dren with a genetic vulnerability to problem behavior who were also exposed to maltreatment. Third, causal models must consider the possibility that subgroups of youth with conduct problems may have distinct causal mechanisms underlying their antisocial and aggressive behaviors. Finally, causal models need to integrate research on the development of conduct problems with research on normally developing youth. For example, research suggests that the ability to adequately regulate emotions and behaviors and the ability to feel empathy and guilt towards others play a role in the development of CD (Frick & Viding, 2009). As a result, understanding the processes involved in the normal development of these abilities is critical for understanding how they may go awry in some children and place them at risk for acting in an aggressive or antisocial manner.

In this section, we provide a causal model for ODD and CD by attempting to integrate previously reviewed research on CD subtypes with the research on the diverse array of risk factors associated with conduct problems. Furthermore, we take a developmental psychopathology approach by linking these risk factors to the specific developmental mechanisms that may lead to the problem behavior.

Dispositional Risk Factors

Genetic Influence

Research employing behavior genetic designs suggests that conduct problems are under at least moderate genetic influence (h^2 = .53–.54; Bornovalova, Hicks, Iacono, & McGue, 2010; Gelhorn et al., 2005). This influence is stronger for aggressive childhood conduct problems (h^2 = .60) than for nonaggressive conduct problems (h^2 = .49; Eley, Lichtenstein, & Stevenson, 1999), and for the childhood-onset subtype than for the adolescent-onset subtype of CD (Moffitt, 2003, 2006). Such findings support the view that the development of conduct problems in the adolescent-onset group is less related to dispositional factors and more related to environmental influences. For those youth with conduct problems and comorbid disorders (e.g., ADHD), research suggests that common genetic factors often explain much of the comorbidity (Bornovalova et al., 2010).

Importantly, the genetic influence on childhood-onset CD seems to be substantially accounted for by youth with significant levels of CU traits (Larsson, Andershed, & Lichtenstein, 2006; Taylor, Loney, Bobadilla, Iacono, & McGue, 2003). The most direct support for this contention comes from a large twin study of 7-year-old children, which reported that the heritability of conduct problems for children high on CU traits was over twice as great (.81) as for children low on CU traits (.30; Viding, Blair, Moffitt, & Plomin, 2005). Differences in heritability could not be attributed to the severity of conduct problems or to levels of impulsivity–hyperactivity (Viding et al., 2005; Viding, Jones, Frick, Moffitt, & Plomin, 2008). In attempting to explore the genetic contributions to CU traits, another twin study reported that left posterior cingulate and right dorsal anterior cingulate gray matter concentrations showed significant heritability (.46 and .37, respectively), and that common genetic factors explained the phenotypic relationship between these regions and CU traits in a sample of boys (Rijsdijk et al., 2010). These data suggest that the genetic contribution to CU traits may be manifested, at least in part, through an impact on anterior and posterior cingulate cortex development.

A particularly promising area of research is investigating potential genetic polymorphisms associated with CU traits. T. Fowler and colleagues (2009) reported that among adolescents (ages 12–19) with childhood ADHD, those either possessing a low-activity monoamine oxidase A receptor (MAOA) allele, homozygous for the low-activity serotonin transporter (5-HTT) allele, or possessing the high activity catechol-*O*-methyltransferase (COMT) Val/Val genotype demonstrated significantly higher levels of CU traits. Also, in a study of 162 children and adolescents (ages 6-16), CU traits were associated with two polymorphisms on the oxytocin receptor (OXTR) gene (Beitchman et al., 2012). Specifically, CU traits were associated with the haplotypes consisting of the OXTR_rs237885 A allele and OXTR_rs2268493es A allele. Since few molecular genetic studies have been undertaken, conclusions about potential genetic polymorphisms that may be related to the development of CU traits should be drawn cautiously. However, these latter findings are particularly promising, given oxytocin's role in affiliation and recognition of others' emotions, both of which are impaired in individuals with CU traits (Campbell, 2010).

Emotional/Temperamental Factors

Various emotional risk factors have been associated with the development of ODD and CD, and problems in emotional regulation play an important role in many theories of their development (Frick & Morris, 2004). There is a robust relationship between ODD and a child

temperament characterized by low effortful control (i.e., poor age-appropriate self-regulation), with more modest associations with child sensory dysregulation and negative affect (Lavigne et al., 2012). Barkley (2010, 2013) has argued that this emotional dysregulation dimension of ODD is largely a consequence of the substantial overlap of ADHD with ODD. He asserts that ADHD, as a disorder of self-regulation, has an inherent deficit in emotional self-control that places children with ADHD at higher risk for comorbid ODD. This deficit in emotional regulation also results in low frustration tolerance, impatience, and quickness to anger. In addition, Barkley argues that children with "pure" ODD are likely to manifest the social conflict aspects of ODD (e.g., arguing) that may be more related to learning within coercive family processes, but are less likely to show its emotional dimension (e.g., anger, irritability, impatience) than are children with both ODD and ADHD.

With respect to CD, emotion regulation problems appear to be more strongly associated with the childhood-onset than the adolescent-onset type (Moffitt et al., 1996). However, within the childhood-onset group, those with and without a CU presentation seem to show different emotional characteristics. Specifically, those without a CU presentation seem to be highly reactive to negative emotional stimuli (Kimonis, Frick, Fazekas, & Loney, 2006; Loney, Frick, Clements, Ellis, & Kerlin, 2003; Muñoz et al., 2008) and to the distress of others (Pardini et al., 2003); they often show high rates of anxiety (Andershed, Gustafson, Kerr, & Stattin, 2002; Frick et al., 1999; Pardini, Lochman, & Powell, 2007); and they appear to be highly distressed by the effects of their behavior on others (Loney et al., 2003; Pardini et al., 2003). These findings suggest that children with conduct problems but without significant levels of CU traits may have difficulties with emotional regulation related to high levels of emotional reactivity.

In contrast, those with non-normative levels of CU traits show deficits in the processing of negative emotional stimuli—and, even more specifically, deficits in their reactivity to signals of fear and distress in others. This is evidenced by their reduced autonomic responses to others' distress (Blair, 1999), reduced recognition of fearful and sad facial expressions (Blair, Colledge, Murray, & Mitchell, 2001; Stevens, Charman, & Blair, 2001), reduced responsiveness to fearful vocal tones (Blair, Budhani, Colledge, & Scott, 2005), reduced focus on the eye region of the face when they are processing fearful expressions (Dadds, El Masry, Wimalaweera, & Guastella, 2008), and reduced attentional orienting to others' distress cues (Kimonis et al., 2006, 2008). Of note, a study by Willoughby, Waschbusch, Propper, and Moore (2011) suggests that these differences in emotional processing between groups of children with conduct problems may be evident very early in life. Specifically, 5-year-old children (n = 178) with high levels of parent-reported CU traits and symptoms of ODD were rated as less soothable and showed less negative reactivity to the "still-face" paradigm (i.e., a parental face showing no emotion or interaction with an infant) at 6 months of age, compared to those with symptoms of ODD but without a CU presentation.

Children with CU traits also tend to show lower levels of fear and anxiety (or neuroticism), especially when research has controlled for co-occurring impulsivity or conduct problems (Frick et al., 2014). For example, Pardini, Stepp, Hipwell, Stouthamer-Loeber, and Loeber (2012) reported on a longitudinal study of 1,862 girls who were ages 5–8 at the initial assessment. Girls with CD who showed significant levels of CU traits exhibited fewer anxiety problems 6 years later than girls with CD but without a CU presentation did. In another study that used a population-based sample (N = 7,000), fearless temperament at age 2 predicted both CU traits and conduct problems at age 13 (Barker, Oliver, Viding, Salekin, & Maughan, 2011). However, in follow-back analyses, youth with high levels of both conduct problems and CU traits at age 13 showed lower fearful responses to punishment cues at age 2, compared to those high on conduct problems but without a CU presentation. These emotional characteristics of children and adolescents with elevated CU traits closely resemble a temperament that has been described as "behaviorally uninhibited" or "fearless." Specifically, uninhibited children tend to seek out novel and dangerous activities, and show less physiological arousal to threats of punishments (Kagan, Reznik, & Snidman, 1988; Rothbart, 1981). Importantly, there is also evidence that children with this uninhibited or fearless temperament are at risk for problems in conscience development (Kochanska, Gross, Lin, & Nichols, 2002; Rothbart, Ahadi & Hershey, 1994), supporting the hypothesis that deficits in the normative development of conscience may be a primary developmental mechanism leading to conduct problems in children with CU traits (Frick & Viding, 2009).

Cognitive Deficits

Consistent with the findings for the other dispositional risk factors, youth with childhood-onset CD tend to

show cognitive deficits in executive functioning and low verbal intelligence (Fergusson, Lynsky, & Horwood, 1996; Kratzer & Hodgins, 1999; Piquero, 2001; Raine, Yaralian, Reynolds, Venables, & Mednick, 2002). Also consistent with findings for the other dispositional risk factors, the specific types of cognitive deficits appear to differ depending on whether or not a youth shows CU traits. Children without CU traits show more severe verbal intelligence deficits (Loney, Frick, Ellis, & McCoy, 1998) and are more likely to attribute hostile intent to the actions of peers (i.e., hostile attribution bias) than those with CU traits (Frick et al., 2003).

In contrast, children and adolescents with conduct problems and CU traits tend to expect more instrumental gain (e.g., obtaining goods or social goals) from their aggressive actions with peers (Pardini et al., 2003). They are also more impaired in their moral reasoning (Blair, 1999; Blair, Monson, & Frederickson, 2001; Dolan & Fullam, 2010). Furthermore, several studies have shown that antisocial youth high on CU traits endorse more deviant values and goals in social situations, such as viewing aggression as a more acceptable means for obtaining goals, blaming others for their misbehavior, and emphasizing the importance of dominance and revenge in social conflicts (Chabrol, Van Leeuwen, Rodgers, & Gibbs, 2011; Pardini et al., 2003; Stickle et al., 2009). On a laboratory task measuring altruistic behavior, adolescents scoring high on conduct problems and CU traits were more likely than controls were to make decisions that benefited themselves while harming others (Sakai, Dalwani, Gelhorn, Mikulich-Gilbertson, & Crowley, 2012).

Perhaps the most striking cognitive characteristics of children with CD and CU traits are found in their emotional learning of the valence of objects and actions following experiences with reinforcement and punishment. In particular, studies demonstrate that youth with high levels of CU traits perform poorly in learning tasks that require them to stop a previously rewarded response following a change in the reinforcement contingency, such that it comes to be progressively more associated with punishment (Fisher & Blair, 1998; O'Brien & Frick, 1996). Youth with CU traits also show impairments in reversal learning, involving learning to reverse the response associated with a stimulus following a change in the reinforcement contingency (Blair, Monson, & Frederickson, 2001; Budhani & Blair, 2005). These studies suggest that youth with CU traits are not simply unresponsive to punishment, as offered by early explanations for psychopathy (Lykken, 1995); more specifically, they have difficulties in reversal learning tasks involving both rewards and punishments (Budhani & Blair, 2005). Performance on these reversal learning tasks is thought to reflect the role of the orbitofrontal cortex in representing the value of the newly correct response, and this value representation should successfully guide the individual's decision making (Bechara, Damasio, & Damasio, 2000). However, the appropriate recruitment of the orbitofrontal cortex in the representation of reinforcement information may be disrupted in youth with CU traits, as suggested by findings that they show atypical orbitofrontal responses during reversal learning tasks (Finger et al., 2008).

Deficits in responding to social cues critical for moral socialization (i.e., others' distress) and in specific forms of emotional learning (i.e., stimulus–reinforcement learning) are believed to interfere with the efficient socialization of individuals with elevated CU traits (Blair, 2007; Frick & Morris, 2004). This interference is thought to underlie the deficits reported in the moral judgments made by children and adolescents with CU traits (Blair, 1999). Moreover, it probably contributes to their increased propensity to show positive outcome expectancies within aggressive situations with peers. As a result, children with CU traits are less likely to be capable of cognitively representing the negative consequences of the victims' distress.

Biological Correlates

As suggested by the behavior genetic studies reviewed previously, biological correlates also tend to be more strongly associated with childhood-onset CD; however, the types of biological correlates differ according to the presence–absence of significant levels of CU traits (Frick & Viding, 2009). Furthermore, these biological correlates tend to support the emotional and cognitive differences between groups of children and adolescents with CD that have been highlighted above. Specifically, research on psychophysiological correlates of CU traits supports the finding that children and adolescents scoring high on CU traits show blunted emotional reactivity to certain types of stimuli. For example, both Anastassiou-Hadjicharalambous and Warden (2008) and de Wied, van Boxtel, Matthys, and Meeus (2012) reported that youth with CD and CU traits showed a lower magnitude of heart rate change to emotionally evocative films, compared to youth with CD but normative levels of CU traits. Moreover, CU traits were negatively related to skin conductance reactivity during responses to peer provocation in a sample of detained

adolescent boys (Kimonis et al., 2008). Finally, children with CU traits have shown blunted cortisol reactivity to experimentally induced stress (Stadler et al., 2011).

To date, there have been three functional imaging studies of children and adolescents with high levels of CU traits. Two of these studies reported that youth with conduct problems and CU traits exhibited less right amygdala activity in response to fearful faces than controls did (Jones, Laurens, Herba, Barker, & Viding, 2009; Marsh et al., 2008). A third imaging study reported that youth with conduct problems and CU traits demonstrated abnormal responses within the ventromedial prefrontal cortex during punished reversal errors, compared to typical controls (Finger et al., 2008). These studies hold promise for potentially clarifying the neurological markers of some emotional and cognitive characteristics that distinguish children and adolescents with CU traits.

Traditionalism

A clear conclusion from this review of dispositional risk factors related to the development of severe conduct problems is that the extant research consistently suggests that most of these risk factors are more strongly related to childhood-onset than adolescent-onset CD. There is, however, one notable exception. Youth with adolescent-onset conduct problems show personality traits that endorse less traditional values, such as viewing societal rules and status hierarchies as less important (Dandreaux & Frick, 2009; Moffitt et al., 1996), and they are more rebellious, such as desiring more autonomy from parents, compared with the childhood-onset type (Piquero & Brezina, 2001). These personality features may increase the likelihood of inappropriate attempts to achieve autonomy (i.e., antisocial behavior) in adolescence that characterize the adolescent-onset group (Dandreaux & Frick, 2009).

Contextual Risk Factors

Prenatal and Early Childhood Factors

Several risk factors present early in life are associated with the development of conduct problems. Some research suggests that risk factors for future conduct problems can be identified in the mother during pregnancy or shortly after birth (Petitclerc, Boivin, Dionne, Zoccolillo, & Tremblay, 2009). For example, maternal prenatal cigarette smoking is a factor consistently associated with childhood conduct problems; however, it is not clear to what extent comorbid ADHD or the transmission of an underlying antisocial tendency from mother to child accounts for this association (D'Onofrio et al., 2010; Latimer et al., 2012; Murray, Irving, Farrington, Colman, & Bloxsom, 2010). Other risk factors that are associated with ODD or CD when they occur during the prenatal period or in the first 5 years of life include alcohol use, stress, and viral illness in the mother during the prenatal period; lead exposure; malnutrition; and adoption (Barker & Maughan, 2009; Marcus, Fulton, & Clarke, 2010; Murray et al., 2010; Petitclerc et al., 2009). The extent to which genetic factors contribute to a child's exposure to these early risk factors is not clear, however, since a parent may transmit an externalizing liability to the child that both places the child at risk for conduct problems and puts the parent at risk for engaging in impulsive and antisocial behaviors and substance abuse (Markon & Krueger, 2005).

Familial Factors

A host of risk factors within the family have been associated with ODD and CD, including low socioeconomic status (SES), parental separation, and maternal depression (Averdijk, Malti, Eisner, & Ribeaud, 2012; Goodman et al., 2011; Lavigne et al., 2012). High rates of family stress and conflict can also lead to the development of conduct problems, with ongoing stress contributing to the stability of ODD (Lavigne et al., 2011, 2012). These factors may also interact with (i.e., moderate) other risk factors in the development of conduct problems. For example, in preschoolers with symptoms of hyperactivity, maternal depression predicted the later development of ODD (Harvey, Metcalfe, Herbert, & Fanton, 2011). The association between risk factors and conduct problems may also be mediated by other, more proximal risk factors, as indicated by a study of 4-year-old community children ($N = 796$; Lavigne et al., 2012). In this study, the effect of low SES on ODD symptoms was mediated by family stress and conflict, parental depression, and parental hostility toward/lack of emotional support to a child. Furthermore, stress and conflict influenced parental depression and dysfunctional parenting, which in turn affected ODD symptoms.

The most central and consistent family influence on the development and maintenance of conduct problems is that of dysfunctional parenting practices. Across a

large number of studies, lack of parental involvement, poor monitoring and supervision, low parental warmth, failure to use positive reinforcement, high parental hostility, and the use of harsh and inconsistent discipline have been linked to the development of ODD and CD (Chamberlain, Reid, Ray, Capaldi, & Fisher, 1997; Frick, 2006; Loeber & Stouthamer-Loeber, 1986; Patterson, 1996). Importantly, dysfunctional parenting often mediates the association between other contextual factors (e.g., poverty, maternal depression, high rates of family conflict) and childhood conduct problems (see, e.g., Lavigne et al., 2011). For example, Shaw, Hyde, and Brennan (2012) found that low-income 18-month-old boys exposed to high levels of dysfunctional parenting and maternal depression were at high risk for a trajectory of early-starting and increasing antisocial behavior to age 17. Thus it is quite possible that many contextual factors have their influence on childhood conduct problems by affecting parents' ability to use effective parenting strategies to socialize their children adequately.

Failures in parental socialization of their children play a role in many theories developed to explain the etiology of childhood conduct problems (e.g., Patterson, 1996). However, as with other risk factors, the role it plays may vary across the different developmental pathways. Specifically, although several studies have reported results showing that children in the childhood-onset subgroup tend to come from homes with greater levels of family instability, with more family conflict, and with parents who use less effective parenting strategies (Aguilar, Sroufe, Egeland, & Carlson, 2000; McCabe, Hough, Wood, & Yeh, 2001; Patterson & Yoerger, 1997; Woodward, Fergusson, & Horwood, 2002), parenting factors have played an important role in theories for the development of adolescent-onset CD as well. For example, poor parental supervision and low parental involvement, especially when combined with association with deviant peers, are often viewed as being critical to the processes that lead some adolescents to be more rebellious than is normative (Moffitt, 2006; Patterson & Yoerger, 1997). For the childhood-onset type without CU traits, conduct problems are viewed as resulting from an interaction between a child's risky temperament (e.g., impulsivity, poorly regulated emotions) and exposure to a problematic socializing environment (e.g., ineffective parental discipline). This interaction disrupts the socialization of the child and leads to enduring vulnerabilities and adjustment problems across the lifespan (Patterson, 1996).

Risky temperaments are likely to originate from genetic predispositions; however, neither genetic vulnerabilities nor environmental risk factors are sufficient in themselves for the development of conduct problems. Rather, mounting evidence suggests that gene–environment interactions play an important role. For example, Lahey and colleagues (2011) found that 4- to 6-year-old children meeting diagnostic criteria for ADHD who were exposed to more negative and less positive parenting practices in early childhood showed greater CD symptoms several years later when they possessed two copies of the 9-repeat allele of the variable-number tandem repeat (VNTR) polymorphism in the 3′ untranslated region (UTR) of the dopamine transporter gene (DAT1), compared to children without this polymorphism. Similarly, Edwards and colleagues (2010) found that community-based men exposed to childhood physical discipline who carried a low-activity risk allele at the promoter region (uVNTR) of the MAOA gene, which is located on the X chromosome, were more likely to engage in delinquent behavior later in life than were males not carrying the risk allele. While children exposed to physical discipline were generally more likely to engage in delinquency, those with the polymorphism in the absence of physical discipline were not. Other studies of gene–environment interaction identify the polymorphism at the COMT Val-158Met, which is also involved in regulating dopamine levels (Albaugh et al., 2010). Together, these studies suggest that ineffective and harsh parenting interacts with a child's genotype to influence the development of conduct problems (see Dodge, 2009).

The extent to which gene–environment interactions relate to the development of conduct problems in children with CU traits is less well understood. Moreover, the role of parenting in the development of conduct problems appears to be quite different for children with CU traits. Specifically, research consistently demonstrates that harsh, inconsistent, and coercive discipline is more highly associated with conduct problems in youth scoring low on CU traits (Edens, Skopp, & Cahill, 2008; Hipwell et al., 2007; Oxford, Cavell, & Hughes, 2003; Pasalich, Dadds, Hawes, & Brennan, 2012; Wootton, Frick, Shelton, & Silverthorn, 1997; Yeh, Chen, Raine, Baker, & Jacobson, 2011). In contrast, low warmth in parenting appears to be more highly associated with conduct problems in youth with CU traits (Kroneman, Hipwell, Loeber, Koot, & Pardini, 2011; Pasalich et al., 2012). Research also documents that dysfunctional parenting practices are related

directly to CU traits themselves (Barker et al., 2011; Waller et al., 2012). For example, in a prospective longitudinal study of a population-based sample (N = 7,000), harsh parenting at age 4 significantly predicted CU traits at age 13, accounting for 10% and 14% of the variance in these traits in boys and girls, respectively (Barker et al., 2011). However, the direction of influence between parenting practices and CU traits is not clear. In the few longitudinal studies that have tested potential bidirectional effects of parenting and child characteristics, CU traits have been more predictive of changes in parenting over time than parenting has been predictive of changes in CU traits over time (Hawes, Dadds, Frost, & Hasking, 2011; Muñoz, Pakalniskiene, & Frick, 2011).

Several studies report an association between CU traits and disorganized attachment styles (Bohlin, Eninger, Brocki, & Thorell, 2012; Fite, Greening, & Stoppelbein, 2008; Pasalich, Dadds, Hawes, & Brennan, 2011). Potentially related to the problems in attachment, Dadds, Jambrak, Pasalich, Hawes, and Brennan (2011) reported that children with high levels of CU traits made less eye contact with both mothers and fathers in free-play and "emotional talk" scenarios. In a second study, Dadds, Allen, and colleagues (2012) reported that children with conduct problems and CU traits also showed lower levels of physical and verbal affection, and made less eye contact with mothers during a task where the mothers said they loved their children and showed affection, compared to controls and children with conduct problems but without CU traits. Together, these studies led Dadds, Allen, and colleagues to suggest that a deficit in the propensity to make eye contact with an attachment figure "signals the absence of a basic building block underlying social and moral development" in children with non-normative levels of CU traits (p. 195).

Peer Relationships

Children and adolescents with ODD and CD often have problems in their peer relationships. The two most common problems are peer rejection (i.e., they have few friends and their peers actively dislike them; Dodge, Bates, & Pettit, 1990; Price & Dodge, 1989) and affiliation with deviant peers who show high levels of antisocial behavior (McCabe et al., 2001). It is less clear, however, whether these problems are differentially associated with the various developmental pathways discussed in this chapter. For example, some studies have found that youth in the adolescent-onset group have more deviant peer associations than youth in the childhood-onset group (McCabe et al., 2001), whereas other researchers have not found such differences (Dandreaux & Frick, 2009; Fergusson et al., 1996; Moffitt et al., 1996, 2002; Patterson & Yoerger, 1997). Furthermore, compared with youth scoring low on CU traits, adolescents with high levels of CU traits may be more likely to commit crimes in groups and show the highest level of association with delinquent and antisocial peers (Goldweber, Dmitrieva, Cauffman, Piquero, & Steinberg, 2011; Kimonis, Frick, & Barry, 2004; Muñoz, Frick, et al., 2008; Pardini & Loeber, 2008).

Thus problems in peer relationships (particularly association with a deviant peer group) may play a role in both childhood-onset and adolescent-onset conduct problems, and in conduct problems with and without non-normative levels of CU traits. However, the developmental processes linking the problematic peer relationships may differ across the different subgroups. For example, many theories consider association with a deviant peer group as being a critical causal process to the adolescent-onset group, with the peer group encouraging and supporting the youth's misguided attempts to achieve autonomy (Moffitt, 1993, 2006; Patterson & Yoerger, 1997). For those in the childhood-onset group (i.e., without CU traits), their problems in emotional and behavioral dysregulation and associated cognitive biases can place the youth at risk for rejection by conventional peers, depriving them of important peer socializing experiences that foster the development of social and cognitive skills (Dodge et al., 1990; Price & Dodge, 1989). Rejection by conventional peers may cause children to seek out associations with nonconventional and deviant peers, particularly when parents provide poor supervision (Coie, Terry, Zakriski, & Lochman, 1995; Dishion, Patterson, Stoolmiller, & Skinner, 1991; McCabe, Rodgers, Yeh, & Hough, 2004; Vitaro, Brendgen, Pagani, Tremblay, & McDuff, 1999).

The potential roles of peer rejection and delinquent peer affiliations for those children and adolescents with CU traits have been the subject of much less research. In one of the few studies of the friendships of youth with CU traits, Muñoz, Kerr, and Besic (2008) reported that in a population-based sample (N = 667) of adolescents (ages 12–15), those with CU traits had as many friends as other adolescents; however, the friendships were less stable and were viewed by the youth high on CU traits as more conflictual. Although the study by Muñoz and colleagues did not examine conduct

problems specifically, Kimonis and colleagues (2004) did; they similarly found that community boys and girls scoring high on CU traits and conduct problems reported having friends, but that their friends tended to be more delinquent than were the friends of youth with CU traits or conduct problems alone. Kerr, Van Zalk, and Stattin (2012) used peer network analyses to test the effects of both the target adolescents' levels of CU traits and their peers' levels of CU traits on the association between antisocial peers and delinquency. Their findings suggest that the delinquent behavior of the target adolescents was less influenced by peer delinquency if they scored high on CU traits. However, if an adolescent had friends who had high levels of CU traits, his or her delinquent behavior was more influenced by their peer delinquency. These findings raise the provocative possibility that the antisocial behavior of the adolescents with CU traits may be less likely to be caused by deviant peers, but that these adolescents may have a strong influence on the antisocial behavior of their peer group.

There is a well-established link between conduct problems and bullying (Crapanzano, Frick, Childs, & Terranova, 2011). ODD and CD are among the most common psychiatric disorders diagnosed in children involved in bullying, particularly those who are also victimized (i.e., "bully-victims"; Kumpulainen, Räsänen, & Puura, 2001). "Bullying" is defined as repeated physical, verbal, or psychological attack or intimidation that is intended to cause fear, distress, or harm to the victim; that occurs within particular interpersonal relationships; and that is characterized by an imbalance of power (Olweus, 1993). It has been described as a form of proactive aggression that involves achieving dominance over peers through intimidation in order to "construct, promote and/or reinforce [a] grandiose self-image" (Washburn, McMahon, King, Reinecke, & Silver, 2004, p. 256). However, youth who engage in bullying behaviors exhibit both proactive and reactive aggression (Camodeca et al., 2002; Salmivalli & Nieminen, 2002). Adolescents with conduct problems who also score high on CU traits are at particularly high risk for bullying. For example, Viding, Simmonds, Petrides, and Frederickson (2009) found that the combination of conduct problems and CU traits predicted greater rates of bullying than either condition alone, among a large (N = 704) sample of young adolescents (ages 11–13 years). Furthermore, CU traits contributed to the statistical prediction of peer-reported bullying, over and above the variance accounted for by conduct problems. In another study capturing a broader adolescent range (ages 12–18 years; M = 14.63 years), CU traits were strongly associated with bullying in Greek Cypriot youth (N = 347; Fanti, Frick, & Georgiou, 2009). Using a longitudinal study design, Fanti and Kimonis (2012) found that adolescents (N = 1,416) with conduct problems and CU traits were at greatest risk for engaging in bullying behaviors across development, compared with those youth exhibiting low or moderate levels of CU traits or conduct problems alone. Together, this research suggests that CU traits, alone or in combination with conduct problems, are associated with greater risk for engaging in bullying.

Neighborhood Characteristics

Children living in dangerous neighborhoods are at risk for developing conduct problems. Within the United States, neighborhood quality and ethnicity are usually confounded because minorities tend to be overrepresented in impoverished neighborhoods. Poor neighborhood quality exposes youth to peers and other individuals with antisocial attitudes and behaviors. Exposure to community violence, which is also common in impoverished neighborhoods, is robustly associated with conduct problems (Cooley-Strickland et al., 2009). Furthermore, the risk for negative child outcomes increases as the violence becomes more physically proximal, with the poorest outcomes for youth directly victimized by violence (P. J. Fowler, Tompsett, Braciszewski, Jacques-Tiura, & Baltes, 2009). Poor neighborhood quality and the stress associated with it may also affect the quality of parenting by causing parents to be more restrictive and harsh, in an effort to keep children under control and protected from negative outside influences (see Campbell, Shaw, & Gilliom, 2000).

Protective Factors

A variety of protective factors have been identified to explain why many children with ODD do not progress to CD, or why adolescents with CD do not progress to antisocial personality disorder in adulthood. More generally, an entire field of resilience research has emerged to explain why children with environmental and/or genetic vulnerabilities do not develop psychopathology (Garmezy, Masten, & Tellegen, 1984). In many cases, protective factors are the opposite of risk factors; for instance, positive parenting operates as a protective factor, and dysfunctional parenting operates as a risk

factor (Burke, Loeber, & Birmaher, 2002). Protective factors buffer the impact of risk factors on children and are often examined by testing whether these factors interact (i.e., moderate) to predict antisocial outcomes. For example, family support interacted with neighborhood disorder to predict antisocial behavior, such that Mexican American (n = 673) and African American (n = 897) children living in dangerous or disadvantaged neighborhoods (i.e., risk factor) showed fewer antisocial behaviors when exposed to higher levels of family support (i.e., protective factor) (Schofield et al., 2012). Protective or resilience factors fall into three primary categories: external societal support systems (e.g., good schools), positive dispositional characteristics (e.g., good cognitive and socioemotional skills), and a nurturing family milieu (e.g., high-quality relationships with parents and other adults) (Masten et al., 1999). Later in development, factors that serve to disconnect individuals from earlier negative influences and provide them with new opportunities in adulthood (e.g., military service, marriage) may protect socially disadvantaged antisocial youth from showing behaviors that persist into adulthood (see Rutter, 2012).

Although there has been relatively little study of protective factors in relation to conduct problem subtypes, maternal support or responsiveness and secure child attachment, which are important protective factors against the development of conduct problems generally (Shaw et al., 2003), may be particularly relevant to the development of CU traits. Research investigating the effects of certain parenting practices indicates that practices not relying solely on punishment-related arousal for internalization of parental norms, but instead focusing on the positive qualities of the parent–child relationship, are more effective in promoting conscience development in relatively fearless children (Kochanska, 1997). Similarly, in a longitudinal study, Pardini and colleagues (2007) found that children exposed to warm and involved parenting showed a reduction in CU traits 1 year later. Thus, warm and involved parenting may buffer against the development of CU traits, in particular among children with risky fearless temperaments. These examples illustrate the importance of testing potential protective factors that can enhance the development of children who may show some of the temperamental risk factors for severe conduct problems. They also suggest that integrating research on normative conscience development with research on children with conduct problems (i.e., a developmental psychopathology perspective) may permit researchers to examine which protective factors might deflect children from this particularly severe and stable course of deviant behavior.

AN OVERARCHING THEORETICAL FRAMEWORK FOR POSSIBLE DEVELOPMENTAL PATHWAYS

Taken together, the many factors associated with the development of conduct problems, combined with the evidence supporting distinct subgroups of youth, lead to a comprehensive and integrative model for understanding the different developmental pathways through which children may develop severe conduct problems (Frick & Viding, 2009). The first pathway supported by this research is the adolescent-onset pathway, in which CD symptoms coincide with the onset of puberty. Children in this pathway show fewer dispositional risk factors, and the developmental mechanism involved seems to be an exaggeration of the normative process of adolescent rebellion and identity formation, rather than an enduring vulnerability. Some level of rebellious behavior is normative in adolescence as part of the typical development of identity. However, youth with adolescent-onset CD are likely to experience factors that lead to a more severe and impairing pattern of rebellion than is typical. Such factors could include association with a deviant peer group, poor supervision by parents, or personality traits characterized by a rejection of traditional status hierarchies.

Children within the childhood-onset pathways show more biological, emotional, cognitive, and contextual risk factors than those in the adolescent-onset group. However, within the childhood-onset pathway, there appear to be important differences between those who do and who do not show elevated CU traits. Those who show normative levels of CU traits are more likely to show deficits in verbal abilities, which, combined with inadequate socializing experiences, could result in problems in the executive control of behavior (such as an inability to anticipate the negative consequences of inappropriate behavior or an inability to delay gratification). Also, the cognitive (e.g., hostile attributional biases) and emotional (e.g., heightened reactivity to negative stimuli) characteristics of children in this group, again combined with inadequate socializing experiences, could lead to problems in regulating emotion. These problems in emotional regulation could result in the children's committing impulsive and unplanned

aggressive and antisocial acts for which they may be remorseful afterward. This dysfunctional transactional process disrupts the children's socialization, leading to poor social relations with persons both inside (e.g., parents and siblings) and outside (e.g., peers and teachers) their families.

Finally, although youth with CU traits (labeled as CD "with limited prosocial emotions" in DSM-5) appear to constitute a minority of those within the childhood-onset group, they show a particularly severe, stable, and aggressive pattern of conduct problems (see Figure 3.1). This group seems to show a distinct temperamental style that places them at risk for missing some of the early precursors to empathic concern, and that may make these children relatively insensitive to the prohibitions and sanctions of parents and other socializing agents. It can lead to problems in the development of conscience, whereby the children become so focused on the potential rewards and instrumental gains of aggression or other antisocial means to solve interpersonal conflicts that they ignore the potentially harmful effects of this behavior on themselves and others.

CURRENT ISSUES AND FUTURE DIRECTIONS

This approach to conceptualizing the development of severe conduct problems has a number of important implications for future research that could advance our understanding of the causes of ODD and CD and improve the assessment, prevention, and treatment of these disorders (Frick, 2012). It is not sufficient for research simply to focus on documenting which risk factors are associated with these disorders or which risk factors account for the most or the most unique variance in measures of antisocial behavior, aggression, or delinquency, since such approaches assume that ODD and CD are unitary outcomes. That is, a variable may be related to the symptoms of CD or may differentiate between children with and without CD in the overall sample; however, this overall association may obscure the fact that it is only related to the behavior of a subgroup of youth with CD. Illustrating this point, dysfunctional/ineffective parenting showed a moderate but significant association with conduct problems in one study after the researchers controlled for several demographic variables; however, this overall association obscured a highly significant positive association for children scoring low on CU traits, versus a weak and nonsignificant negative association for those scoring high on CU traits (Wootton, Frick, Shelton, & Silverthorn, 1997).

A key component to the developmental models outlined in this chapter relates to the different temperamental predispositions (e.g., fearlessness and low behavioral inhibition; high levels of emotional reactivity) and related neurological systems (e.g., reduced amygdala responses; abnormal responses of the orbitofrontal cortex) that may place a child at risk for manifesting severe conduct problems. However, the vast majority of research has focused on children and adolescents who already show severe and impairing conduct problems. Therefore, it will be critical for future research to study children with the hypothesized temperamental and/or biological risk factors early in life, to determine how well these factors predict later severe antisocial behavior. Such longitudinal research is not only important for providing strong tests of the predictive utility of the developmental model; it could also identify protective factors reducing the likelihood that a child with a temperamental risk factor will develop severe conduct problem behaviors. For example, children who display a fearless and uninhibited temperament may show enhanced conscience development and, as a result, lower levels of conduct problems, if they are exposed to consistent, strong, and warm parenting (Cornell & Frick, 2007; Kochanska, 1997; Kochanska & Murray, 2000).

Although there have been many studies showing different correlates to the different conduct problem pathways, there have been far fewer studies directly comparing the specific biological vulnerabilities across subgroups. Future research comparing biological vulnerabilities across the developmental pathways could help to document how the genetic vulnerability to severe conduct problems might lead to the various cognitive and emotional deficits displayed by youth with ODD and CD. For example, Frick and Viding (2009) reviewed molecular genetic studies suggesting that the MAOA low-activity risk polymorphism may relate specifically to children who show primarily impulsive and reactive types of conduct problems. Furthermore, they reported that other studies have identified an increased vulnerability to antisocial behavior in the presence of the MAOA high-activity allele (e.g., Manuck, Flory, Ferrell, Mann, & Muldoon, 2000). Thus it is possible that different alleles of the same gene may predispose youth to different conduct problem pathways by having opposite effects on affective lability.

Given that conduct problems are related to both genetic and environmental risk factors, twin and adoption

studies offer another promising research methodology for investigating various types of gene–environment correlations and interactions. For example, risk factors that have been traditionally conceptualized as environmental (e.g., parenting practices) may actually be evoked partly by children's heritable temperamental features (gene–environment correlation; Larsson, Viding, Rijsdijk, & Plomin, 2008). Moreover, there may be genetically influenced individual differences in the sensitivity to environmental risk factors such as maltreatment (gene–environment interaction). For example, the genetic vulnerability to CD conferred by the MAOA low-activity allele may only manifest itself in the presence of an environmental trigger such as maltreatment (Caspi et al., 2002; Kim-Cohen et al., 2006). Unfortunately, possible unique gene–environment correlations or interactions across each of the different developmental pathways to conduct problems have not been examined to date.

Research on the different developmental pathways to ODD and CD could have important implications for preventing and treating severe conduct problems in children and adolescents. One key implication of this approach is the importance of prevention. As noted previously, the most aggressive youth, and the youth most likely to continue their antisocial behavior into adulthood, tend to show a childhood onset to their behavior. Furthermore, several interventions have proven effective in treating early-emerging conduct problems, but have shown a great decrease in their effectiveness with older children and adolescents (Eyberg, Nelson, & Boggs, 2008; McMahon et al., 2006). Another implication from this research on the developmental pathways to conduct problems is that no risk factor—whether genetic, temperamental, or environmental—operates in isolation. Thus it is not surprising that some of the most effective interventions for severe conduct problems involve multiple components, rather than targeting only a single risk factor (e.g., Conduct Problems Prevention Research Group, 2010). Perhaps the most important implication of this research on developmental pathways for treatment is that optimal interventions for children and adolescents with ODD and CD must not only be comprehensive; they also need to be tailored to each child's and family's individual needs, which are likely to differ depending on the specific mechanisms underlying the child's behavioral disturbance. As a result, some of the most effective treatments for older children and adolescents with CD are comprehensive and individualized interventions (Burns et al., 2003; Butler, Baruch, Hickey, & Fonagy, 2011; Henggeler, Schoenwald, Borduin, Rowland, & Cunningham, 2009).

Research on the different developmental pathways to conduct problems has great potential for informing these individualized approaches to treatment (Frick, 2012). For example, the most effective interventions for youth in the adolescent-onset pathway are likely to be somewhat different from the most effective interventions for other youth with CD. Specifically, interventions focusing on enhancing identity development in adolescents and increasing contact with prosocial peers, such as mentoring programs (Grossman & Tierney, 1998) or programs that provide structured afterschool activities (Mahoney & Stattin, 2000), may be particularly effective for youth within the adolescent-onset pathway. In contrast, interventions that focus on anger control (Larson & Lochman, 2002) or on reducing harsh and ineffective parenting (e.g., Forgatch & Patterson, 2010; McMahon & Forehand, 2003) may be more effective for children within the childhood-onset pathway who do not exhibit elevated CU traits, but who often show problems with emotional regulation and come from families that employ dysfunctional parenting practices (see McMahon & Pasalich, in press, for a review).

Given that shared genetic factors contribute to ODD/CD and ADHD, which is highly heritable (Faraone et al., 2005; Faraone & Mick, 2010), early intervention with children diagnosed with ADHD appears important to preventing the later development of ODD and perhaps CD. The best-supported intervention for children with ADHD is medication management with or without behavioral treatment (MTA Cooperative Group, 1999, 2004), such as parent management training. Such medications may not only reduce the inattentive and impulsive behavior of ADHD that feeds forward into ODD and CD risk, but may particularly improve the emotional impulsivity and poor emotional self-regulation associated with ADHD (Barkley, 2010). Similarly, the failure to treat comorbid ADHD among children with ODD or CD may predict poorer treatment response.

Finally, interventions emphasizing reward-oriented approaches that target youth's self-interests (rather than punishment-based approaches), and that increase parental warmth and involvement, may be more effective for children with CU traits (Caldwell, Skeem, Salekin, & Van Rybroek, 2006; Dadds, Cauchi, Wimalaweera, Hawes, & Brennan, 2012; Somech & Elizur, 2009). The important advances that have been made in in-

corporating the different developmental pathways into current diagnostic classification systems are critical to encouraging continuing research and the testing of innovative interventions for youth on different developmental pathways to childhood and adolescent conduct problems.

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CHAPTER 4

Adolescent Substance Use Disorders

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Adolescent substance use and substance use disorders (SUDs) are topics of clinical and public health concern because of their prevalence and associated negative consequences. There are also substantial economic costs. Considering all age groups, recent estimates suggest costs in the United States of $193 billion for tobacco use (Centers for Disease Control and Prevention, 2008), $223 billion for excessive alcohol use (Bouchery, Harwood, Sacks, Simon, & Brewer, 2011), and $193 billion for the use of illegal drugs (National Drug Intelligence Center, 2011). Moreover, although many adolescents experiment without experiencing adverse consequences, adolescent substance use is associated with increased risk for all three of the leading causes of death in adolescence (accidents, suicide, and homicide), as well as increased risk for sexually transmitted disease and the development of clinical substance use disorder (Institute of Medicine, 1994; Moritsugu & Li, 2008). Although the magnitude, specificity, and durability of effects are unclear, there is also concern that adolescent substance use can impair emerging neurocognitive functioning (see Squeglia, Jacobus, & Tapert, 2009, for a review), as well as developmental competence and psychosocial functioning (Baumrind & Moselle, 1985; Chassin, Pitts & DeLucia, 1999; Chassin et al., 2010).

This chapter describes the features and epidemiology of adolescent substance use and SUDs, and examines etiological factors with an emphasis on recent evidence. The chapter is not intended to be comprehensive; for example, we do not consider issues of treatment or prevention. (For discussions of treatment, see Becker & Curry, 2008; Deas & Thomas, 2001; Hser et al., 2001; Liddle, 2004; and Waldron & Kaminer, 2004. For discussions of prevention, see Bukoski, 1997; Spoth, Greenberg, & Turrissi, 2008; Substance Abuse and Mental Health Services Administration [SAMHSA], 1999, 2000; and Winters, Fawkes, Fahnhorst, Botzet, & August, 2007.) Moreover, because many empirical studies consider only substance use, we include coverage of adolescent substance use as well as SUDs, while noting the distinctions between them. Finally, our discussion spans developmental periods ranging from early childhood precursors of adolescent SUDs to the period of "emerging adulthood" (ages 18–25), when SUDs reach their peak.

HISTORICAL CONTEXT

A historical perspective on adolescent substance use and SUDs must be placed within the broader context

of historical changes in the definitions of adolescence. Prior to the 19th century, the transition from childhood to adulthood was short; after puberty children often gained many of the freedoms and responsibilities of adulthood, including substance use (Lender & Martin, 1987). However, as the American economy changed in the 19th century, adult occupations required greater training and maturity. Adolescence began to be viewed as a period that required moral instruction as well as preparation for the economic and social demands of adulthood. As adolescence became more strongly differentiated from adulthood, societal attitudes toward adolescent substance use became more negative (Lender & Martin, 1987).

Coincident with changes in attitudes toward adolescent substance use in 19th-century America was a rise in alcohol temperance movements that peaked with the Prohibition (1919–1933). Since then, societal movements against psychoactive substances have included movements against opiates in the early 20th century, marijuana in the 1920s, narcotics in the 1950s, and cocaine (including crack) in the 1980s (Bukstein, 1995).

The origins of the current "war on drugs" can be tied to the rise of the counterculture of the late 1950s and 1960s. This era brought increases in the use and social acceptance of many psychoactive drugs, particularly marijuana and LSD. As substance use became more common among middle-class American college students in the 1960s, there was increased societal concern about drug use and increased antidrug legislation. The Drug Abuse Control Amendment of 1965 and the Controlled Substances Act of 1970 brought hallucinogens, stimulants, and depressants under the regulatory control of the federal government, whereas before the 1960s only narcotics were controlled substances (Maisto, Galizio, & Connors, 1999). In the 1970s, national epidemiological studies were undertaken to monitor trends in adolescent substance use (e.g., the Monitoring the Future Study [MTF], to be discussed later, began in 1975). The "war on drugs" under Presidents Ronald Reagan and George H. W. Bush saw increases in federal funding of nearly 700% for federal drug programs, the appointment of a federal "drug czar," and increased military activity to counter drug supply (Humphreys & Rappaport, 1993). Societal conceptualizations of and attitudes toward adolescent substance use continue to evolve today, with recent trends including increases in the legal drinking age, controversies over medical marijuana laws, a reconceptualization of tobacco use as an addictive behavior, and U.S. Food and Drug Administration regulation of tobacco products pursuant to the Family Smoking Prevention and Tobacco Control Act of 2009.

DEFINITIONAL AND DIAGNOSTIC ISSUES

Current Diagnostic Criteria

In the United States, the most commonly used diagnostic system is the *Diagnostic and Statistical Manual of Mental Disorders* (DSM). At this writing, a new version has just been released, DSM-5 (American Psychiatric Association, 2013). One major change from DSM-IV (American Psychiatric Association, 1994) is the removal of the distinction between substance abuse and substance dependence, which have been replaced with a single diagnosis of SUD (which can be applied to alcohol; cannabis; hallucinogens; inhalants; opioids; sedatives, hypnotics, and anxiolytics; stimulants; and tobacco). The DSM-5 criteria for SUD include tolerance (needing greater amounts of a substance in order to become intoxicated, or experiencing reduced effects from the same amount of consumption); withdrawal (cognitive and physiological changes upon discontinuing the substance); taking the substance in greater amounts or over longer times than intended; giving up important activities because of use; unsuccessful attempts to cut down or a persistent desire to cut down on use; spending much time in obtaining, using, or recovering from using the substance; continuing to use the substance despite physical, psychological, social, or interpersonal problems that are being exacerbated by this consumption; failing to meet important obligations at home or school/work; and use in hazardous situations. A new symptom added for DSM-5 is craving, which is defined as a powerful urge or desire to use the substance; also, the DSM-IV substance abuse criterion of recurrent legal problems has been removed from DSM-5. In DSM-5, an SUD is diagnosed if two or more symptoms occur within a 12-month period (with two to three symptoms indicating mild disorder, four or five indicating moderate disorder, and six or more indicating severe disorder).

As in prior versions of the DSM, adolescent SUDs are diagnosed with the same criteria that are applied to adults. However, the empirical support for this practice has been questioned. Studies using DSM-IV criteria have reported a category of "diagnostic orphans" (i.e., adolescents who endorse one or two symptoms but do

not qualify for a substance-related diagnosis, despite problematic use). Rates of these diagnostic orphans are substantial. For example, in studies of adolescents who regularly use alcohol, these rates have ranged from 13 to 30% (Harrison, Fulkerson, & Beebe, 1998; Lewinsohn, Rohde, & Seeley, 1996; Pollock & Martin, 1999). However, some recent data suggest that individuals who are categorized as "diagnostic orphans" by DSM-IV criteria will be likely to meet criteria for alcohol (Agrawal, Heath, & Lynskey, 2011) or marijuana (Mewton, Slade, & Teeson, 2013) disorder, according to the new DSM-5 criteria.

There are several reasons why recent diagnostic criteria (both DSM-IV and DSM-5) may be inadequate for adolescents. First, because adolescents are just beginning consumption, it is more normative for adolescents than for adults to show increases in tolerance (Martin, Steinley, Verges, & Sher, 2011; Winters, Martin, & Chung, 2011), so increased tolerance may not have the same meaning for the two age groups. Second, withdrawal is reported by a very small percentage of adolescents (Winters, 2013). Third, the hazardous use criterion may be less likely for adolescents because they have less access to motor vehicles (Martin, Sher, & Chung, 2011; Winters, 2013). In general, the degree to which criteria for SUDs capture (or fail to capture) the unique features of adolescents versus adults suggests that some modifications to adult classification systems might be necessary (Colby, Tiffany, Shiffman, & Niaura, 2000; Mikulich, Hall, Whitemore, & Crowley, 2001; Winters, Latimer, & Stinchfield, 1999). The possibility that the SUD diagnostic criteria are developmentally inappropriate when applied to adolescents may explain some findings that adolescents meet diagnostic criteria at lower levels of consumption than do adults (Langenbucher et al., 2000). However, because it has been reported that adolescents may be neurobiologically more sensitive to some of the effects of consumption (Adriani & Laviola, 2004; Spear, 2011), a greater neurobiological vulnerability might also lead adolescents to meet diagnostic criteria at lower levels of use compared to adults.

Given the overlap between DSM-IV and DSM-5 symptoms, many of the concerns that were raised with respect to diagnosing adolescent SUDs in DSM-IV are also likely to apply to DSM-5, although combining substance abuse and dependence into a single SUD diagnosis is empirically supported for adolescents (Winters et al., 2011). In addition, the DSM-5 removal of the legal-problems symptom is likely to improve diagnosis for adolescents because this symptom has been thought to relate more to associated conduct problems than specifically to SUD. However, concerns for DSM-5 include the need for clear operationalization of craving (a new criterion) and concern about whether the two-symptom threshold for diagnosis will overdiagnose SUDs (Martin, Steinley, et al., 2011; Winters et al., 2011). Overdiagnosis may be particularly likely among adolescents compared to adults, given that tolerance is relatively normative and that adolescents report using in "larger amounts than intended" for reasons of social conformity in peer contexts (Martin, Steinley, et al., 2011).

Related Symptoms and Disorders

SUDs in adolescence are typically accompanied by a number of clinical and subclinical symptoms. Most notably, adolescents with SUDs are likely to show polydrug use (Roberts, Roberts, & Xing, 2007). The most frequently occurring combination is alcohol and marijuana, followed by alcohol and hallucinogens, although one recent study involving college students found that nearly 10% used alcohol in combination with prescription drugs (Deas, Riggs, Langenbucher, Goldman, & Brown, 2000; Martin, Kaczynski, Maisto, & Tarter, 1996; McCabe, Cranford, Morales, & Young, 2006). Among adolescents in general, there is support for a developmental sequence of substance use involvement—beginning with the use of "gateway drugs" (alcohol and nicotine), followed by marijuana, and then other illegal drugs (Kandel, Yamaguchi, & Chen, 1992).

Adolescents with SUDs are further characterized by functional impairment in numerous domains. They exhibit poorer academic achievement and higher rates of academic failure than either youth who do not use substances or those without SUDs (Haller, Handley, Chassin, & Bountress, 2010; Moss, Kirisci, Gordon, & Tarter, 1994; Tarter, Mezzich, Hsieh, & Parks, 1995). Adolescents with SUDs tend to associate with deviant peer groups; to engage in delinquent behaviors (Blackson et al., 1999; Branstetter, Low, & Furman, 2011; Fergusson, Boden, & Horwood, 2008; Hawkins, Catalano, & Miller, 1992) and risky sexual behaviors (Malow, Devieux, Jennings, Lucenko, & Kalichman, 2001); and to experience negative interactions with their parents (Kuperman et al., 2001; Mezzich et al., 1997).

One of the most consistent findings in the literature is that adolescent SUDs are often comorbid with DSM-IV disruptive behavior disorders (Costello, Mustillo,

Erkanli, Keeler, & Angold, 2003; Elkins, McGue, & Iacono, 2007; Wilens et al., 2010). Cohen and colleagues (1993) and Costello and colleagues (2003) found that at least half of adolescents with SUDs were also diagnosed with disruptive behavior disorders. Among those with diagnosed SUDs, odds ratios for diagnoses of disruptive behavior disorders have been reported from 0.4 to 30.7, with the larger odds ratios pertaining to conduct disorder (CD), as compared to attention-deficit/hyperactivity disorder (ADHD) or oppositional defiant disorder (ODD) (Costello et al., 2003; Fergusson, Horwood, & Lynskey, 1993; Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993). Although the relations between SUDs and conduct problems appear unique, the link between ADHD and SUDs is more controversial, and the effect of ADHD is often eliminated after the effect of CD is taken into account (Brook, Brook, Zhang, & Koppel, 2010; Costello, Erkanli, Federman, & Angold, 1999; Fergusson & Horwood, 1995; Fergusson, Horwood, & Ridder, 2007; Glass & Flory, 2011; Weinberg, Rahdert, Colliver, & Glantz, 1998). In fact, one group found that the relation between ADHD and substance use problems was fully mediated by CD symptoms (Brook et al., 2010). Others report that ADHD and CD interact to increase risk for SUDs in adolescence (Flory & Lynam, 2003). Still others suggest that those with the different types of ADHD are at differential risk for substance problems, with hyperactivity–impulsivity being uniquely related to substance problems over and above CD symptoms, and inattention not being related to substance problems (Elkins et al., 2007). Because adolescent substance use problems rarely occur in the absence of other disruptive problem behaviors, heavy adolescent substance use is often considered a specific manifestation of broader-based problem behaviors (Donovan & Jessor, 1985). Some suggest that adolescent SUDs are the culmination of a deviant developmental trajectory, manifested in childhood and early adolescence by behavioral undercontrol and by antisocial and oppositional behavior (King, Iacono, & McGue, 2004; Tarter, Sambrano, & Dunn, 2002; Tarter & Vanyukov, 1994).

The relation between SUDs and internalizing disorders is less clear. Some have found that depression, social anxiety, and generalized anxiety are related to the onset of adolescent substance use (Costello et al., 1999; King et al., 2004; Schneier et al., 2009), although separation anxiety may actually reduce the likelihood of onset (Kaplow, Curran, Angold, & Costello, 2001), perhaps by decreasing time spent away from parents and in peer contexts. Other studies have found that depression and anxiety occur with adolescent SUDs, but that the relations with depression are stronger (Fergusson et al., 1993; Kandel et al., 1997; King et al., 2004; Lewinsohn et al., 1993). There have also been reports of interactions among different forms of internalizing symptoms in predicting substance use. For example, Valentiner, Mounts, and Deacon (2004) found that among late adolescents with panic attacks, depression predicted substance use, but depression was not a significant predictor of substance use among those without panic attacks. Because some of these studies examined slightly older samples, the associations between substance use outcomes and emotional disorders may increase with age, and emotional disorders may be the result of continued substance use. Moreover, some studies suggest that associations between emotional disorders and substance use outcomes are stronger for females than for males, with the exception of social phobia (social anxiety disorder), for which the link is stronger for boys (e.g., Bukstein, Glancy, & Kaminer, 1992; Federman, Costello, Angold, Farmer, & Erkanli, 1997; Sung, Erkanli, Angold, & Costello, 2004; Tarter, Kirisci, & Mezzich, 1997; Whitmore et al., 1997; Wu, Goodwin, et al., 2010).

EPIDEMIOLOGY

Prevalence Rates

Several national epidemiological studies were launched in the 1970s to monitor trends in adolescent substance use prevalence over time. The Monitoring the Future Study (MTF) began in 1975 as a school-based survey of substance use among the nation's high school seniors, and is administered annually to over 45,000 students in 8th, 10th, and 12th grades in 435 schools nationwide (Johnston, O'Malley, & Bachman, 2000, 2001, 2002, 2005; Johnston, O'Malley, Bachman, & Schulenberg, 2006, 2008, 2012). The National Household Survey on Drug Abuse (NHSDA) has been conducted since 1971, and obtains information from over 70,000 civilians age 12 or older across the nation in face-to-face interviews (SAMHSA, 2000, 2001).

Because parents are likely to be unaware of their adolescents' substance use, epidemiological studies on adolescent use rely on the adolescents' self-reports. Indeed, parent and adolescent reports show low levels

of agreement (Cantwell, Lewinsohn, Rohde, & Seely, 1997; Fisher et al., 2006). A large literature has addressed the validity of adolescent self-reports, including their validation with biological measures (e.g., Dolcini, Adler, & Ginsberg, 1996; Dolcini, Adler, Lee, & Bauman, 2003; Murray, O'Connell, Schmid, & Perry, 1987), and these data suggest that self-reports can be valid if they are obtained under conditions of anonymity and privacy, and if there is minimal motivation to distort responses. Data suggest that self-administered questionnaires substantially improve reporting, compared to data obtained via interviewer-style questioning (Etter, Houzec, & Perneger, 2003; Rogers, Miller, & Turner, 1998).

Data from the MTF suggest that adolescent substance use is relatively common by the end of the 12th grade. For example, the MTF data from 2011 showed that 20.1% of 8th graders and 49.9% of 12th graders had used some illegal drug in their lifetimes (Johnston et al., 2012). Marijuana was the most frequently used illegal drug, with 12.5% of 8th graders and 36.4% of 12th graders reporting use in the past year (Johnston et al., 2012). The use of substances that are legal for adults (i.e., alcohol and tobacco) was even more common, with 70% of high school seniors having tried alcohol at least once, and 40% reporting drinking in the past month (Johnston et al., 2012). As of 2011, 40% of 12th graders had tried cigarettes, and approximately 20% were current smokers (i.e., within the last 30 days; Johnston et al., 2012). In regard to prescription drug use, 21.7% of 12th graders had ever used at least one such drug without a doctor's order (Johnston et al., 2012). The use of different drugs is highly interrelated in both epidemiological and clinical samples of adolescents (Clayton, 1992; Johnston et al., 2001; Kandel, Davies, Karus, & Yamaguchi, 1986; Single, Kandel, & Faust, 1974; Young et al., 2002). For example, the 1985 NHSDA data showed that 24% of those who reported any illicit drug use used more than one drug at the same time within the past year, and 43% had used alcohol along with an illicit drug (Clayton, 1992).

In addition to finding that substance use generally increases during adolescence, the MTF data also reveal interesting patterns of change in drug use over time. In general, adolescent substance use peaked in the mid-1970s and early 1980s, and then declined. Substance use increased again in the early 1990s, but has since leveled off. At this writing (2013), there are declining trends for cigarettes and alcohol, Ecstasy (MDMA), Oxycontin, and Vicodin. On the other hand, the past-year use of stimulant drugs (e.g., Adderall) without a doctor's order has steadily increased, reaching 6.5% among high school seniors in 2011 (Johnston et al., 2012). Other drugs have shown more nuanced increases and decreases in use over time. For example, past-year cocaine use among 12th graders peaked in the early/mid-1980s, showed dramatic declines between 1986 and 1992, and then began to increase again until 2000. Between 2000 and 2006, cocaine use leveled off, and it has decreased steadily since 2006 (Johnson et al., 2012). Past-year inhalant use for high school seniors peaked in the mid-1990s and declined until the early 2000s, at which time use increased slightly and then began to decline again (Johnston et al., 2012). Johnston and colleagues (2012) also note that as older drugs wane in popularity, new drugs replace them. For instance, LSD and methamphetamine showed an increase in the 1960s; and heroin, crack and other forms of cocaine, and phencyclidine made a comeback in the 1990s after being initially unpopular (Johnston et al., 2005). Moreover, sometimes the popularity of a specific drug revives after a period of low use. Johnston and colleagues (2001, 2005, 2012) suggest that the use of a particular drug makes such a comeback because knowledge of its risks and negative effects gets lost from the adolescent culture after a period of nonuse. This phenomenon has been called "generational forgetting."

Substantial numbers of adolescents who use alcohol or drugs also report some problems associated with their substance use. For example, Zoccolillo, Vitaro, and Tremblay (1999) found that among adolescents using alcohol more than five times, 70% of boys and 53% of girls reported experiencing at least one alcohol-related problem, and 20% of boys and 11% of girls reported three or more problems. Of those who had used other drugs more than five times, 94% of boys and 85% of girls reported at least one drug-related problem, and 68% of boys and 52% of girls reported three or more problems. Among adolescents ages 13–17, rates of diagnosable disorders are about 2–7% for alcohol use disorders and 3–9% for other drug use disorders (Fergusson et al., 1993; Kessler et al., 2012; Merikangas et al., 2010; Roberts, Roberts, & Xing, 2007, 2008). Among older adolescents and emerging adults (ages 17–20), rates are approximately 12–18% for alcohol use disorders and 4–11% for other drug use disorders (Cohen et al., 1993; Merikangas & McClair, 2012; SAMHSA, 2001; Young et al., 2002). In general, rates of SUDs rise throughout adolescence, peak during emerging adulthood, and then decline.

Demographic Correlates

Gender

Numerous studies have documented gender differences in substance use prevalence. That is, girls, compared to boys, use fewer types of drugs, use them with less frequency, and drink less alcohol in a single sitting (Johnston et al., 2000, 2002; Wallace et al., 2003). In the MTF data, 12th-grade males have reported substantially higher prevalence rates for the annual use of heroin, LSD, ketamine, hallucinogens, cocaine, steroids, and smokeless tobacco, as well as in the daily use of marijuana and alcohol. At younger grades, however, males and females show similar rates of drug use for many drugs, and females even have higher rates of annual use of inhalants, tranquilizers, and amphetamines in 8th grade. This pattern may reflect a developmental phenomenon, with accentuating gender differences emerging over the course of adolescence; or a cohort effect, with gender differences decreasing among more recent cohorts of adolescents. Support for both potential explanations has been found. For example, Cohen and colleagues (1993) and Johnston and colleagues (2008, 2012) found that gender differences for alcohol use disorders and for illicit drug use increased as individuals moved into late adolescence (17–20 years of age). In addition, Chen and Jacobson (2012) found that although females drank, smoked, and used marijuana more than males in early adolescence, males' substance use increased at a higher rate than females', culminating in their higher use by the end of adolescence and into adulthood. However, Wallace and colleagues (2003) found that 12th-grade boys drank alcohol and used marijuana more frequently than their female counterparts, but that the magnitude of these differences decreased from the 1990s into the 2000s.

In addition to differential prevalence rates, males and females may use drugs for different reasons. Indeed, younger females (under 15 years old) report higher levels of social enhancement and coping motives than do younger males, although this difference is reversed in older adolescents (18–19 years old; Cooper, 1994). In a study of individuals ages 16–22, females were more likely than males to report using drugs to lose weight, stay awake, lose inhibitions, stop worrying, and enjoy the company of friends (Boys, Marsden, & Strang, 2001). Comeau, Stewart, and Loba (2001) found in their sample of adolescents (mean age 15) that males were more likely to drink alcohol to conform. Studies of tobacco use have found that females report stronger weight regulation and anxiety reduction motives than do males, who are more likely to smoke to enhance self-confidence (Berlin et al., 2003; Grunberg, Winders, & Wewers, 1991; Piko, Wills, & Walker, 2007; Rose, Chassin, Presson, & Sherman, 1996; see also Amaro, Blake, Schwartz, & Flinchbaugh, 2001, for a review of drug use among adolescent girls, and White & Huselid, 1997, for a review of gender differences in adolescent alcohol use).

Socioeconomic Status

Adolescent drug use has also been associated with socioeconomic status (SES). Goodman and Huang (2012) found that among 12- to 18-year-olds, adolescents with more educated parents drank alcohol and smoked cigarettes less frequently than did those with less educated parents. In the MTF data, lower parent education was associated with greater illegal drug use in the middle school years, but not in the high school years (Johnston et al., 2008, 2012). These diminished differences may reflect differential school dropout as a function of parental education or substance use, or a developmental phenomenon, with use becoming equally common across SES levels by the end of adolescence (Johnston et al., 2008). They might also reflect a cohort effect, such that substance use is becoming more concentrated in less educated subgroups among more recent cohorts (as has been argued for cigarette smoking; Fiore, Newcomb, & McBride, 1993).

Weaker relations have been reported between adolescent substance use and other indicators of SES, including family income (Goodman & Huang, 2012; Parker, Calhoun, & Weaver, 2000) and subjective ratings of familial SES (Fawzy, Combs, Simon, & Bowman-Terrell, 1987). It has also been suggested that low SES increases risk for adolescent substance use only when poverty co-occurs with childhood behavior problems (Hawkins et al., 1992). Moreover, the relation between adolescent substance use and SES may also vary with different drugs. For example, with the rise in prevalence of crack cocaine in the early 1980s, lower-SES populations exhibited increases in cocaine use, while their higher-SES counterparts showed declining use. Although this trend ended in 1985, it illustrates how social and economic factors—in this case, the increased opportunity to acquire this cheaper form of cocaine—can influence the SES distribution for specific drugs.

One reason for the weak and inconsistent associations between SES and adolescent substance use is that

the association may be curvilinear, such that SES may only influence adolescent substance use at its extreme ends. Interestingly, both high- and low-SES neighborhoods have been linked with increased adolescent substance use. Research indicates that decreased parental availability and supervision (Luthar & Latendresse, 2005), increased financial resources (Hanson & Chen, 2007), increased achievement pressures (Luthar & Becker, 2002), and increased parental drinking (Chuang, Ennett, Bauman, & Foshee, 2005) may mediate the influence of neighborhood affluence on adolescent substance use, whereas the influence of neighborhood *disadvantage* may be mediated by decreased social cohesion (Duncan, Duncan, & Strycker, 2002), greater acceptance of substance use, lower perceived harmfulness of substance use (Lambert, Brown, Phillips, & Ialongo, 2004), decreased after-school supervision (Luthar & Latendresse, 2005), and increased peer drinking (Chuang et al., 2005).

Ethnicity

In regard to ethnic correlates of use, MTF data show that African American high school seniors have the lowest prevalence rates (lifetime, annual, monthly, and daily) for use of alcohol, cigarettes, and all illegal drugs, compared to non-Hispanic European American and Hispanic American high school seniors. In 6th and 8th grades, Hispanic American students report more use than do European Americans, but this difference reverses at 12th grade, when European Americans tend to have the highest rates of drinking and illegal drug use, compared to African American and Hispanic American adolescents (Johnston et al., 2008, 2012). Possible reasons for this crossover between Hispanic Americans and European Americans are the comparatively high dropout rate of Hispanics, which may diminish initial ethnic differences, and/or the findings that European Americans begin using drugs later in adolescence and eventually overtake the prevalence rates of Hispanic Americans (Johnston et al., 2000, 2008). Native American adolescents also show high rates of use (Plunkett & Mitchell, 2000; Wallace et al., 2003), although their levels of use vary by geographic location. By contrast, Asian American high school seniors report very low levels of drug use, although this trend may be mostly driven by the very low rate of drug use by Asian American females (Wallace et al., 2003).

Research on ethnic differences in diagnosed adolescent SUDs appears to be mixed. For example, Costello, Farmer, Angold, Burns, and Erkanli (1997) found that Native American adolescents had significantly higher odds of receiving an SUD diagnosis than did European American adolescents; however, Mitchell, Beals, Novins, Spicer, and the American Indian Service Utilization, Psychiatric Epidemiology, Risk and Protective Factors Project Team (2003) found that 15- to 24-year-old Native Americans showed extremely low levels of SUDs. Results from another large-scale study (Kandel et al., 1997) showed that European American and African American adolescents were more likely to be diagnosed with an SUD than were Hispanic adolescents (for reviews of ethnic differences in drug use, see Barrera, Castro, & Biglan, 1999; Kandel, 1995). However, others (Roberts, Roberts, & Xing, 2006) found that European American adolescents were most likely to be diagnosed with an SUD, and African American adolescents were least likely to be diagnosed, with Mexican American adolescents being in the middle in terms of risk.

It may also be that apparent ethnic differences in substance use may in part reflect ethnic differences in reporting bias. For instance, Bauman and Ennett (1994) found that when self-report data were validated against a biological measure of tobacco use, African American adolescents underreported their smoking, whereas European American adolescents overreported their smoking. However, recent work using larger and more ethnically heterogeneous samples has suggested that the validity of self-reports is comparable across ethnic groups (Brener et al., 2002; Wills & Cleary, 1997).

In addition to varying by ethnicity, adolescent substance use seems to vary across cultures. Specifically, the frequency of drunkenness and smoking is higher in most European countries and in Australia than in the United States (Kuntshe, Knibbe, Kuntsche, & Gmel, 2011); McMorris, Hemphill, Toumbourou, Catalano, & Patton, 2007; Piko, Luszczynska, Gibbons, & Tekozel, 2005). However, in one study, lifetime marijuana use was greater in the United States than in Australia (McMorris et al., 2007). Research has also documented that there is higher lifetime alcohol use in the Commonwealth of Puerto Rico than in the rest of the United States (Warner, Canino, & Colon, 2001). Therefore it appears that prevalence rates of adolescent substance use vary by substance across countries, continents, and cultures.

As these data illustrate, rates of adolescent substance use vary with gender, SES, and ethnicity. However, these conclusions may oversimplify a more complex

picture, in that prevalence rates may vary as a function of complex interactions among gender and ethnicity, and also as a function of type of substance (Griesler & Kandel, 1998). In addition, the correlated effects of ethnicity and SES are difficult to disaggregate. Moreover, the mechanisms underlying these demographic differences have not been well articulated, and methodological artifacts such as sampling and reporter biases may affect the results of these studies.

DEVELOPMENTAL COURSE AND PROGNOSIS

Both substance use and SUDs show systematic age-related patterns from adolescence to adulthood—patterns that have led some researchers to view SUDs as developmental disorders (Masten, Faden, Zucker, & Spear, 2008; Sher & Gotham, 1999). Substance use is typically initiated in adolescence, and there are multiple reasons why adolescents may be vulnerable to substance use initiation. Recent data suggest that adolescence as a developmental period is characterized by a gap between changes in dopaminergic reward systems (producing increases in sensation seeking and reward seeking beginning at puberty) and the slower and more gradual development of top-down cognitive control, correlated with increased myelination both within prefrontal cortex and between cortical and subcortical areas (Steinberg, 2008). In addition, adolescence is characterized by greater time spent in peer activities beyond the supervision of parents, and the presence of peers has been shown to activate the same reward centers that lead to risky behavior (Chein, Albert, O'Brien, Uckert, & Steinberg, 2011). Finally, adolescents may be particularly vulnerable to substance use effects that make escalation of substance use particularly likely. For example, adolescents are more sensitive to some of the positive effects of substances, but less sensitive to some of the aversive effects (Spear, 2011).

Over the adolescent years, alcohol and drug use increase in quantity and frequency to reach a peak in the age period that Arnett (2000) has referred to as "emerging adulthood" (18–25 years of age). The prevalence of diagnosed SUDs also peaks in this age period (e.g., Grant et al., 1994). Then, in the mid- to late 20s, the consumption of alcohol and illegal drugs begins to decline. SUDs that decline in young adulthood have been referred to as "developmentally limited" (Zucker, 1987).

However, "maturing out" of substance use is likely to be more complex than originally proposed. For example, Lee, Chassin, and Villalta (2013) found that declines in drinking were not uniform, but rather were more common among individuals with heavier, problematic drinking than among those with other types of drinking, and that declines among those with heavy drinking reflected moderation rather than cessation of drinking. Verges and colleagues (2012) found that although persistence in DSM-IV alcohol dependence was somewhat lower in early adulthood than later in life, age-related declines in alcohol dependence were largely produced by reductions in new onset. Their findings suggest that alcohol dependence may be thought of as either "short-duration" or "chronic and episodic" (although "short-duration" alcohol use disorders may be more common at earlier ages).

Taking on adult roles in emerging adulthood has been thought to explain the "maturing out" of substance use and SUDs, given that substance use is incompatible with the demands of the roles of worker, spouse, and parent (Yamaguchi & Kandel, 1985). However, multiple factors may influence the maturing out of substance use. First, as described earlier, neurobiological research has documented a gradual maturation of cognitive control areas that continues into the early to mid-20s (Steinberg, 2008); these increases in cognitive control would be likely to reduce risk-taking behavior in general and substance use more specifically. Moreover, recent studies have demonstrated that age-related changes in personality—including declines in behavioral disinhibition/impulsivity and negative emotionality/neuroticism, and increases in conscientiousness—are correlated with declines in alcohol use in emerging adulthood (Littlefield, Sher, & Wood, 2009). There is also some recent evidence of a reverse direction of effect, such that alcohol use might influence age-related personality change, although the results are not totally consistent (Hicks, Durbin, Blonigen, Iacono, & McGue, 2012; Littlefield, Verges, Wood, & Sher, 2012).

Finally, there is substantial heterogeneity in age-related trajectories of substance use and SUDs. Several studies have suggested that an early age of substance use onset is one predictor of subsequent course and of clinical impairment. For example, Grant and Dawson (1997) found that alcohol use initiation before age 14 was associated with elevated risk for the development of alcohol use disorders. Similarly, Robins and Pryzbeck (1985) reported that early onset of illegal drug use (before age 15) was associated with increased likelihood of later drug use disorders. There is also heterogeneity in the speed of transition from initiation of use to

the development of clinical disorder. For example, adolescents whose parents have alcohol use disorders and those with externalizing symptoms move more quickly from onset to clinical disorders (Hussong, Bauer, & Chassin, 2008).

Researchers using mixture modeling have empirically identified multiple developmental trajectories of substance use within longitudinal studies. A particularly high-risk pattern combines early age of onset with a steeply escalating course of use. This has been found both for cigarette smoking (Chassin, Presson, Pitts, & Sherman, 2000) and for heavy drinking (Chassin, Pitts, & Prost, 2002; K. Hill, White, Chung, Hawkins, & Catalano, 2000). Moreover, studies of these early-escalating subgroups have shown them to be associated with a family history of use or disorder and high levels of conduct problems (Chassin et al., 2002; Costello et al., 1999; S. Y. Hill, Shen, Lowers, & Locke, 2000; Loeber, Stouthamer-Loeber, & White, 1999).

Conversely, longitudinal studies of adolescents have also identified a late-onset subgroup (at least late in the adolescent age period) whose smoking or heavy drinking does not begin until after the high school years (Chassin et al., 2002). For these adolescents, substance use initiation may be associated with decreases in parental supervision, perhaps during the transition out of the parental home. Adolescent substance use that begins after the high school years has been relatively neglected by researchers, and most prevention programs (with the exception of college student drinking initiatives) have been targeted at younger age groups. This represents an important area for future research.

RISK FACTORS AND ETIOLOGICAL MODELS

Risk factors for adolescent substance use and SUDs have been identified on multiple levels ranging from intrapersonal to macroenvironmental (see Hawkins et al., 1992), and have also been integrated into biopsychosocial theoretical models of etiology (see e.g., Sher, 1991). Given the heterogeneity of SUDs, it is unlikely that any one factor or etiological pathway could explain their development. For example, theory and research in alcoholism have suggested that subtypes of this disorder may have different etiological antecedents. In particular, researchers have distinguished between early-onset alcoholism (which has a higher prevalence in males, typically begins in adolescence, and is strongly associated with antisociality) and later-onset alcoholism (which is more strongly associated with neuroticism and negative affectivity; see, e.g., Cloninger, 1987).

Here we review some of the major risk factors and etiological models, with an emphasis on recent empirical evidence. These models suggest that the antecedents and etiological pathways into adolescent SUDs have their roots in earlier stages of development. In discussing the etiology of these SUDs, it is important to remember that they represent only a segment of a larger series of stages in substance use progression. These stages include initiation, experimental or occasional use, regular or escalating use, and problem use, as well as cycles of cessation and relapse (Flay, d'Avernas, Best, Kersell, & Ryan, 1983; Glantz & Pickens, 1992). As such, it is likely that movement through the different stages has different etiological determinants. However, existing empirical studies have often blurred these distinctions, and many of the existing data refer to predictors of adolescent substance use rather than clinical SUDs. Thus the existing database makes it difficult to specify etiological models of transition that are unique to different stages of substance use behavior.

Family History and Genetic Risk

A robust finding in the literature is that adults whose parents have a history of SUDs are at elevated risk for substance use and SUDs (McGue, 1994; Milne et al., 2009), although the magnitude of the risk varies substantially across samples. For example, parent alcoholism raises risk for offspring alcoholism anywhere from a risk ratio of 2–3 in community samples, to a risk ratio of 9 in severely alcohol-dependent and antisocial samples (McGue, 1994; Russell, 1990). There is also elevated risk (as high as eightfold) for SUDs among relatives of probands with SUDs (Merikangas et al., 1998).

Family history risk is also associated with adolescent substance use, including adolescent onset of substance use (Chassin et al., 2000; Costello et al., 1999), persistence of substance use over time (Chassin et al., 2000), and trajectories of heavy substance use and SUDs starting in adolescence (Chassin, Flora, & King, 2004; Jackson, Sher, & Wood, 2000). Studies suggest that this family history risk for substance use and SUDs in adolescence has both heritable and environmental mediators, and that the relative influence of each changes over the course of development. Adolescent substance use phenotypes are strongly influenced by common environmental factors. However, over the course of adolescence the influence of genetic factors on these

phenotypes tends to increase, while the influence of environmental factors tends to decrease (Dick, Pagan, et al., 2007; Kendler, Schmitt, Aggen, & Prescott, 2008; Rose, Dick, Viken, & Kaprio, 2001; Rose, Dick, Viken, Pulkkinen, & Kaprio, 2001).

These findings may in part be explained by the fact that adolescents are relatively less able than adults are to choose their social environments. This difference in autonomy may result in lowered opportunities for adolescents to express their genetic predispositions (Meyers & Dick, 2010). On the other hand, adults have greater control over their environments, and this "niche picking" may result in greater gene–environment covariation in adult social environments. Supporting this notion are findings reported by Dick, Pagan, and colleagues (2007) demonstrating that genetic influences on adolescent smoking decreased, and environmental influences increased, with higher levels of parental monitoring. Accordingly, these data suggest that the greater observed effects of the environment on adolescent substance use may result in part from the more restrictive environments of adolescents compared to adults. In addition, developmentally limited forms of adolescent substance use may mask genetic effects that become more prominent once these forms of use have remitted.

Studies have also revealed differences in the heritability of different developmental stages of substance use. For example, some research indicates that shared environmental influences play a more prominent role in substance use initiation, whereas genetic and unique environmental influences play a larger role on heavier/problematic use in both adolescents and adults (Fowler et al., 2007). However, other studies report a greater genetic influence on substance initiation compared to heavier/problematic use, conditional on the substance being investigated and on gender (McGue, Elkins, & Iacono, 2000; Rhee et al., 2003).

Another important consideration in the heritability of adolescent substance use comes from recent evidence indicating that this problem behavior is simply one way in which genetic risk for a spectrum of externalizing disorders is manifested. For example, a robust finding in the literature is that shared genetic factors account for the co-occurrence of childhood CD symptoms and both concurrent and later substance use (e.g., Hicks, Krueger, Iacono, McGue, & Patrick, 2004; Krueger et al., 2002; Slutske et al., 1998; Young, Stallings, Corley, Krauter, & Hewitt, 2000). In an adolescent sample, Young and colleagues (2000) found that CD, ADHD, substance experimentation, and novelty seeking were accounted for by a single, highly heritable, latent phenotype; Krueger and colleagues (2002) similarly found that a higher-order, highly heritable externalizing factor linked SUDs, antisocial behavior, and dishinhibited personality in 17-year-old twins. In addition, several candidate gene studies have found that adult substance use problems and adolescent behavioral problems may share genes (e.g., Dick et al., 2006; Dick, Agrawal, et al., 2007; Latendresse et al., 2011). Together, these findings suggest that the co-occurrence among externalizing disorders is in part accounted for by a common genetic vulnerability. Furthermore, researchers have posited that the underlying inherited phenotype that unifies the externalizing disorders is behavioral undercontrol/disinhibition (Zucker, Heitzeg, & Nigg, 2011).

The current literature emphasizes the importance of the environment's potential moderating effects in genetic studies of adolescent substance use. Although the literature with measured genes is just developing and there is concern about failures to replicate, several gene × environment interaction (G×E) studies have uncovered stronger genetic predispositions towards substance use in the context of higher-risk environments. Some of the environmental variables that have been shown to moderate genetic risk for adolescent substance use in this manner across both candidate gene and twin studies include parental monitoring (Dick et al., 2009; Dick, Pagan, et al., 2007; Latendresse et al., 2011), religiosity (Koopmans, Slutske, van Baal, & Boomsma, 1999), peer alcohol use (Dick, Pagan, et al., 2007), rural versus urban residency (Rose, Dick, Viken, & Kaprio, 2001), and parental rule setting (van der Zwaluw et al., 2010). Another framework within which to conceptualize G×E is the differential-susceptibility model, which posits that certain genes may render individuals more susceptible to the environment, regardless of whether the environment is positive or negative (Belsky et al., 2009). Thus individuals who possess "plasticity" genotypes would have the worst outcomes in the context of high-risk environments, but the best outcomes in the context of positive environments. For example, Laucht and colleagues (2012) found that adolescents homozygous for the Met allele of the COMT $Val^{158}Met$ polymorphism had higher levels of drinking under conditions of lower parental involvement and supervision, but also had reduced levels of drinking under conditions of higher parental involvement and supervision.

Research has also highlighted the importance of endophenotypes in genetic studies of adolescent sub-

stance use. "Endophenotypes" are measurable indices that are associated with a phenotype of interest, are heritable, may cosegregate with disease, and are often known or hypothesized to have a closer proximity to the biology underlying the disorder (Gottesman & Gould, 2003; Lynskey, Agrawal, & Heath, 2010). Identifying endophenotypes of SUDs and studying their genetic correlates will be advantageous because endophenotypes can lead to the identification of cases that are less likely to be etiologically heterogeneous than SUD status would be. Endophenotypes may aid in determining the mechanisms through which genes affect SUDs, and they may reduce the number of false positives and negatives in case status determination (Iacono, Carlson, & Malone, 2000). In adolescence, some endophenotypes of substance use have been proposed, including reduced P300 (Carlson, Iacono, & McGue, 2004), neurobehavioral disinhibition (Tarter, Kirisci, Habeych, Reynolds, & Vanyukov, 2004), subjective response to substances (e.g., Ehringer et al., 2007), and impulsivity (Esposito-Smythers, Spirito, Rizzo, McGeary, & Knopik, 2009). Although some work has linked genes to endophenotypes of adolescence substance use (e.g., Esposito-Smythers et al., 2009; Zeiger et al., 2008), more research is needed to identify other relevant endophenotypes in adolescence and the genetic correlates of these constructs.

Over the past several years, the literature on gene identification has grown rapidly. One difficulty associated with gene identification efforts in adolescents is categorizing those individuals who carry an unaffected status only because they have yet to manifest the disorder. This ambiguity can make it difficult to correctly identify those genomic regions that contribute to risk for substance use in adolescence. Although a review of this literature is beyond the scope of this chapter, several studies specifically examining the genetics of adolescent substance use include Stallings and colleagues (2003), Corley and colleagues (2008), and Zeiger and colleagues (2008). Reviews of the broader molecular genetics literature as it relates to substance use can be found in Foll, Gallo, Strat, Lu, and Gorwood (2009), Agrawal and Lynskey (2009), Dick and Foroud (2003), and Edenberg and Foroud (2006). Provided in this chapter are examples of some of the genomic regions that have been implicated in the etiology of adolescent substance use and SUDs through their influences on deviant peer affiliation and parenting behaviors, as well as their interactions with environmental variables.

Although studies indicate significant heritability for substance use and SUDs in adolescence, family history risk can also exert influence through fetal exposure mechanisms. For example, one study found that prenatal exposure to marijuana was associated with greater frequency of adolescent marijuana use, even after the researchers controlled for potential confounding variables such as adolescents' current substance use, pubertal stage, sexual activity, delinquency, peer drug use, family history of drug disorder, and home-environmental variables (Day, Goldschmidt, & Thomas, 2006). Similarly, Disney, Iacono, McGue, Tully, and Legrand (2008) found that prenatal exposure to alcohol raised risk for CD symptoms (a behavioral correlate of alcohol and drug use) in adolescents, even after the investigators controlled for parental SUDs, antisocial/behavioral disorders, and other potential confounding variables. On the other hand, using a more comprehensive measure of familial risk for alcohol problems that assessed both first- and second-degree relatives, S. Y. Hill, Lowers, Locke-Wellman, and Shen (2000) found no effect of prenatal alcohol and nicotine exposure on child/adolescent externalizing problems above and beyond this familial risk. Although conflicting data exist, a review of the literature by Glantz and Chambers (2006) concluded that prenatal exposure to illicit drugs increased risk for offspring SUDs beyond the risk contributed by parental SUDs, although the extent of this increased risk is unknown.

Given that a family history of SUDs is a well-established and robust risk factor for adolescent SUDs, an important goal for research is to understand how this risk is mediated. As described above, studies have demonstrated that there are both genetic and environmental components to the intergenerational transmission of risk. Risk may be mediated through personality and temperamental characteristics (e.g., propensities for negative affectivity, poor self-regulation, impulsivity, sensation seeking); through individual differences in the pharmacological effects and reinforcement value of substances; and through the effects of risky environments. Given the complexity of these processes, researchers have postulated multiple and interrelated pathways of risk that are biopsychosocial in nature. A heuristic model of such pathways has been offered by Sher (1991) and provides the guiding framework for the current review. Sher hypothesizes that vulnerability to SUDs can be described by three submodels or pathways: a deviance-proneness pathway, a pathway emphasizing stress and negative affect, and a pathway that focuses on substance use effects (the enhanced-reinforcement pathway). These pathways are not meant to be mutually exclusive; indeed, the same factors can

contribute to more than one pathway. Although Sher's model was proposed to explain the effects of familial alcoholism on vulnerability to alcoholism, the same pathways can be examined with respect to SUDs more broadly.

THE DEVIANCE-PRONENESS SUBMODEL

Sher's (1991) deviance-proneness submodel is depicted in Figure 4.1 (with the exception of contributions from negative affect, which are considered within the stress and negative affect submodel). In general, the deviance-proneness submodel suggests that the development of SUDs occurs within a broader context of the development of conduct problems and antisociality. Adolescents at risk for SUDs are thought to be temperamentally "difficult," with a heritable predisposition to behavioral undercontrol (Iacono, Malone, & McGue, 2008). They are also considered to be prone to cognitive deficits—including deficits in verbal skills and executive functioning (e.g., working memory, response inhibition, and attentional control)—that contribute to a lack of behavioral and emotional self-regulation. In addition, high-risk children are thought to receive poor parenting (and indeed to evoke poor parenting because behaviorally undercontrolled children are difficult to parent). This combination of temperamental, cognitive, and environmental risk factors sets the stage for failure at school and ejection from the mainstream peer group, which may result in affiliation with deviant peers who provide opportunities, models, and approval for alcohol and drug use. Because this submodel considers substance use within the broader context of antisocial behavior, it is quite similar to theories that attempt to explain the etiology of aggression and conduct problems more generally (see Kimonis, Frick, & McMahon, Chapter 3, this volume).

Temperament and Personality

Numerous studies report that temperamental and personality traits reflecting behavioral undercontrol and poor self-regulation are associated with adolescent substance use problems. For instance, in two reviews, the personality characteristics most consistently associated with adolescent substance use included unconventionality, low ego control, sensation seeking, aggression,

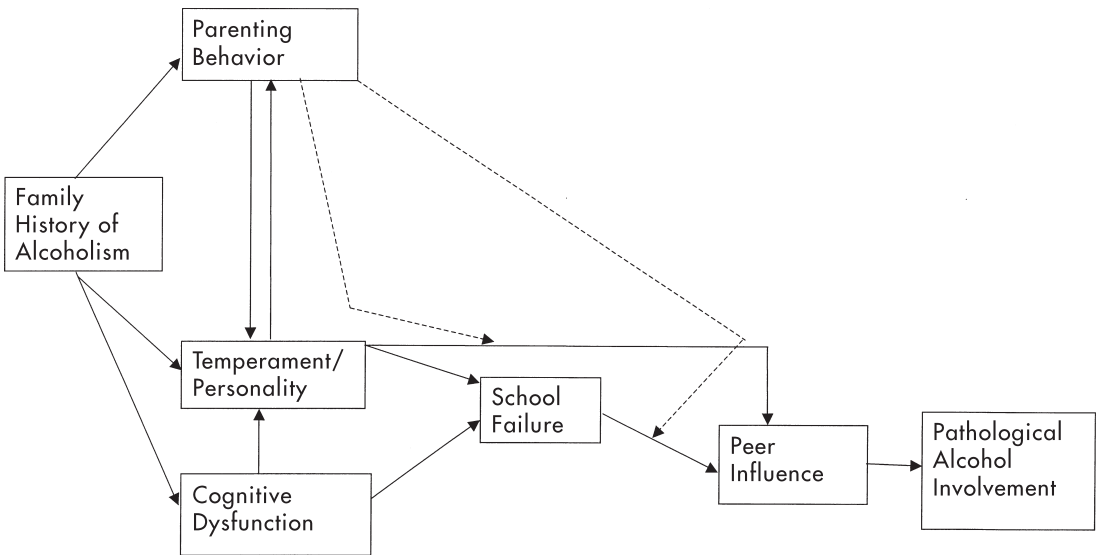

FIGURE 4.1. Schematic diagram of Sher's (1991) deviance proneness submodel. Mediating paths are indicated by solid lines; moderating paths are indicated by dashed lines. The effects of emotional distress (depicted in Sher's original 1991 model) are omitted here and depicted in the stress and negative affect submodel (Figure 4.2). From Sher (1991). Copyright 1991 by University of Chicago Press. Adapted by permission.

impulsivity, and an inability to delay gratification (Bates, 1993; Hawkins et al., 1992).

Longitudinal research has demonstrated that childhood temperamental characteristics reflecting undercontrolled behavior are longitudinally predictive of later substance use problems in adolescence and young adulthood. For instance, Block and colleagues (Block, Block, & Keyes, 1988; Shedler & Block, 1990) found that adolescents who used marijuana at least weekly were characterized as children by heightened levels of behavioral undercontrol and interpersonal alienation, and these traits were observable as early as 3–4 years of age. Similarly, Caspi, Moffitt, Newman, and Silva (1996) found that 3-year-old boys described by others as impulsive, restless, and distractible were at increased risk for an SUD diagnosis by age 21. Lerner and Vicary (1984) found that 5-year-old children with "difficult" temperamental profiles, including high levels of behavioral reactivity/emotionality and slow adaptability, were more likely to use substances in adolescence and young adulthood than children not characterized as "difficult" were. Brook, Whiteman, Cohen, Shapiro, and Balka (1995) found that childhood characteristics of unconventionality and poor control of emotions were associated with increased levels of drug use in adolescence and young adulthood. Such findings suggest that poor self-regulation and undercontrolled behavior are not simply correlates of problematic substance use, but prospectively predict future adolescent drug and alcohol problems, although causal mechanisms are not known.

As noted earlier, several biobehavioral markers of behavioral undercontrol, and consequent risk for adolescent substance use problems, have been identified. One is a diminished P3 component in event-related potentials (ERPs). P3 components of ERPs occur approximately 300 milliseconds after the presentation of a novel or task-relevant stimulus. Reductions in P3 amplitude have been reported for several forms of undercontrolled behaviors, including antisocial personality disorder, ADHD, and aggression, as well as SUDs (Begleiter & Porjesz, 1999; Iacono, Carlson, Taylor, Elkins, & McGue, 1999; Klorman, 1992). Moreover, young children of parents with alcohol use disorders also show reduced P3 amplitude even before the onset of drinking (Begleiter & Porjesz, 1999), and reduced P3 amplitude predicts drinking onset in this population (S. Y. Hill, Shen, et al., 2000; Iacono et al., 1999). Given these data, reductions in P3 amplitude have been viewed as a potential marker for behavioral undercontrol as a diathesis for early-onset substance use. Other candidate biobehavioral markers for behavioral undercontrol and risk for substance use include neurochemical and neuroendocrine responses, as well as ability to modulate autonomic nervous system reactivity (Iacono et al., 1999; see Tarter et al., 1999, for a review).

Additional data suggest that the intergenerational transmission of adolescent substance use problems may be mediated by a predisposition toward behavioral undercontrol. For instance, research has consistently found that children of parents with alcohol use disorders (a population at heightened risk for the development of alcohol problems) show high levels of impulsivity, aggression, and high levels of motor activity (e.g., Blackson, 1994; Jansen, Fitzgerald, Ham, & Zucker, 1995; Martin et al., 1994; Tarter, Alterman, & Edwards, 1985); these traits are observed in their alcoholic parents as well (e.g., Blackson, 1994). Data from twin studies further suggest that indicators of behavioral undercontrol have substantial heritability, and may serve to increase risk for substance use problems in adolescents, particularly in the context of familial alcoholism. Ongoing longitudinal data from the Minnesota Family Twin Study (Iacono et al., 1999) have shown substantial heritability for various indices of undercontrol, including reduced constraint, poor psychophysiological modulation in response to stress, and high levels of externalizing behavior. These traits were also more likely to characterize children with a family history of alcoholism. Specifically, sons of "undersocialized alcoholics" (i.e., parents with alcohol use disorders and comorbid externalizing disorders) were more likely than sons of "socialized alcoholics" (i.e., parents with alcohol use disorders but without comorbid externalizing disorders) or sons of nonalcoholic parents to meet diagnostic criteria for ADHD, CD, or antisocial behavior; to have had contact with the police; and to have a personality style typified by low constraint. In turn, these risk factors were strongly associated with a diagnosis of adolescent SUDs, even after the researchers controlled for effects of paternal alcoholism. Taken together, these findings support a genetic diathesis model for adolescent substance use problems, with the diathesis consisting of heritable individual differences in behavioral undercontrol.

However, although behavioral undercontrol is a well-recognized risk factor for adolescent substance use, it is important to note that behavioral undercontrol is a complex and heterogeneous construct. For example, from a personality perspective, the "propensity to rash action" has been proposed to comprise five dis-

tinct dimensions, including sensation seeking, lack of perseverance, lack of premeditation (acting without planning), and positive and negative urgency (Birkley & Smith, 2011; Lynam, 2011). In general, it has been suggested that three types of processes—those involving reward sensitivity and the seeking of reward; harm avoidance and the avoidance of punishment; and inhibitory control and the ability to restrain behavior to avoid negative consequences—are particularly important for substance use and SUDs (Castellanos-Ryan, Rubia, & Conrod, 2011; Goldstein & Volkow, 2002). Thus adolescents who show elevated levels of sensation seeking and reward seeking, those who show low levels of harm avoidance, and those with low levels of inhibitory control are at risk for substance use. Moreover, dual-process models (e.g., Wiers, Ames, Hofman, Krank, & Stacy, 2010) propose that substance use behavior is the result of an interaction between automatic associations that promote approach or avoidance of substances and inhibitory control. Thus, for example, positive automatic associations with substance use behavior will be more likely to drive behavior in circumstances when more effortful, reflective, top-down cognitive control is weakened. Because cognitive control is likely to be weakened in contexts of high emotional arousal, highly arousing peer social contexts may create a particularly high risk for adolescent substance use.

Although temperament is presumed to reflect a relatively stable behavioral style, the effects of temperament on developmental outcomes are also presumed to be modified by the environment, particularly by parenting and family environments. In studies of adolescent externalizing behavior, it has been reported that poor parenting is particularly detrimental when adolescents show high levels of temperamental reactivity or deficient regulation (e.g., Bates, Pettit, Dodge, & Ridge, 1998; Stice & Gonzales, 1998). Similar results have been reported with respect to adolescent substance use. Specifically, Wills, Sandy, Yaeger, and Shinar (2001) examined moderating effects of temperament and parenting on adolescent substance use (including alcohol, tobacco, and marijuana use), and found that parental risk factors (i.e., substance use, conflict) differentially exacerbated risk for substance use among adolescents with high activity levels and high levels of negative emotionality. Such findings suggest that despite their heritable bases, the effects of temperamental characteristics on substance use outcomes may be either exacerbated or buffered by the type of parenting that adolescents receive. However, studies have also found that the protective effects of parenting and family environment on substance use outcomes are reduced at higher levels of behavioral undercontrol and familial alcoholism, and are absent at the highest levels of risk (King & Chassin, 2004; Zhou, King & Chassin, 2006).

Cognitive Functioning

Additional evidence for deficient self-regulation as a risk factor for adolescent substance use and SUDs may be found at the level of cognitive functioning, in the form of deficits in executive functioning. "Executive functioning" is a multidimensional construct that encompasses a variety of related higher-order cognitive processes allowing for future-goal-oriented behavior. A myriad of different processes have been included in this construct, including planning, organizational skills, selective attention, hypothesis generation, cognitive flexibility, working memory, maintenance of cognitive set, decision making, judgment, inhibitory control, and self-regulation (Lezak, Howieson, Bigler, & Tranel, 2012; Spreen & Strauss, 1998).

From the point of view of risk for adolescent SUDs, a common theme is that deficits in executive functioning make it difficult for children both to create strategic and goal-oriented responses to environmental stimuli, and to use feedback to modify behavior in response to environmental events (Peterson & Pihl, 1990). Such cognitive difficulties in creating goal-directed responses to environmental stimuli then produce heightened levels of behavioral undercontrol, such as impulsive and externalizing behavior, which raise risk for substance use and SUDs (Peterson & Pihl, 1990).

Adolescents with SUDs have shown deficits in cognitive functioning. For example, Brown and colleagues reported that relative to youth without alcohol problems, alcohol-dependent adolescents were characterized by poorer retention of verbal and nonverbal information, poorer attentional capacities, and deficits in visual–spatial planning (Brown, Tapert, Granholm, & Delis, 2000; Tapert & Brown, 1999). Moreover, substance-dependent adolescents with poor cognitive skills and poor coping skills were also more likely to continue using alcohol and drugs over time (Tapert, Brown, Myers, & Granholm, 1999). Similarly, Giancola, Mezzich, and Tarter (1998) found that adolescent girls with SUDs exhibited poorer executive functioning than that of controls.

Deficits in executive functioning have also been found to be associated with alcohol use in communi-

ty samples in late adolescence. For example, Deckel, Bauer, and Hesselbrock (1995) found that lower levels of executive functioning were associated with earlier drinking onset, greater frequency of drinking to get drunk, and higher scores on the Michigan Alcoholism Screening Test in a sample of young adults. Research with college students has yielded similar findings. Giancola, Zeichner, Yarnell, and Dickson (1996) found that lower levels of executive functioning were associated with more adverse consequences of drinking, even after the investigators controlled for absolute levels of alcohol consumption. Sher, Martin, Wood, and Rutledge (1997) found that first-year undergraduates with diagnoses of alcohol use disorders performed more poorly than did students without such diagnoses on measures of visual–spatial ability, motor skill, and attention. However, these studies were cross-sectional in design, and thus could not speak to the directionality of effects.

Several studies have also suggested that executive functioning deficits are found in children of parents with alcohol use disorders—even at early ages, before alcohol problems have developed (e.g., Corral, Holguin, & Cadaveira, 1999; Drejer, Theilgard, Teasdale, Schulsinger, & Goodwin, 1985; Giancola, Martin, Tarter, Pelham, & Moss, 1996; Harden & Pihl, 1995; Peterson, Finn, & Pihl, 1992; Poon, Ellis, Fitzgerald, & Zucker, 2000). These data suggest that executive functioning may be an antecedent risk factor rather than a result of alcohol consumption in this population. Similarly, Deckel and Hesselbrock (1996) found that children of alcoholic parents with poorer executive functioning showed greater increases in alcohol consumption over a 3-year period than did children of alcoholic parents with higher levels of executive functioning, suggesting that executive functioning might be a prospective predictor of substance use among high-risk adolescents. In a separate longitudinal investigation, Atyaclar, Tarter, Kirisci, and Lu (1999) reported significant independent effects of paternal substance abuse and executive functioning on several measures of adolescent drug use, including the lifetime number of drugs used, lifetime exposure to cannabis and tobacco, and severity of consequences resulting from drug use.

Although these findings suggest that executive functioning impairments play an important role in the pathogenesis of substance use, particularly among those at high risk because of parental alcoholism, it is important to note that these studies have not been consistently replicated. Many investigators have not found differences in cognitive functioning between children of alcoholic parents and controls (e.g., Bates & Pandina, 1992; Wiers, Gunning, & Sergeant, 1998). Moreover, measures of attention and working memory have not consistently been found to predict adolescent substance use (Castellanos-Ryan et al., 2011; Handley et al., 2011), and at least one review of the literature has concluded that evidence for executive functioning deficits in children of alcoholic parents is weak and inconsistent across studies (Hesselbrock, Bauer, Hesselbrock, & Gillen, 1991). Response inhibition has been found to have a unique effect on alcohol-related problems and illegal drug use, over and above externalizing symptoms (Nigg et al., 2006), but other studies have not found a relation between response inhibition and cannabis use (Griffith-Lendering, Huijbregts, Vollebergh, & Swaab, 2012) or found that response inhibition predicted conduct problems but not substance use (Castellanos-Ryan et al., 2011; Handley et al., 2011). Given the lack of consistent effects of executive functioning on adolescent substance use, one possibility is that executive functioning is better conceptualized as a moderator of more automatic processes (as proposed by dual-process models; Wiers et al., 2010) than as a main-effect predictor. Alternatively, it has been argued that inconsistent findings for executive functioning measures may be due to problems with the measures themselves, including problems of reliability and weak ecological validity (Barkley, 2012).

Finally, adolescent substance use is related to performance on task measures of risk taking and affective decision making, such as the Balloon Analogue Risk Task (BART; Lejuez et al., 2002) and the Iowa Gambling Task (IGT; Bechara, Damasio, Damasio, & Anderson, 1994), as well as delay discounting. Greater delay discounting of reward (Reynolds & Fields, 2012), poorer performance on the IGT (Goudriaan, Grekin, & Sher, 2007; Xiao et al., 2013), and greater risk taking on the BART (Aklin, Lejuez, Zvolensky, Kahler, & Gwadz, 2005; Lejuez et al., 2002) are associated with more adolescent substance use. However, these are complex tasks for which performance is determined by multiple processes. Thus the mechanisms that link performance on these tasks to adolescent substance use are not always clear.

Parenting and Socialization

Parenting that combines high levels of nurturance with consistent discipline—in other words, what Baumrind

(1991) has termed "authoritative" parenting—has been associated with a lowered risk of adolescent substance use (Adalbjarnardottir & Hafsteinsson, 2001; Hawkins et al., 1992). For example, low levels of parental social support and discipline prospectively predict increases in adolescent substance use over time (King & Chassin, 2004; Stice & Barrera, 1995; Wills, Resko, Ainette, & Mendoza, 2004). In addition, higher levels of harsh parenting (Brody & Ge, 2001) and family conflict have been found to be associated with higher levels of adolescent substance use and SUDs, at least in African American youth. This relation may also be stronger for females than males and for those with elevated negative emotionality (Skeer et al., 2011; Skeer, McCormick, Normand, Bika, & Gilman, 2009; Webb & Baer, 1995; Wills, Sandy, Yaeger, & Shinar, 2001).

Low levels of parental monitoring/knowledge have also been shown to prospectively predict both the onset of substance use and heavy drinking in adolescence, although this effect may differ for males and females (Barnes, Hoffman, Welte, Farrell, & Dintcheff, 2006; Borawaski, Ievers-Landis, Lovegreen, & Trapl, 2003; Coley, Votruba-Drzal, & Schindler, 2008; Dishion, Nelson, & Kavanagh, 2003; King & Chassin, 2004; Reifman, Barnes, Dintcheff, Farrell, & Uhteg, 1998; Steinberg, Fletcher, & Darling, 1994). However, research concerning parent monitoring suggests that, for the most part, parents obtain information about their adolescents because the children choose to disclose information, rather than because parents ask their children about their lives (Fletcher, Steinberg, & Williams-Wheeler, 2004; Laird, Pettit, Bates, & Dodge, 2003; Stattin & Kerr, 2000). Therefore, findings supporting a link between parental monitoring/knowledge and adolescent substance use may really reflect the fact that adolescents who use substances tell their parents less about their lives. Research examining the ease with which adolescents talk to their parents suggests that among sons, communication with fathers is protective against marijuana use and cigarette smoking (Luk, Farhat, Iannotti, & Simons-Morton, 2010).

Finally, parental divorce and living in single-parent families (Duncan, Duncan & Hops, 1996; Waldron, Bucholz, Madden, & Heath, 2009) have been associated with higher levels of adolescent substance use, although some have found that this effect only holds for those not associating with deviant peers (Eitle, 2005). It is also unclear whether single-parent family structure or correlated processes (such as increased conflict or disrupted parent–adolescent relationships) more strongly predict substance use (Brody & Forehand, 1993).

Not only is adolescent substance use related to general parenting style, family climate, and parent–adolescent relationships, but data also suggest that adolescent substance use may be related to parents' specific socialization about the use of substances. That is, parents set not only general rules and expectations for adolescent behavior, but also rules and policies about the use of tobacco, alcohol, and other drugs. They may discuss reasons not to use these substances, and may punish substance use behavior. Cross-sectional and longitudinal studies have suggested that these forms of socialization that are specific to substance use may deter adolescents' substance use behavior (Chassin et al., 2005; Chassin, Presson, Todd, Rose, & Sherman, 1998; de Leeuw, Scholte, Harakeh, Leeuwe, & Engels, 2008; Jackson & Henriksen, 1997).

Thus available data suggest that parent socialization—either in the form of general parenting and parent–adolescent relationships, or in the form of specific attempts to deter substance use—may influence the development of adolescent substance use behavior. Moreover, although data are not extensive, several mediational models suggest that the effects of parenting on adolescent substance use may be mediated through the effects of parenting on affiliations with deviant peers, as specified in various versions of the deviance-proneness pathway (Chassin, Curran, Hussong, & Colder, 1996; Dishion, Capaldi, Spracklen, & Li, 1995; Dishion, Patterson, & Reid, 1988; Roberts et al., 2012).

Recent work on the effects of parenting on adolescent substance use has examined whether these effects are unique, over and above gene–environment covariation (in this case, the relation between genetic risk and parenting). There is likely to be both evocative gene–environment covariation (such that adolescents at genetic risk evoke particular parenting) and passive gene–environment covariation (such that parents pass on a genetic predisposition to substance use) (Reiss, Neiderhiser, Hetherington, & Plomin, 2000). Studying the effects of parenting on adolescent substance use without considering correlated genetic risk is potentially misleading because parenting may be simply a marker of genetic risk or may be a mediator of genetic effects on substance use. Twin studies have found that genetic factors play a significant role in predicting parental affection, conflict, control, and knowledge of children's activities (Cleveland & Crosnoe, 2004; Plomin, Reiss, Hetherington, & Howe, 1994; Reiss et al.,

2000), suggesting the importance of gene–environment covariation.

Recent work has begun examining the link between specific genes and parenting behaviors, with the serotonin transporter polymorphism (5-HTTLPR), the oxytocin receptor gene (OXTR), and the dopamine D2 receptor gene (DRD2) receiving some support for their links to anxiety and mood, which are implicated in parental sensitivity, engagement, and secure parent–child attachment (Bakermans-Kranenburg & van IJzendoorn, 2006; Gillath, Shaver, Baek, & Chun, 2008; Laucht et al., 2012). In addition to research focusing on genes that might predict how caregivers parent their children, there is also work implicating particular receptor systems in child behaviors that evoke certain responses from parents. For example, because of their link to reward, other genes from the dopamine, gamma-aminobutyric acid (GABA), and opioid systems may affect adolescents' risk-taking behavior and likelihood of associating with deviant peers, which may in turn affect the parenting that they receive (Edenberg & Foroud, 2006; Foley et al., 2004; Fowler, Settle, & Christakis, 2011; Rowe et al., 2001; Vaughn, Beaver, DeLisi, Perron, & Schelbe, 2009).

As discussed earlier, there is also work suggesting that genes and parenting interact to predict adolescent substance use outcomes. Although, as noted earlier, there is a need for replication, some data suggest that genes are more predictive of substance use and related outcomes at higher levels of environmental risk (e.g., lower levels of parental monitoring/knowledge; Dick et al., 2009; Dick, Pagan, et al., 2007). Others have found that individuals at higher risk on "plasticity genes" are more vulnerable to both positive and negative environments (Bakermans-Kranenburg & van IJzendoorn, 2006; Belsky & Pluess, 2009).

Finally, less is known about how parenting and family environment factors might differentially affect adolescent SUDs across different ethnic or cultural groups. Although there is evidence for generalizability of familial influences across ethnic groups (Barrera et al., 1999; Nowlin & Colder, 2007), other studies have reported differential magnitudes of relations between parenting and substance use across ethnicity (e.g., Bohnert, Rios-Bedoya, & Breslau, 2009, and Griesler & Kandel, 1998, for tobacco use), or have suggested that the relations between authoritative parenting and adolescent deviance-proneness may vary as a function of ethnicity and community context (Lamborn, Dornbusch, & Steinberg, 1996).

School Failure and Academic Aspirations

Children who are temperamentally poorly regulated, who receive poor parental nurturance and involvement and deficient parental monitoring and discipline, who have parents with less education, and who have cognitive deficits in executive and verbal functioning are at heightened risk for school failure (Blair & Diamond, 2008; Bryant & Zimmerman, 2002; Patterson, 1986; Valiente et al., 2011). Moreover, school failure itself may further elevate risk for the onset of adolescent substance use through several mechanisms. First, school failure is a source of stress and negative affect, which can raise risk for substance use to regulate that affect. Second, school failure can weaken school attachment (e.g., aspirations for higher education, values placed on academic success, participation in mainstream school activities). Many theories of adolescent substance use and deviant behavior—including social control theory (Elliott, Huizinga, & Ageton, 1985), the social development model (Catalano, Kosterman, Hawkins, Newcomb, & Abbott, 1996), and problem behavior theory (Jessor & Jessor, 1977)—suggest that estrangement from mainstream social institutions makes adolescents more vulnerable to engaging in problem behaviors (including substance use) because they feel less bound by conventional social norms and values. Moreover, adolescents who are not committed to academic success will experience less role conflict between the demands of academic roles and the impairment produced by alcohol and drug use, so that they have less reason to refrain from substance use. Third, school failure can increase risk for adolescent drug use because it raises risk for adolescents' ejection from a mainstream peer group, particularly if the school failure is associated with aggressive or underregulated behavior (Bryant, Schulenberg, O'Malley, Bachman, & Johnston, 2003; Dishion, Patterson, Stoolmiller, & Skinner, 1991; Flicek, 1992). Adolescents who are ejected from a mainstream peer group are more likely to affiliate with deviant peers, who model and approve of substance use behavior. Consistent with these mechanisms, available empirical evidence suggests that adolescents with poor grades (Bachman, Staff, O'Malley, Schulenberg, & Freedman-Doan, 2011; Crosnoe, 2006; S. C. Duncan, Duncan, Biglan, & Ary, 1998; Ellickson, Tucker, & Klein, 2008; Gau et al., 2007; Kandel, 1978; Luthar & D'Avanzo, 1999), those with low educational aspirations (Bachman et al., 2011; Paulson, Combs, & Richardson, 1990), those who are unhappy with school

(Fitzpatrick, Piko, Wright, & LaGory, 2005), and those who have low value and expectations for attaining educational success (Bergen, Martin, Roeger, & Allison, 2005; Jessor & Jessor, 1977; Luthar & Ansary, 2005) are more likely to use alcohol or drugs. However, it is important to note a potential exception to this pattern: Extremely high levels of pressure for academic success have been suggested to serve as a risk factor for substance use among affluent adolescents (Luthar & Latendresse, 2005).

Peer Influences

There is a strong relation between an adolescent's substance use and the substance use of the adolescent's friends (Bullers, Cooper, & Russell, 2001; Hawkins et al., 1992; Kandel, 1978; Rosenquist, Murabito, Fowler, & Christakis, 2010). Affiliation with a drug-using peer group elevates risk for adolescent substance use by providing models and opportunities for engaging in, as well as norms for, drug use (Oetting & Donnermeyer, 1998). When adolescents are in the presence of their peers, they take significantly more risks, suggesting that the presence of peers is particularly rewarding (Steinberg, 2008). Indeed, Chein and colleagues (2011) found that situations in which peers were present activated adolescent brain regions associated with reward.

Siblings are an additional source of peer influence on adolescent drug use (Conger & Rueter, 1996; Duncan, Duncan, & Hops, 1996; McGue, Sharma & Benson, 1996). For example, older siblings' drug use during adolescence and early adulthood has been found to prospectively predict younger siblings' use (Bricker, Peterson, Sarason, Andersen, & Rajan, 2007; van der Vorst, Engels, Meeus, Dekovic, & Leeuwe, 2007). However, the strength of the older siblings' influence is moderated by sibling relationship quality, such that a warm and supportive relationship with a delinquent older sibling represents high risk for substance use for the younger sibling (East & Khoo, 2005; Slomkowski, Rende, Conger, Simons, & Conger, 2001; Slomkowski, Rende, Novak, Lloyd-Richardson, & Niaura, 2005). In addition, the transmission of substance use from an older to a younger sibling occurs more often when the two are the same gender and close in age (Trim, Leuthe, & Chassin, 2005).

Even though peer use has been regarded as the strongest predictor of adolescent substance use, researchers have also questioned the interpretation of this relation. Because most studies ask adolescents to report on both their own use and the behavior of their friends, the magnitude of the correlation between peer use and adolescent use is inflated because adolescents who themselves use drugs overestimate their friends' use (Bauman & Ennett, 1996). Correlations between adolescents' and friends' drug use are lower—although still significant—when peers are surveyed directly (Kandel, 1978).

Although there are consistent relations between adolescent substance use and peer substance use in adolescence, these correlations are likely to result from two different processes: peer selection and influence. Individuals who use alcohol are likely to select similar alcohol-using friends (i.e., peer selection), and individuals whose friends either use alcohol or approve of alcohol use are likely to increase their alcohol use (i.e., peer influence). Numerous studies have tested whether selection or influence is driving the relation between an individual's substance use and that of his or her friends (Bauman & Ennett, 1996; Dishion & Owen, 2002; Simons-Morton & Farhat, 2010), with longitudinal studies reporting both peer selection and peer influence effects (Bullers et al., 2001; Dishion & Owen, 2002; Rosenquist et al., 2010).

However, some have found that peer selection effects are stronger than are influence effects (Bullers et al., 2001; Simons-Morton & Farhat, 2010). This has led researchers to speculate about the possibility of an active gene–environment correlation, such that adolescents with a particular genotype seek similar friends or friends who encourage substance use (Loehlin, 2010; Reiss et al., 2000). Indeed, genetic influences on affiliations with deviant or substance-using peers have been found both in twin studies (Cleveland, Wiebe, & Rowe, 2005; Fowler et al., 2007; Kendler & Baker, 2007) and with measured genes (Beaver, Wright, & DeLisi, 2008; Fowler et al., 2011; Vaughn et al., 2009). It is also possible that peer influences mediate the effects of genetic risk on substance use. That is, individuals of particular genotypes select substance-using friends, and those friends in turn influence them to use substances (Reiss et al., 2000). For example, Chassin and colleagues (2012) found that, for males, mu-opioid receptor (OPRM1) genetic variation predicted affiliations with alcohol-use-promoting peers, who increased risk for alcohol-related problems.

In addition to mediating genetic risk, it is possible that peer influences moderate genetic risk. Guo, Elder, and Hamilton (2009) found that the effects of genetic risk on adolescent drinking were larger for those with

heavier-drinking peers. Similarly, Agrawal and colleagues (2010) found that regular substance use was more heritable for women who reported more peer substance use. Peer environments that support alcohol use may act to expose genetic vulnerability and thus show larger genetic effects on drinking, whereas peer environments that constrain drinking may suppress effects of genetic risk. This G×E pattern may also vary with age. Kendler, Gardner, and Dick (2011) found that the interaction between peer group deviance and genetic risk on drinking was strong in early adolescence, weaker in middle adolescence, and nonsignificant in early adulthood. Finally, few G×E studies have been conducted with measured genes and peer influences. van der Zwaluw, Larsen, and Engels (2012) found no significant interactions between best friends' drinking and the dopamine D4 receptor (DRD4) in predicting adolescent drinking, but Johnson and colleagues (2010) found a significant interaction between peer influence and CHRNA5 in predicting problems with nicotine.

Childhood Conduct Problems

A central assumption of the deviance proneness model is that adolescent substance use disorders are related to the broader development of conduct problems and antisociality, and this assumption has widespread empirical support (Hawkins et al., 1992). Conduct problems and aggression predict adolescent substance use (Henry et al., 1993; Kellam, Brown, Rubin, & Ensminger, 1983), escalations in use over time (K. Hill et al., 2000; Hussong, Curran, & Chassin, 1998) and later SUD diagnoses (Chassin, Pitts, & DeLucia, 1999). Moreover, CD is a strong risk factor for adolescent SUDs (Clark, Parker, & Lynch, 1999; Costello et al., 1999; Disney, Elkins, McGue, & Iacono, 1999; Weinberg & Glantz, 1999), and conduct problems have been found to predict SUDs for both boys and girls (Chassin, Pitts, Delucia, & Todd, 1999; Costello et al, 1999; Disney et al., 1999). Interestingly, the relation has been somewhat specific to conduct problems, rather than including all externalizing disorders in general. For example, although ADHD is associated with SUDs, these associations seem largely mediated by the development of associated CD rather than specific to ADHD per se (Costello et al., 1999; Disney et al., 1999; Lynsky & Fergusson, 1995; Molina, Smith, & Pelham, 1999). An exception to this pattern occurs for tobacco problems, which have been linked to attention deficits even in the absence of CD (Disney et al., 1999; Elkins et al., 2007; McMahon, 1999).

THE STRESS AND NEGATIVE AFFECT SUBMODEL

Stress and negative affect mechanisms can be used to hypothesize that individuals who use substances in order to regulate or cope with stress and negative affect are at high risk for SUDs. Accordingly, children and adolescents who experience a high level of environmental stress and/or are temperamentally prone to experience negative affect may be at risk for substance use and SUDs to the extent that they use alcohol or drugs as a way to decrease this negative affect (i.e., as a form of self-medication). Sher's (1991) elaboration of this submodel is depicted in Figure 4.2. Although this submodel is intuitively appealing, it has not enjoyed consistent empirical support and remains less well established in the adolescent literature than the deviance-proneness submodel.

Numerous studies have shown that high levels of negative affect and internalizing symptoms commonly co-occur with adolescent substance use outcomes, including alcohol use, heavy drinking, alcohol use disorder, smoking, tobacco use disorder, cannabis use, nonmedical use of prescription drugs, and other illicit drug use (Deykin, Buka, & Zeena; 1992; Hussong, Jones, Stein, Baucom, & Boeding, 2011; Kassel, Stroud, & Paronis, 2003; Patton et al., 2002; Rohde, Lewinsohn, & Seeley, 1996; Waller et al., 2006; Wu, Ringwalt, Mannelli, & Paktar, 2008). In addition, multiple studies have provided strong evidence that adolescents who experience high levels of environmental stress are more likely to use substances (including alcohol, tobacco, and other drugs), and to escalate the quantity and frequency of their use over time (Chassin et al., 1996; Dube et al., 2006; Hoffman, Cerborne, & Su, 2000; Hussong & Chassin, 2004; Wills, Sandy, & Yaeger, 2002). Moreover, children and adolescents who are exposed to traumatic events, particularly childhood maltreatment (sexual, physical, or emotional abuse and emotional or physical neglect), may also be at risk for substance use problems. These include early onset of substance use (Keyes, Hatzenbuehler, & Hasin, 2011; Whitesell, Beals, Mitchell, Manson, & Turner, 2009), binge drinking (Cisler et al., 2011), alcohol-related problems (Sartor, Agrawal, McCutcheon, Duncan, & Lynskey, 2008), cannabis disorder symptoms (Rogosch, Oshri, & Cicchetti, 2010), and SUDs (Whitesell et al., 2009). Finally, support for a link between adolescent stress/negative affect and substance use is also provided by studies of adolescents in treatment for SUDs, which show that stress, negative affect, and depression are

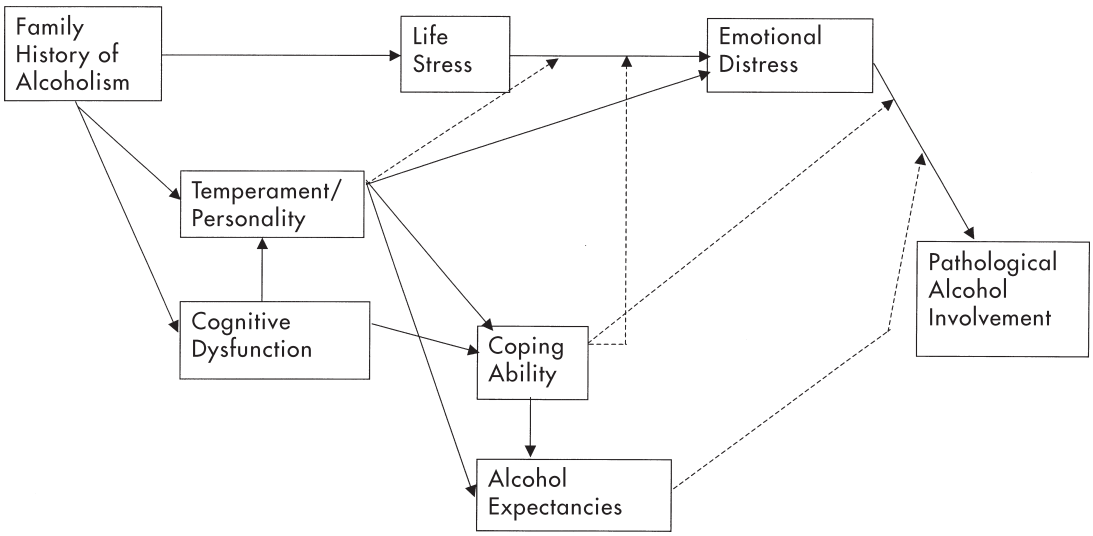

FIGURE 4.2. Schematic diagram of Sher's (1991) stress and negative affect submodel. Mediating paths are indicated by solid lines; moderating paths are indicated by dashed lines. From Sher (1991). Copyright 1991 by University of Chicago Press. Adapted by permission.

associated with relapse after treatment (Cornelius et al., 2003; McCarthy, Tomlinson, Anderson, Marlatt, & Brown, 2005; White et al., 2004).

Although it is clear that stress and negative affect are associated with adolescent substance use involvement, it is less clear whether negative affect and internalizing symptomatology are causes or consequences (or both) of adolescent substance use. Although several prospective studies have linked childhood and adolescent internalizing symptoms to future substance use initiation (King et al., 2004), increases in substance use over time (Mason, Hitchings, & Spoth, 2009), substance-related problems (Mason, Hitchings, & Spoth, 2007), and SUDs (Sung et al., 2004; Wittchen et al., 2007), effects are typically small and are only found for certain subgroups of individuals or at certain developmental periods. Moreover, many other prospective studies have failed altogether to find a significant internalizing pathway to substance use and SUDs during adolescence and early adulthood (Chassin, Pitts, DeLucia, & Todd, 1999; Hansell & White, 1991; K. Hill et al., 2000; Hussong et al., 1998).

One reason for these mixed findings is that adolescent internalizing symptoms often co-occur with externalizing symptoms (e.g., Lewinsohn, Shankman, Gau, & Klein, 2004), which have much stronger and more consistent effects on substance use outcomes (Dierker, Vesel, Sledjeski, Costello, & Perrine, 2007; Hallfors, Waller, Bauer, Ford, & Halpern, 2005; Hussong et al., 1998; King et al., 2004; Ohannessian & Hesselbrock, 2008). Although internalizing and externalizing mechanisms may each contribute unique risk for substance use outcomes, they may also interact with each other over development (Hussong et al., 2011). Unfortunately, the high rates of comorbidity among internalizing and externalizing symptoms during adolescence make it difficult to disentangle these effects (Hussong et al., 2011). Nonetheless, adolescents who display high levels of both internalizing and externalizing symptoms are likely to be at particularly high risk for substance use problems (Pardini, White, & Stouthamer-Loeber, 2007).

Another explanation for the inconsistent empirical support for stress and internalizing symptomatology as prospective predictors of substance use outcomes is that studies often use inappropriate time lags between assessments. Because self-medication is likely to involve using substances close to the time of experiencing a negative event (Park, Armeli, & Tennen, 2004), studies that examine associations between stress/negative affect and substance use over long periods of time may present a poor match between method and theory. Daily

diary and experience-sampling methods (e.g., Hussong, Hicks, Levy, & Curran, 2001) may be better suited for testing self-medication models of substance use. Conversely, others have argued that the time lag between assessments may not be long *enough*, given that an internalizing pathway to SUDs is typically characterized by late-onset substance use problems. Although research on the development of alcohol use disorders typically targets adolescents and young adults, negative affect alcoholism subtypes, such as Cloninger's (1987) Type 1 alcoholism and Zucker's (2006) negative affect alcoholism, posit *adult* rather than adolescent onset.

Among adolescents, however, direct and prospective internalizing effects may only be found for a small subgroup who have both early-onset and clinically significant internalizing symptomatology. Sihvola and colleagues (2008) found that early-onset (i.e., age 14) depression significantly predicted numerous substance use outcomes 3.5 years later, including daily smoking, illicit drug use, and frequency of alcohol use, even after the researchers controlled for comorbid disorders and baseline use. Yet, for most adolescents, early internalizing symptoms will *not* progress to substance use problems; whether negative affect/internalizing symptoms predict problematic substance use outcomes will depend on the extent to which these symptoms cause impairment in other, more proximal domains, such as involvement with deviant peers, social incompetence/rejection, and academic failure (Hussong et al., 2011; Zucker, 2008). In other words, the effects of stress and negative affectivity on substance use during adolescence may be better characterized as indirect than as direct.

The associations between adolescent negative affect/internalizing symptoms and substance use also appear to vary according to the specific type of affect (for a review, see Colder, Chassin, Lee, & Villalta, 2009). As a result, studies that aggregate different types of affect (e.g., depression, anger, anxiety) and internalizing symptoms may obscure their relations with substance use. With respect to depression, research indicates that adolescent depression and substance use may interact with each other to reciprocally influence the severity and course of each problem (Colder et al., 2009). Depressed adolescents may find that experimenting with substances temporarily relieves their mood, reinforcing additional substance use and resulting in the development of SUDs; conversely, repeated substance use may lead to biochemical changes that induce additional depressive episodes (Rao, 2006). Although anger is cross-sectionally related to substance use, it has failed to prospectively predict substance use outcomes (e.g., Swaim, Deffenbacher, & Wayman, 2004; Weiner, Pentz, Turner, & Dwyer, 2001). Affect regulation models of substance use also posit a motivation to use substances in order to increase positive affect (Cooper, Frone, Russell, & Mudar, 1995). Among the few studies that have examined positive affect separately from negative affect, low positive affect has been linked with substance use and substance use escalation (Wills, Sandy, Shinar, & Yaeger, 1999), as well as with adolescent substance use problems among adolescents with high levels of impulsivity (Colder & Chassin, 1997). However, other studies find that positive affect and adolescent substance use are unrelated (Hussong & Hicks, 2003).

The link between anxiety and substance use vulnerability appears to depend on the type of anxiety symptoms. For instance, late childhood separation anxiety may actually reduce the likelihood of substance use during adolescence (Kaplow et al., 2001), whereas adolescent symptoms of generalized anxiety have been linked to increased risk for adolescent substance use onset and frequency (Fröjd, Ranta, Kaltiala-Heino, & Marttunen, 2011; Kaplow et al., 2001) and young adult alcohol use disorders (Sartor, Lynskey, Heath, Jacob, & True, 2007). Posttraumatic stress disorder (PTSD) symptoms have been linked to increased risk for alcohol use initiation (Wu, Bird, et al., 2010) and young adult cannabis use disorders (Cornelius et al., 2010); however, further longitudinal studies of PTSD are warranted before the role of PTSD in youth substance use can be determined. Interestingly, adolescent social anxiety has been linked to *decreased* substance use during adolescence (Fröjd et al., 2011), but to *increased* risk for later adult SUDs (Buckner et al., 2008; Zimmermann et al., 2003). Perhaps social anxiety lowers risk for adolescent substance use because socially anxious adolescents are less likely to select into (or to be selected into) peer contexts that promote substance use, but it raises risk for substance use problems during adulthood, when drinking and other substances use is more common and accessible.

Studies examining negative affect pathways to adolescent substance use also highlight the importance of various moderators, suggesting that internalizing processes may play a larger role for a subset of vulnerable youth. For instance, the effects of stress and negative affect on substance use may be stronger for adolescents with various genetic predispositions (e.g., Audrain-

McGovern, Lerman, Wileyto, Rodriguez, & Shields, 2004; Covault et al., 2007). The association between negative affect and substance use may also be stronger in adolescents who have less social support (Hussong et al., 2001), poorer parental emotion socialization (Hersh & Hussong, 2009), and more positive expectancies about the effectiveness of substance use as a coping mechanism (Hussong, Galloway, & Feagans, 2005; Kassel et al., 2007). Indeed, Sher's (1991) model suggests that the relation between stress or negative affect and substance use should be stronger for those who expect substance use to relieve their emotional distress. Although only a minority of adolescents and young adults report using alcohol to cope with negative affect (1–7% in alcohol studies reviewed by Kuntsche, Knibbe, Gmel, & Engels, 2005), those who do may be at particularly high risk for developing alcohol-related problems and disorders (see Hussong et al., 2011).

Gender may also be an important moderator. Although the literature on gender differences in internalizing pathways to substance use is quite complex, with many contradictory findings, it generally appears that the association between negative affect and substance use may be stronger for girls than for boys (Armstrong & Costello, 2002; Mason et al., 2007; Poulin, Hand, Boudreau, & Santor, 2005). However, boys with *early-onset* depression appear to be at markedly high risk for substance use problems, compared to girls and nondepressed boys (Crum, Storr, Ialongo, & Anthony, 2008; Kovacs, Obrosky, & Sherrill, 2003). Researchers have theorized that early mood symptoms may be more likely to manifest themselves subsequently as mood disorders for girls, whereas subsequent substance use and SUDs are more likely for boys (Klein & Corwin, 2002).

Finally, the effects of stress and negative affect on substance use may also be mediated and/or moderated by individual differences in response to stress. For instance, stress/negative affect mechanisms may be stronger for adolescents who use maladaptive coping strategies (e.g., Kassel, Jackson, & Unrod, 2000; Laurent, Catanzaro, & Callan, 1997; Wills, Sandy, Yaeger, Cleary, & Shinar, 2001), who have ruminative stress response styles (Skitch & Abela, 2008), and who have dysregulated biological stress response systems (De Bellis, 2002; Schepis, Rao, Yadav, & Adinoff, 2011). Importantly, research has also shown that early trauma and chronic stress may lead to dysregulation of the hypothalamic–pituitary–adrenocortical axis and other neurobiological mechanisms underlying stress regulation, which may increase risk for early initiation of substance use and later SUDs (Andersen & Teicher, 2009; De Bellis, 2002). Therefore, early adversity may have long-lasting implications for developmental trajectories of substance use via stress-induced changes to the brain that increase vulnerability to stress and negative affect.

THE SUBSTANCE USE EFFECTS SUBMODEL

The discussions above of the deviance-proneness submodel and the stress and negative affect submodel of adolescent substance use serve to illustrate the importance of considering some of the functions that substance use might serve for adolescents. The deviance-proneness submodel highlights the fact that adolescent substance use occurs in a broader social context of low behavioral constraint and drug-use-promoting peer networks. Within these peer social networks, adolescent substance use may serve to communicate a social image of toughness and precocity, and to express an adolescent's actual or ideal self-concept (Barton, Chassin, Presson, & Sherman, 1982; Jessor & Jessor, 1977; Sussman, Dent, & McCullar, 2000). Moreover, the acquired preparedness model suggests that disinhibition biases the learning process, so that impulsive and sensation-seeking adolescents will be more likely to focus on positive substance use effects (see, e.g., Corbin, Iwamoto, & Fromme, 2011). The stress and negative affect submodel highlights the affect-regulating functions that alcohol and drug use may fulfill for adolescents. As such, it is important to remember that alcohol and drug consumption involves reinforcing pharmacological effects, and to consider these effects within etiological models of adolescent SUDs. Sher's (1991) substance use effects submodel is depicted in Figure 4.3. In this model, a family history of alcoholism (or, in our extrapolation, other SUDs) is thought to be associated with individual differences in sensitivity to the pharmacological effects of alcohol and other drugs (as well as with the temperamental and cognitive variables discussed earlier). As people experience different effects of their substance use, these experiences then influence their expectancies about the effects of future consumption. These expectancies in turn influence the likelihood of future substance use involvement.

A large literature has examined the effects of alcohol and drug self-administration in both human and animal laboratory studies, and this literature is beyond the scope of the current chapter. Moreover, for ethical

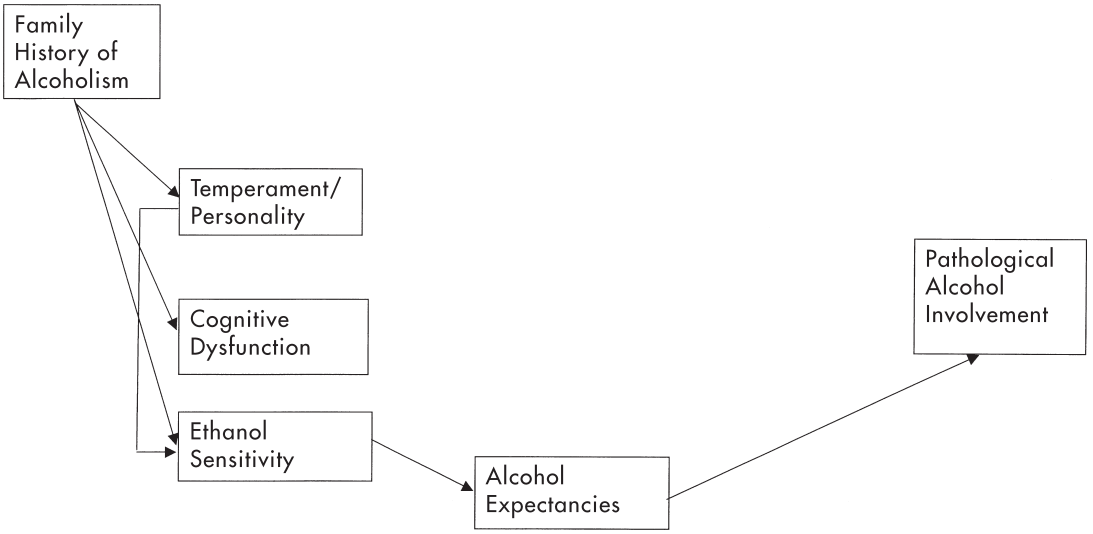

FIGURE 4.3. Schematic diagram of Sher's (1991) substance use effects submodel. From Sher (1991). Copyright 1991 by University of Chicago Press. Adapted by permission.

reasons, human laboratory studies of alcohol or drug administration have been confined to adult participants, so that little is known about the relation between alcohol or drug effects in the laboratory and adolescent alcohol or drug use in the natural environment. Rather, researchers who are interested in child and adolescent populations have focused on their beliefs or expectancies about substance use effects. These expectancies can be measured in young children even before substance use begins, and they become increasingly complex and more positive in adolescence (Dunn & Goldman, 1996). Moreover, adolescents' expectancies about substance use effects are systematically related to their consumption. For example, adolescents' expectancies that alcohol has positive effects prospectively predict their drinking behavior (Smith, Goldman, Greenbaum, & Christiansen, 1995; Stacy, Newcomb, & Bentler, 1991), and expectancies concerning marijuana and stimulants are also associated with adolescent drug preferences and drug use (Aarons, Brown, Stice, & Coe, 2001). Finally, in addition to self-reported beliefs and expectancies about substances, studies have assessed adolescents' implicit attitudes (more automatic positive and negative associations to substances) that are measured indirectly by tasks such as reaction times to pair substance use stimuli with positive and negative words. Measures of more automatic associations have prospectively predicted adolescents' cigarette use (Sherman, Chassin, Presson, Seo, & Macy, 2009) and changes in cannabis use (Cousijn, Goudriaan, & Wiers, 2011), and dual-process models of adolescent substance use propose that the effects of automatic associations are particularly powerful when processes of reflective, cognitive control are weakened (see Wiers et al., 2010).

NEIGHBORHOODS AND OTHER MACRO-LEVEL INFLUENCES

Sher's (1991) deviance-proneness, stress and negative affect, and substance use effects submodels do not explicitly focus on the effects of social influences that are broader than peer and family environments. However, researchers have become increasingly interested in ways in which broader, macro-level environments such as neighborhoods, schools, and SES might influence adolescent substance use and SUDs (mirroring broader trends in the study of macro-level influences on developmental psychopathology). It is likely that these macro-level influences interact with parenting and peer variables, the family environment, personality characteristics, and other etiological factors to influence

adolescent substance use. Neighborhoods, schools, and other social contexts could influence risk for substance use and disorder by providing social norms about the relative acceptability of use, by providing different ease of access to different substances, and by providing different degrees of punishment or sanctions for use. Theoretically, these factors would influence the prevalence of use for adolescents in all three of Sher's etiological pathways.

Several neighborhood characteristics have been linked to increased substance use among youth, including alcohol outlet density, lack of neighborhood strength (e.g., lack of community identity, lower participation in local activities), residential mobility and instability, high population density, high levels of crime or violence, and positive community norms about substance use (Buu et al., 2009; Gibbons, Gerrard, Wills, Brody, & Conger, 2004; Huckle, Huakau, Sweetsur, Huisman, & Caslwee, 2008; Lambert et al., 2004; Leventhal & Brooks-Gunn, 2000; Tobler, Komro, & Maldonado-Molina, 2009; Wilson, Syme, Boyce, Battistich, & Selvin, 2005).

Although neighborhoods with high concentrations of ethnic minorities are often characterized as disadvantaged and high-risk, research indicates that minority youth are generally *less* likely to use alcohol and other substances than are European American youth (SAMHSA, 2001). Some studies suggest that ethnic differences in youth substance use are more likely to be explained by differences in family and peer processes than by compositional characteristics of neighborhoods. For instance, lower rates of substance youth among both Hispanic American (Cox, Burr, Blow, & Parra Cardona, 2011) and African American (Watt & Rogers, 2007) youth have been linked to a greater emphasis on family relationships and lower susceptibility to peer influences. It should be noted, however, that higher levels of acculturation have been shown to erode some of these protective factors for Hispanic American youth (Cox et al., 2011).

Schools are also an important social context for the development of substance use. For instance, research indicates that risk for substance use and SUDs is higher for adolescents who attend schools where substance use is perceived as normative and socially acceptable, and where low levels of school connectedness and poor student–teacher relationships exist (Bond et al., 2007; Botticello, 2009; Fletcher, Bonell, & Hargreaves, 2008). Similarly, school intervention studies have shown that increasing school participation, improving relationships between students and adults (e.g., teachers, coaches) at school, increasing enjoyment and interest in school, and reducing truancy may effectively reduce substance use, especially for boys (Fletcher et al., 2008). In regard to school policies about substance use, consistent enforcement of school antismoking policies has been linked to reduced youth tobacco use, although little is known about how school policies on alcohol and other drugs influence use (Evans-Whipp et al., 2004).

In addition to factors such as neighborhoods, schools, and SES, adolescent substance use is also shaped by public policies, particularly with respect to legal drugs (i.e., alcohol and tobacco). Research has shown that increases in alcohol (Chaloupka, Grossman, & Saffer, 2002) and cigarette taxes/prices (Carpenter & Cook, 2008) significantly reduce youth drinking and smoking. Likewise, increasing the minimum drinking age, lowering the allowable blood alcohol concentration for drivers under the age of 21, regulating the density of alcohol and tobacco outlets, limiting the proximity of alcohol and tobacco outlets to schools, and reducing the permissible volume of alcohol and tobacco advertising/media exposure have all been linked with reduced youth alcohol (Anderson, Chisholm, & Fuhr, 2009; Paschall, Grube, & Kypri, 2009) and tobacco (Henriksen et al., 2008) use and consequences.

CONCLUSIONS AND FUTURE DIRECTIONS

As illustrated by the discussion above, much is known about the nature of adolescent substance use and SUDs, as well as about etiological factors; moreover, much effort has already gone into the development of empirically evaluated treatment and prevention programs. For example, a large and diverse literature has produced a consensus across studies that a family history of SUDs, childhood conduct problems, temperament or personality traits reflecting behavioral undercontrol, and affiliations with drug-using peer networks all raise risk for substance use and SUDs.

However, there are also many unanswered questions and areas for future research. The adequacy of existing diagnostic criteria as they are applied to adolescents must be clarified, and the impact of the two-symptom threshold in DSM-5 requires evaluation. In regard to etiology, although the role of family history risk is well established, less is known about the mechanisms underlying the intergenerational transmission of risk, or about the protective factors that might

buffer this risk. The increasing number of genetically informative studies has suggested that a heritable predisposition to behavioral undercontrol is an important risk factor, and more needs to be known about G×E in the externalizing and internalizing developmental pathways. In terms of externalizing pathways, recent studies have reinforced the notion that behavioral undercontrol is a complex and multifaceted concept. More needs to be known about different aspects of behavioral undercontrol, how they develop, how malleable they are by environmental influences, and how they are related to adolescent substance use outcomes. A better understanding of the multiple processes that drive overall performance in laboratory decision-making and risk-taking tasks is also needed. In regard to the internalizing pathway, studies are needed to clarify its role in the context of strong externalizing effects, and to clarify the roles of different types of negative affect (particularly the importance of moderating variables, including coping and behavioral undercontrol). That is, rather than considering internalizing and externalizing pathways in isolation, it may be more useful to focus on behavioral undercontrol and underregulation as moderators of the relation between environmental stress or negative affect and subsequent substance use outcomes. In general, our understanding of adolescent substance use will benefit from research advances in studying the development of emotional, cognitive, and behavioral self-regulation.

Moreover, in studying these etiological models, it is important to retain a developmental perspective. Recent studies have begun to illuminate ways in which early adversity might influence later deficits in self-regulation (including G×E), which can in turn increase risk for adolescent substance use disorders. Similarly, adolescent substance use itself may further contribute to risk because of particular neurobiological sensitivity to substance use effects, and more data are needed about the magnitude and duration of the effects of substance use on adolescent neurobiological development. For all the etiological models, data are also needed about ways in which our existing findings might vary across particular gender and ethnic subgroups. Moreover, this topic is in need of stronger theory development, which would help guide our interpretations of why particular risk or protective factors might operate in particular ways within certain gender or ethnic subgroups. Beyond questions of gender and ethnic variation, the examination of other macro-level societal and cultural factors (neighborhood effects, school effects, and effects of social policies like taxation) has often been conducted in isolation from more individual-level factors. Research is needed to study neighborhood, school, and social policy influences as they interact with individual, family, and peer factors.

Finally, as is evident from our review, it is unlikely that a single etiological pathway will be capable of explaining the development of adolescent SUDs. Thus we are in need of studies and methods that are capable of differentiating among multiple pathways that might underlie different trajectories of substance use. To accomplish these ambitious goals requires studies that are multilevel and multidisciplinary, and that embed studies of SUDs within a broader developmental perspective. Given the clinical and public health importance of adolescent substance use and SUDs, it is likely that the field will continue to expand in these future directions.

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PART III

MOOD DISORDERS AND SUICIDE

CHAPTER 5

Child and Adolescent Depression

CONSTANCE L. HAMMEN
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DEFINING CHILD AND ADOLESCENT DEPRESSION

Joey is a 10-year-old boy whose mother and teacher have shared their concerns about his irritability and temper tantrums displayed both at home and at school. With little provocation, he bursts into tears, yells, and throws objects. In class, he seems to have difficulty concentrating and seems easily distracted. Increasingly shunned by his peers, he plays by himself at recess—and at home, spends most of his time in his room watching TV. His mother notes that he has been sleeping poorly and has gained 10 pounds over the past couple of months from constant snacking. A consultation with the school psychologist has ruled out learning disabilities or attention-deficit/hyperactivity disorder (ADHD); instead, she says, he is a deeply unhappy child who expresses feelings of worthlessness and hopelessness—and even a wish that he would die. These experiences probably began about 6 months ago when his father—divorced from the mother for several years—remarried and moved to another town, where he spends far less time with Joey.

Diagnostic Criteria

The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association, 2013) provides essentially the same criteria for major depressive disorder (MDD) for both adults and children. The criteria are shown in Table 5.1. Persistent depressive disorder (dysthymic disorder) is a diagnosis of chronic, mild to moderate depressive (or for children, irritable mood) symptoms, with a duration of at least 1 year (in adults, duration is at least 2 years). With the new category of persistent depressive disorder, DSM-5 differs from DSM-IV, which defined chronic major depression and dysthymic disorder in separate sections; DSM-5 now emphasizes *persistence* rather than severity. Even the fairly mild symptoms typical of persistent depressive (dysthymic) disorder beginning in childhood or adolescence do not mean that it is a relatively benign condition, however. Such chronic symptoms commonly predict the development of major depressive episodes (MDEs), and may predict a long-term course with significant psychosocial impairment—especially if the symptoms are associated with familial depression and poor parent–child relationships, as is often the case (Klein, Shankman, & Rose, 2008).

In recognition that irritability is a common expression of distress in depressed youngsters (as shown in the case of Joey), DSM-5 specifies that irritable mood may be substituted for depressed mood. However, irritability occurring in MDEs or persistent depressive (dysthymic) disorder is to be distinguished from a new DSM-5 depressive disorder, disruptive mood dysregula-

TABLE 5.1. DSM-5 Diagnostic Criteria for Major Depressive Disorder

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
Note: Do not include symptoms that are clearly attributable to another medical condition.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (**Note:** In children and adolescents, can be irritable mood.)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.
(**Note:** In children, consider failure to make expected weight gain.)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly ever day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

Note: Criteria A–C represent a major depressive episode.

Note: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual's history and the cultural norms for the expression of distress in the context of loss.

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There has never been a manic episode or a hypomanic episode.
Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

Coding and Recording Procedures

The diagnostic code for major depressive disorder is based on whether this is a single or recurrent episode, current severity, presence of psychotic features, and remission status. Current severity and psychotic features are only indicated if full criteria are currently met for a major depressive episode. Remission specifiers are only indicated if the full criteria are not currently met for a major depressive episode.

In recording the name of a diagnosis, terms should be listed in the following order: major depressive disorder, single or recurrent episode, severity/psychotic/remission specifiers, followed by as many of the following specifiers without codes that apply to the current episode.

Specify:

With anxious distress
With mixed features
With melancholic features

(continued)

TABLE 5.1. *(continued)*

With atypical features
With mood-congruent psychotic features
With mood-incongruent psychotic features
With catatonia
With peripartum onset
With seasonal pattern

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tion disorder, which was intended to provide an alternative to the excessive diagnosis of bipolar disorders in children when the presentation is marked by severe and persistent temper outbursts and irritability rather than classic episodic mood changes (for further discussion, see Youngstrom & Algorta, Chapter 6, this volume). Disruptive mood dysregulation disorder in children is defined by pronounced and frequent temper outbursts, with rage, aggression, and persistently angry mood (see Table 5.2). Evidence of its validity as a depressive disorder is scant at present, however, and critics have argued that it may not be either distinguishable from oppositional defiant disorder or conduct disorder, or predictive of a depressive course (e.g., Axelson et al., 2012).

TABLE 5.2. DSM-5 Diagnostic Criteria for Disruptive Mood Dysregulation Disorder

A. Severe recurrent temper outbursts manifested verbally (e.g., verbal rages) and/or behaviorally (e.g., physical aggression toward people or property) that are grossly out of proportion in intensity or duration to the situation or provocation.
B. The temper outbursts are inconsistent with developmental level.
C. The temper outbursts occur, on average, three or more times per week.
D. The mood between temper outbursts is persistently irritable or angry most of the day, nearly every day, and is observable by others (e.g., parents, teachers, peers).
E. Criteria A–D have been present for 12 or more months. Throughout that time, the individual has not had a period lasting 3 or more consecutive months without all of the symptoms in Criteria A–D.
F. Criteria A and D are present in at least two of three settings (i.e., at home, at school, with peers) and are severe in at least one of these.
G. The diagnosis should not be made for the first time before age 6 years or after age 18 years.
H. By history or observation, the age at onset of Criteria A–E is before 10 years.
I. There has never been a distinct period lasting more than 1 day during which the full symptom criteria, except duration, for a manic or hypomanic episode have been met.
   Note: Developmentally appropriate mood elevation, such as occurs in the context of a highly positive event or its anticipation, should not be considered as a symptom of mania or hypomania.
J. The behaviors do not occur exclusively during an episode of major depressive disorder and are not better explained by another mental disorder (e.g., autism spectrum disorder, posttraumatic stress disorder, separation anxiety disorder, persistent depressive disorder [dysthymia]).
   Note: This diagnosis cannot coexist with oppositional defiant disorder, intermittent explosive disorder, or bipolar disorder, though it can coexist with others, including major depressive disorder, attention-deficit/hyperactivity disorder, conduct disorder, and substance use disorders. Individuals whose symptoms meet criteria for both disruptive mood dysregulation disorder and oppositional defiant disorder should only be given the diagnosis of disruptive mood dysregulation disorder. If an individual has ever experienced a manic or hypomanic episode, the diagnosis of disruptive mood dysregulation disorder should not be assigned.
K. The symptoms are not attributable to the physiological effects of a substance or to another medical or neurological condition.

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Developmental differences in the expression of depressive symptoms have been noted, even if these are not codified in the formal diagnostic criteria. As summarized by Avenevoli, Knight, Kessler, and Merikangas (2008; see also Rao & Chen, 2009), somatic complaints are more common among younger samples, who also express less subjective dysphoria and hopelessness; hypersomnia increases during adolescence, and appetite decreases (in girls). Depressed boys are at the greatest risk of suicidal behaviors in late adolescence, whereas girls are at the highest risk during middle adolescence. Yorbik, Birmaher, Axelson, Williamson, and Ryan (2004) compared the symptoms of nearly 900 depressed children and adolescents, and found that depressed adolescents exhibited significantly more fatigue, hypersomnia, suicidal thoughts and attempts, hopelessness/helplessness, and weight loss than children.

It is possible that additional research on developmental expressions of depression will suggest further age-appropriate modifications of the diagnostic criteria. For example, a longitudinal study of MDD in preschoolers found that although the DSM-IV criteria validly defined a group of young children with depression and homotypic continuity into early childhood (Luby, Si, Belden, Tandon, & Spitznagel, 2009), the minimum duration and frequency criteria might not necessarily apply. Children who met full symptom criteria but not duration and frequency did not differ in severity, impairment, or risk of MDD 2 years later (Gaffrey, Belden, & Luby, 2011). Further study of developmentally relevant modifications is needed, and potential alterations may be especially important for significant but subclinical cases that might otherwise not be identified.

Like adult depression, childhood depression sometimes includes psychotic symptoms and endogenous (melancholic) features indicative of severe depression. However, the symptom manifestations that have attracted most attention among children and adolescents are suicidal thoughts and actions, which are commonly but not exclusively associated with depressive disorders (see Cha & Nock, Chapter 7, this volume). The topic has attracted widespread attention for two reasons. First, the U.S. Food and Drug Administration issued a "black box" warning of suicidality as an alleged side effect of antidepressant medications among children, adolescents, and young adults; a discussion of this is beyond the scope of this chapter (but see *www.nimh.nih.gov/health/topics/child-and-adolescent-mental-health/antidepressant-medications-for-children-and-adolescents-information-for-parents-and-caregivers.shtml*). Second, suicidality certainly underscores the severity and lethality of depressive disorders, reminding us that these disorders are serious problems and not merely expressions of youthful turmoil. A review by Bridge, Goldstein, and Brent (2006) notes that suicidal ideation is very common in adolescence with reported point prevalence rates of 15–25%, whereas actual suicide attempts occur in 1–4% of adolescent males and 1.5–10% of females. Completed suicides increase in frequency from childhood to older adolescence, and are considerably higher in males than in females (e.g., 17% for males vs. 3% for females among older adolescents in the United States). Depressive disorders appear to be present in approximately 40% of completed suicides, and even higher rates are seen in youth for whom depression is comorbid with substance use and disruptive behavior disorders (Bridge et al., 2006). Rates of depression have been reported as 40–80% among those who attempt suicide (Cash & Bridge, 2009). In samples of clinically referred youth with depressive disorders, 85% report suicidal ideation, and 32% make a suicide attempt during adolescence or young adulthood (Kovacs, Goldston, & Gatsonis, 1993).

Continuity of Depression Severity

Depression in its "clinical" forms is represented by diagnostic categories as discussed thus far, but DSM classifications, despite their value in improving reliability and communicability, have the disadvantage of implying that individuals either do or do not "have" the disorders in question. In the context of depression, taxometric analyses of the latent structure of DSM-IV MDD symptoms in a sample of 845 youth (ages 9–17) suggested that depression is continuously, rather than categorically, distributed for both children and adolescents and boys and girls (Hankin, Fraley, Lahey, & Waldman, 2005). These authors recommend dimensional assessment of the severity of depression in order to fully capture the phenomena. Importantly, subsyndromal or subclinical depressions that fall short of full diagnostic criteria may nevertheless predict negative outcomes and commonly warrant intervention. Among adults, for example, subclinical levels of symptoms and minor depression portend degrees of functional impairment and use of services often approximating those of individuals with MDD (e.g., Backenstrass et al., 2006; Cuijpers, de Graaf, & van Dorsselaer, 2004). In a youth sample, subclinical depression at ages 17–18 predicted

elevated rates of MDD and depressive symptoms and other disorders (as well as treatment seeking) in two subsequent follow-ups to age 25, compared to those without depressive symptoms (Fergusson, Horwood, Ritter, & Beautrais, 2005; see also Shankman et al., 2009).

Many of the studies of depression in children and adolescents reported in this chapter do not rely on diagnostic assessments, but instead are based on elevated scores on a continuous measure of depression severity covering various symptoms of the syndrome. Commonly used self-report scales are the Children's Depression Inventory (Kovacs, 1980) and the Center for Epidemiologic Studies Depression Scale (Radloff, 1977), both well-validated measures of severity of depressive symptoms, although questions arise about their specificity to depression versus more general negative affect. Similar to studies of clinical compared to subclinical diagnoses, a youth's high scores on self-report measures may portend significant clinical and functional impairment even if the person is not diagnosable (e.g., Gotlib, Lewinsohn, & Seeley, 1995). Use of the self-report Patient Health Questionnaire for Depression (Kroenke & Spitzer, 2002), which assesses the presence of the nine MDD symptoms and has been adapted for children and adolescents, has been recommended in DSM-5 as a supplement to diagnostic evaluation, providing a continuous score of severity of depression.

Clinical Course of Depression

Age of Onset

The prototypical depression is MDD with adolescent onset. In the National Comorbidity Survey Replication—Adolescent Supplement (NCS-A), the median age of onset for DSM-IV mood disorders was 13 (Merikangas et al., 2010). Retrospective assessment among community adults typically indicates that middle to late adolescence is the most common age of onset for a first episode of MDD or significant symptoms (e.g., Burke, Burke, Regier, & Rae, 1990; see also Kessler, Berglund, Demler, Jin, & Walters, 2005). In their community sample, Lewinsohn, Pettit, Joiner, and Seeley (2003) reported mean onset of MDD at around 14 years and mean onset of dysthymic disorder at around 11 years for both boys and girls. As discussed in the section on gender and depression, early adolescence is the point at which the rates of major depression increase sharply for girls and exceed depression rates in boys.

Age of onset appears to be an important potential marker for the course of a depressive disorder and the possibility of etiologically different subtypes. Compared to childhood onset, adolescent onset predicts greater homotypic continuity, whereas childhood onset is more commonly associated with heterotypic continuity. For example, Weissman, Wolk, Wickramaratne, and colleagues (1999) followed a clinically ascertained group of prepubertally depressed youngsters for 10–15 years into adulthood, and found that the majority did not go on to have adult depressive experiences. These youngsters had high rates of psychological disorders and significant maladjustment, but there was poor specificity for depressive disorders. Similar results were reported by Harrington, Fudge, Rutter, Pickles, and Hill (1990) in a follow-back study of the adult functioning of individuals who had been treated for depression as children or adolescents. Thus, across these studies, *childhood* onset of depression may predict significant disorder but not specifically recurring depression, except in subsamples characterized by less comorbidity, recurrent MDDs, and family history of depression. Many children presenting with depression plus externalizing disorders may have an etiologically different depression, or actually may not have depressive disorder as such, but rather suffer from marked emotional and behavioral dysfunction that eventually coalesces into nondepressive psychopathology. As reported later in the section on genetic factors in depression, studies of heritability typically find much stronger evidence of heritability for adolescent-onset depression (similar to adult depression) than for childhood onset (e.g., Rice, 2010).

Recurrence

Data on continuity of *adolescent* depressive disorders into adulthood are strongly consistent and underscore the premise that much depression seen in adults is actually recurrent adolescent-onset depression. Several large-scale prospective community samples reported on the outcomes in young adulthood of those who had been found to have a diagnosis of MDD during adolescence. The Queensland High Risk Study (Hammen, Brennan, Keenan-Miller, & Herr, 2008), the Dunedin (New Zealand) Multidisciplinary Health and Development Study (Bardone, Moffitt, Caspi, Dickson, & Silva, 1996), the Ontario Child Health Study (Fleming, Boyle, & Offord, 1993), the Oregon Adolescent Depression Project (Lewinsohn, Rohde, Klein, & Seeley, 1999),

and the Upstate New York study (Pine, Cohen, Gurley, Brook, & Ma, 1998) all reported high rates of recurrence of MDD in young adulthood (approximately 25–45% within 4 years). Recurrence rates of 40–60% are typical of clinically ascertained samples. A large-scale 10-year study of clinic-referred adolescents followed up to a mean age of 26 found that only 37% survived without an episode of MDD in adulthood (Weissman, Wolk, Goldstein, et al., 1999).

Among those with childhood onset of depression, true childhood-onset unipolar depression is relatively rare, but appears to be associated with a high risk of recurrence; many with unipolar depression have been found to have early-onset dysthymic disorder followed by MDEs (so-called "double depression"), as well as a high degree of depressive disorders in relatives (Birmaher et al., 2004; Kovacs, Akiskal, Gatsonis, & Parrone, 1994; Kovacs, Devlin, Pollock, Richards, & Mukerji, 1997; Weissman, Wolk, Wickramaratne, et al., 1999). Several studies have found a strong association between childhood anxiety symptoms and inhibited or withdrawn behavior, and later anxiety and depressive disorders (e.g., Goodwin, Fergusson, & Horwood, 2004; Katz, Conway, Hammen, Brennan, & Najman, 2011).

It should be noted that a significant minority of children initially (mis)diagnosed with unipolar depression in clinical settings eventually evidence hypomania or mania, which enables a bipolar disorder to be diagnosed (reviewed in Kovacs, 1996; see Youngstrom & Algorta, Chapter 6, this volume). For instance, Kovacs, Akiskal, Gatsonis, and Parrone (1994) found that 13% of their sample initially diagnosed with depression "switched" to bipolar disorder if followed long enough. Geller, Fox, and Clark (1994) found that among a clinical sample of severely depressed children (ages 6–12), 32% switched to bipolar I or II during a 2- to 5-year follow-up. Although symptom predictors of switching have yet to be validated, having a family member with a bipolar disorder increases the likelihood that a child's depression may be an early manifestation of a bipolar disorder. Biederman and colleagues (2009) found that depressed children and adolescents with comorbid ADHD or conduct disorder at baseline also had an increased likelihood of eventual bipolar diagnoses.

Comorbidity

The co-occurrence of disorders has attracted considerable attention in recent years, and comorbidity has now become widely recognized as the rule rather than the exception among depressed youngsters. Community studies permit the best tests of comorbidity rates, inasmuch as clinical populations may be biased because treatment seeking is more common among those with multiple conditions, which in turn are associated with greater impairment of functioning. In a large British community survey, children ages 5–15 with depression were most likely of those with any disorder to have at least one current comorbid diagnosis (66%) (Ford, Goodman, & Meltzer, 2003). Depressed children and adolescents are especially likely to experience anxiety disorders, but also conduct/behavioral disorders, as well as substance use disorders (in adolescents). Angold, Costello, and Erkanli (1999) conducted a meta-analysis of comorbidity in community studies of youngsters and reported a median odds ratio (degree of association) of 8.2 for depression and anxiety disorders, 6.6 for depression and conduct/oppositional defiant disorder, and 5.5 for depression and ADHD. It should be noted that patterns of comorbidity and timing of disorders may differ somewhat by developmental stage and gender (see O'Neil, Conner, & Kendall, 2011; Zahn-Waxler, Shirtcliff, & Marceau, 2008).

To a considerable extent, depression usually occurs after an earlier-onset disorder. A particularly striking case is that of anxiety disorders. Rohde (2009) reported that anxiety disorders occurred first in 85% of youth with comorbid depressive/anxiety disorders (see also Essau, 2003), although depression also may be followed by anxiety disorders in some cases. Externalizing disorders often have earlier onset than comorbid depressive disorders, although the pattern is variable across studies (Rohde, 2009). Kessler, Avenevoli, McLaughlin, and colleagues (2012) retrospectively evaluated temporal patterns of disorders in the NCS-A: They factor-analyzed disorders into classes labeled Fear (e.g., social and specific phobia, panic disorder), Distress (generalized anxiety or separation anxiety disorders and depressive disorders), Behavior (e.g., oppositional defiant disorder, conduct disorder, ADHD), and Substance disorders. The investigators determined that within-class associations were significantly stronger than cross-class associations (e.g., Distress disorders predicted other Distress disorders). Fear disorders were the strongest cross-class predictors, consistent with the common observation of early-onset anxiety disorders preceding depressive disorders.

The magnitude of depression comorbidity raises important clinical, conceptual, and methodological questions. Clinically, the presence of comorbid conditions

with depression predicts greater impairment of functioning, sometimes elevated rates of suicidal behavior, and greater treatment utilization, but less successful treatment outcomes (reviewed in Rohde, 2009). Conceptually, extensive comorbidity means that research findings attributed to depression may sometimes reflect effects due to unreported comorbid conditions or to the greater severity/impairment typically associated with comorbidity. The high rates of comorbidity have been variously hypothesized to arise from deficiencies in the diagnostic system, such as overlapping symptoms, shared etiological factors, or a functional relationship between disorders (e.g., disruptive behavior disorders may cause stressful consequences that provoke depressive reactions). Notably, there are significant bodies of research on shared etiological features of depression and anxiety disorders (e.g., genetic, personality/temperament, and neurotransmitter/neurocognitive factors), and on differentiating shared and unique predictive factors (e.g., Anderson & Hope, 2008; Clark & Watson, 1991).

A full discussion of the origins and meaning of depression comorbidity is beyond the scope of the present chapter. However, it is worth noting the emergence of analytic and assessment strategies to deal with the joint problems of the heterogeneity of the depression phenotype and diagnostic comorbidity, which are barriers to precision in the understanding of depression and its unique risk factors and consequences. Of relevance to depression is the use of quantitative approaches to aggregating manifest DSM diagnoses into superordinate categories, based on the assumption that disorders within the superordinate category reflect a common cause. Numerous studies mostly on adults have supported general internalizing and externalizing factors (e.g., Eaton et al., 2012; see Krueger & Markon, 2006), but Kessler, Avenevoli, McLaughlin, and colleagues (2012) also demonstrated the broad internalizing factor among adolescents with diagnoses may be subdivided into Fear and Distress factors. Such transdiagnostic approaches to the study of child and adolescent depression/anxiety might yield new insights beyond those of studies more narrowly focused on specific DSM diagnoses. In addition, the National Institute of Mental Health has developed the Research Domain Criteria (Sanislow et al., 2010) as a research strategy intended to study specific functions across multiple units of analysis, to cut across diagnostic boundaries, and to try to translate basic research into an improved and integrative understanding and treatment of psychopathology. This strategy is somewhat similar to the search for "endophenotypes" or "intermediate phenotypes." An endophenotype is the more specific representation or element of a disorder that is between the disease and likely distal heritable aspect of the mechanism of the disorder but is not the same as the diagnostic entity. In youth depression, for example, bias toward negative emotions (negative mood), or impaired reward functioning (anhedonia), or a particular biological function such as amygdala reactivity to emotional stimuli are a potential endophenotype that might provide a more focused target of study independent of the diagnostic heterogeneity of MDD and comorbidity (e.g., Hasler, Drevets, Manji, & Charney, 2004). Further developments in our understanding of youth depression are likely to require assessment strategies and case identification methods that go beyond use of DSM categories.

Summary

Depressive disorders and significant symptoms in children and adolescents often portend serious psychological and functional adjustment problems—sometimes recurring depression, but other times different forms of maladjustment into later adolescence and adulthood. Adolescent-onset depression is virtually the "prototype" of what we mean by MDD in adults. However, the differences among presentations of depression by age, clinical features, comorbidities, and outcomes are obstacles to research. Thus further study of developmentally appropriate diagnostic and assessment methods, as well as both transdiagnostic and endophenotypic approaches to characterization of the phenomena, are warranted.

EPIDEMIOLOGY

Prevalence/Incidence

Recent years have seen an increase in epidemiological surveys of child and adolescent disorders using diagnostic interviews and representative samples, although variations in assessment and informant methods have precluded precise comparability across studies. A review of 28 U.S. and international surveys using standardized diagnostic criteria was reported by Avenevoli and colleagues (2008), who found a range of 2–13% in 6- or 12-month prevalence of MDD among adolescents (approximately 13–18 years), and about 1–3% among

school-age children (7–12 years). The NCS-A, the largest and most nationally representative U.S. diagnosis-based survey, reported a 12-month prevalence rate of 8.2% for MDD or dysthymia in the 13- to 17-year-old sample (Kessler, Avenevoli, Costello, Georgiades, et al., 2012); about one-third of adolescents with depression were characterized as having "severe" cases, as defined by functional impairment represented by a score of 50 or less on the Children's Global Assessment Scale (Kessler, Avenevoli, Costello, Green, et al., 2012). Merikangas and colleagues (2010) reported a lifetime rate of 11.7% with MDD or dysthymia in the NCS-A, including 8.7% with severe depression. Avenenvoli and colleagues (2008) found that rates of dysthymia are typically are higher than those of MDD among children, but lower than those of MDD among adolescents.

Epidemiological samples also report markedly high rates of elevated depressive symptoms. A U.S. school-based survey of 11-to 15-year-olds obtained self-reports of DSM criteria for MDE in the past 12 months, and found that 18% of youth overall met the criteria (25% females, 10% males; Saluja et al., 2004). In the National Longitudinal Study of Adolescent Health of youth in grades 7–12 (AddHealth), 29% of youth reported depressive symptoms for the past week meeting the "moderately severe" cutoff of 16 on the Center for Epidemiologic Studies Depression Scale, and 9% met the "severe" cutoff of >24 (Rushton, Forcier, & Schectman, 2002). One year later, 44% of youth with severe symptoms continued to report the same high levels.

Gender, Socioeconomic, and Race/Cultural Differences in Depression

Besides evidence for higher rates of depression among adolescents than children, other notable epidemiological issues concern distributions by gender and additional sociodemographic factors. Most studies indicate that boys and girls have largely similar rates of depression in childhood, but by early adolescence, girls' rates of depressive disorders accelerate dramatically to approximately twice the rates as for boys, and the female–male gender difference remains throughout adulthood and occurs cross-nationally (e.g., Kessler, Avenevoli, Costello, Georgiades, et al., 2012; Merikangas et al., 2010; Nolen-Hoeksema & Girgus, 1994).

The female preponderance of depression is a significant challenge to theories about the origins of these disorders. Several theoretical perspectives highlight the interactive contribution of sex-linked differences in hormonal and biological functioning, stress-related processes, and interpersonal relatedness to the emerging sex difference during adolescence (e.g., Cyranowski, Frank, Young, & Shear, 2000; Hilt & Nolen-Hoeksema, 2009; Rudolph, 2009). Collectively, these perspectives suggest that complex associations among puberty-linked gonadal hormones and brain neurotransmitters affect mood and biological processes in response to stressful circumstances during adolescence in vulnerable individuals. Risk is also thought to be intensified in girls relative to boys due to girls' greater exposure and reactivity to social challenges during this time (Rudolph, 2002; Shih, Eberhart, Hammen, & Brennan, 2006), which in turn are believed to result from both biological sex differences in affiliative needs and socialization experiences that create a heightened focus on interpersonal connectedness and social-evaluative concerns (Cyranowksi et al., 2000; Hilt & Nolen-Hoeksema, 2009; Rudolph, 2009). Girls also are exposed more often to traumatic sexual abuse experiences, which can further affect their biological and psychological reactivity to social stressors (Hilt & Nolen-Hoeksema, 2009). There are additional differences between the genders in the ways they cope with stressful life events and depressed mood, with women tending to adopt a more passive, internalized, ruminative style that amplifies depressive symptoms, compared to males' more active/distracting and instrumental coping that dissipates negative emotionality (Nolen-Hoeksema, 2000). During the transition through puberty, interpersonal vulnerability, social risk, and normative developmental challenges (e.g., physical-maturational, cognitive-developmental, and social-contextual changes) collectively contribute to the emerging sex difference in depression (Rudolph, 2009). Moreover, this developmental context of risk is particularly salient in girls who progress through puberty earlier than their peers—as reflected in prospective links between early maturation and heightened depressive symptoms—suggesting that puberty and its timing may be more important predictors of the emerging sex difference than chronological age per se (Rudolph, 2014). Clearly, complex, integrative models are necessary to account for the emergence of marked sex differences in rates of depression across adolescence.

Sociodemographic variables that represent relatively adverse environmental conditions also are generally associated with higher rates of depression in adult samples, but the evidence is less consistent for youth (e.g., Kessler, Avenevoli, Costello, Georgiades, et al., 2012).

Poverty was not associated with lifetime depressive disorders in youth in the NCS-A study (Merikangas et al., 2010). In their meta-analysis of depressive symptomatology in adolescent samples, Twenge and Nolen-Hoeksema (2002) found no association between socioeconomic status and depression. Similarly, evidence of systematic differences in depression by race/ethnicity has been mixed, with some studies showing elevated rates of depressive disorders and symptoms in African American, Hispanic/Latino, and Asian American samples compared with European American samples, but other studies showing no differences (e.g., Anderson & Mayes, 2010; Latzman et al., 2011). Higher rates of mood disorders were seen in Hispanic adolescents than in non-Hispanic European American adolescents in the NCS-A lifetime rates (Merikangas et al., 2010). Twenge and Nolen-Hoeksema (2002) also found that Hispanic samples scored higher levels of depressive symptoms than did African American or European American samples. Further studies are needed to explore race and ethnicity effects by addressing methodological shortcomings, and to separate out effects that might be caused by different cultural expressions of depressive symptoms and adverse conditions that could be associated with ethnic status (e.g., Anderson & Mayes, 2010).

Birth Cohort Effects

Earlier reports of birth cohort effects showing higher rates of major depression in those born more recently (e.g., Klerman et al., 1985) have been replicated in the United States and internationally by the Cross-National Collaborative Group (1992), indicating growing rates of childhood or adolescent onset of depression among those born in more recent decades. Results from the original National Comorbidity Study also showed evidence of increasing prevalence of MDEs in those born since 1960 (Kessler, Avenevoli, & Merikangas, 2001). Various analyses of the sources of such increasing rates generally have argued against methodological artifacts as explanations, such as memory or increasing willingness to admit to depressive experiences. Most of the research has been based on retrospective accounts; obviously, longitudinally collected information is needed to examine the issue more directly. Twenge and Nolen-Hoeksema (2002) examined longitudinal studies of depressive symptoms (controlling for age and period effects) and found evidence of decreasing symptoms for boys and no changes for girls, contrary to the findings of earlier retrospective studies. It is likely that rates of depressive disorders did increase among youth in recent years—clearly accompanied by higher rates of treatment seeking, impairment, and suicidality—but whether the effect has now diminished, or was in fact due in significant part to changes in perceptions and awareness of depression, remains unresolved.

ETIOLOGY OF DEPRESSION

Biological Vulnerability to Depression

Brain Structures and Neural Circuitry

Efforts to understand the neural underpinnings of depression have commonly focused on brain structures associated with detecting, responding to, and regulating emotional information—mostly in limbic and cortical circuits, including prefrontal cortex (PFC), amygdala, hippocampal, ventromedial striatum, and related areas. The amygdala is involved in detection of stimuli that are salient for the individual's immediate well-being. Meta-analyses of structural findings have largely confirmed reductions in amygdala *volume* in adults with depression (especially those who are unmedicated), compared with controls (Hamilton, Siemer, & Gotlib, 2008). According to a review of imaging studies of depressed children and adolescents, there is similar but not entirely consistent evidence of amygdala volume differences in depressed and nondepressed youth (Hulvershorn, Cullen, & Anand, 2011); however, certain cortical areas, such as the PFC, orbitofrontal cortex (OFC), and anterior cingulate cortex (ACC), more consistently show volume abnormalities similar to those seen in adult depression.

Smaller amygdala volume is associated with greater responsivity to emotional stimuli. Studies of amygdala *activation* commonly present stimuli such as emotional faces. Depressed adults who were scanned while viewing fearful faces displayed greater amygdala activation compared to nondepressed controls (e.g., Monk, 2008). Similar paradigms generally yield parallel findings in youth, although with small samples and some inconsistencies between child and adolescent samples (Hulvershorn et al., 2011). Yang and colleagues (2010) presented an emotional face-matching task to adolescents with depression and to matched controls, and observed abnormally hyperactive left amygdala in the depressed youth. Increased amygdala activation also has been observed in adolescents at risk for depression due to maternal depression (Monk et al., 2008). Using a neu-

ral activation paradigm, Joormann, Cooney, Henry, and Gotlib (2012) demonstrated that at-risk girls were less successful in cognitive control (i.e., using positive autobiographical memories to "repair" sad mood induced by a film). Compared to the control daughters, the at-risk daughters showed less activation of dorsal areas of the PFC to recruit positive memories to reduce sad mood, and showed sustained greater amygdala activation. The authors speculate that these neural patterns reflect a trait marker stemming from difficulty in regulating negative affect, potentially portending development of depression (especially in the face of stressors). Emotion regulation processes based in limbic–cortical interactions also may be disrupted in youth with very early-onset MDD. Pagliaccio and colleagues (2012) studied school-age children who had experienced preschool onset of depression, using a version of the sad mood elaboration task of Joormann and colleagues, and found similar hypoactivity in areas of the PFC.

It should be noted that research has yet to determine the origins of depression-related cortical–limbic abnormalities—whether they are acquired, genetic, or both. Several studies have demonstrated the role of gene variants in neural correlates of disorder. Studies of both adults and children show increased activation of the amygdala to negative emotional stimuli among those with the short alleles of the serotonin transporter gene (5-HTTLPR; e.g., Furman, Joormann, Hamilton, & Gotlib, 2011; Hariri et al., 2002). Lau and colleagues (2010) found greater amygdala activation to emotional faces among brain-derived neurotrophic factor (BDNF) Met-allele carriers compared to Val/Val homozygotes in a sample of adolescents with depressive or anxiety disorders. Pagliaccio and colleagues (2012) found that severity of initial preschool depression was associated with later dysfunctional brain activity, and hypothesized that the depression symptoms may play a causal role in decreasing ability to effectively exert cognitive or prefrontal control over one's emotions.

Another element of cortical, limbic, and striatal brain regions implicated in emotion-processing neural circuits that are believed to be dysregulated in MDD is the hippocampus (HC), adjacent to the amygdala. The HC plays a major role in consolidation of information into long-term memory as well as in emotional responding, and is an important regulator of PFC function. It contains high levels of glucocorticoid receptors and is involved in the regulation of the hypothalamic–pituitary–adrenocortical (HPA) axis through its projections to the hypothalamus. It is vulnerable to stress-related steroids, which have been speculated to cause HC atrophy under conditions of severe and prolonged stress. Considerable evidence has shown reduced HC volume in depressed adult patients (e.g., Kempton et al., 2011; MacQueen & Frodl, 2011), and HC dysfunction contributes to sustained dysregulation of the stress response. Child and adolescent studies have generally found similar reduced HC volumes (Hulvershorn et al., 2011). Rao and colleagues (2010) found lower HC volumes in both depressed adolescents and at-risk adolescents (due to parental depression), and lower HC volume was associated with higher levels of early life adversity. Chen, Hamilton, and Gotlib (2010) similarly found lower HC volumes in girls ages 9–15 at risk for depression due to maternal depression. Several studies have noted potential genetic and environmental effects on reduced HC volume. For example, Frodl and colleagues (2010) found that adults' reports of childhood stress interacted with the presence of short alleles of the 5-HTTLPR gene to predict hippocampal volume. They speculated that genetic processes predictive of depression partly affect the extent of HC changes in response to stress.

Another conceptual paradigm for studying emotional mechanisms underlying depressive disorders has focused on biological bases of reward processing, involving affective, motivational, and decisional components, behaviorally reflected in depressed individuals' low mood and reduced experiences of pleasure, and biased perceptions of and attention to negative outcomes. Considerable evidence has emerged from task-based imaging studies of abnormalities in the striatum, amygdala, and OFC in depressed adults (e.g., Diekhof, Falkai, & Gruber, 2008). Studies of the reward behaviors and neural patterns of depressed children and adolescence also indicate abnormalities such as blunting of reward-related activation (e.g., Forbes et al., 2009). Similarly, even before the development of depression, girls at risk due to maternal depression displayed abnormal patterns under conditions of reward and loss in the striatum and the dorsal ACC, compared to a no-risk comparison group (Gotlib et al., 2010).

Reward circuitry also has been discussed in terms of asymmetries in PFC function associated with approach- and withdrawal-related mood and emotion, with left-sided hypoactivation associated with depression and reduced perception and pursuit of positive incentives, and right-sided hyperactivation associated with inhibition and anxiety (Davidson, Pizzagalli, Nitschke, & Putnam, 2002). Both infants of depressed

mothers and depressed adolescents display relatively reduced left frontal activation measured by electroencephalogram (reviewed in Davidson et al., 2002). These authors speculate that the interconnections of the PFC and other cortical and subcortical structures represent a dysfunctional circuit in which there is deficient regulation of the amygdala, potentially resulting in prolonged processing of negative affect, and insufficient modulatory control by other cortical functions. These ideas are bolstered by a decade of neuroimaging research, as noted above. However, it is important to acknowledge not only that the childhood/adolescent literature on brain functions is relatively small, but that the origins of abnormal neural structures and circuits are matters of speculation. There also is a paucity of longitudinal research clarifying the developmental course of functional brain abnormalities and their clinical consequences. The potential role of gonadal hormones in the development of depression, for example, is enormously complex, in part due to the crucial links among hormones, brain structures and functions, and neurotransmitters (Blanton et al., 2012).

Hypothalamic–Pituitary–Adrenocortical Axis

Dysregulation of the HPA axis is one of the most robust biological correlates of adult depression, with evidence of elevated cortisol levels, elevated corticotropin-releasing hormone (CRH), and impaired negative feedback control of the HPA axis. It is generally hypothesized that exposure to stressful events and chronic circumstances triggers the development of depression in part through the HPA axis and its associated brain connections, with the supposition that severe and/or early stress exposure may alter neural and HPA axis functioning (e.g., Heim, Newport, Mletzko, Miller, & Nemeroff, 2008). Some individuals also are presumed to have preexisting genetically or environmentally mediated abnormalities in the stress response system, which make them vulnerable to depressive reactions to stress (e.g., Halligan, Herbert, Goodyer, & Murray, 2007).

Earlier studies of child and adolescent depressed samples provided supportive but inconsistent evidence of HPA axis dysregulation, but more recent meta-analyses and reviews have drawn different conclusions. Guerry and Hastings (2011; see also Lopez-Duran, Kovacs, & George, 2009) examined studies based on different methods: dexamethasone suppression, basal cortisol, CRH infusion, psychological challenges, and children of depressed parents. Noting numerous methodological deficiencies, Guerry and Hastings (2011) and Lopez-Duran and colleagues (2009) nevertheless found that when studies were grouped by methods, there was fairly consistent evidence of abnormalities in HPA axis functioning in depressed or at-risk children and youth, including elevations in basal levels of cortisol, greater cortisol response to psychological stressors, and a predictive association between elevated cortisol and later development of depression. Moreover, differences between depressed and nondepressed youth generally appeared to be smaller in scale than between depressed and nondepressed adults, suggesting the need for developmentally informed hypotheses and methods. Indeed, research indicates that baseline cortisol levels and reactivity to stress increase across adolescence and pubertal development (e.g., Gunnar, Wewerka, Frenn, Long, & Griggs, 2009).

Guerry and Hastings (2011) suggested that cortisol differences are particularly observed under stressful conditions, such as laboratory stressors and both acute and chronic stress exposure (including having a depressed mother). Examining cortisol in the context of stressful situations, rather than naturally occurring levels, may improve prediction of future depressive symptoms. In one study, Susman, Dorn, Inoff-Germain, Nottelmann, and Chrousos (1997) found that cortisol reactivity to a stressful situation (blood draw) predicted depressive symptoms 1 year later. In another study, Rudolph, Troop-Gordon, and Granger (2011) found that exposure to the stressful experience of actual peer victimization interacted with heightened anticipatory cortisol while awaiting a laboratory peer-related stressor to predict depressive symptoms 1 year later. These findings suggest that sensitivity of the HPA axis to ongoing stressors, particularly in youth with a history of stress exposure, may serve as a risk factor for subsequent depression.

Adam, Sutton, Doane, and Mineka (2008) also emphasized the need for longitudinal studies of youth prior to the development of depression, and accentuated the importance of the "cortisol awakening response" (CAR, which occurs approximately 40 minutes after waking up) as a particularly potent predictor of future depression onset. Adam and colleagues (2010) found that elevated baseline CAR, but not other measures of cortisol such as bedtime or daily slope, predicted a significantly increased rate of depressive disorder over the next year in a community sample of late adolescents. It was suggested that the CAR measure is uniquely pre-

dictive of future depression, whereas other measures of cortisol functioning covary with current depression. Because the CAR marks the highest cortisol level of the day, Adam and colleagues speculate that over time high levels contribute to changes in brain glucocorticoid receptors involved in the negative feedback regulation of the HPA axis, including changes in the hippocampus and amygdala and their dysfunctional effects in the cortical–limbic circuits underlying emotion regulation. As to the origins of elevated CAR, these authors note the possibility of genetically transmitted characteristics, but emphasize the likelihood that adverse experiences in childhood modify the developing brain and its HPA axis characteristics.

Genetics

There have been enormous empirical and methodological advances in genetic research in recent years, and these offer a wide array of approaches to the study of genetic contributions to psychological disorders. Depression, while one of the most prevalent of all public health issues, unfortunately offers a substantially heterogeneous phenotype for study, varying in symptomatology, comorbidity, severity, age of onset, course, and impairment. The topic of child and adolescent depression contributes its own unique issues and questions: Do genetic features apply similarly to child, adolescent, and adult populations? How are we to characterize nature–nurture questions? What is the nature/mechanism of genetic effects on depression in youth?

It has been well established in reviews and meta-analyses that depression runs in families (e.g., Rice, Harold, & Thapar, 2002), but the contributions of heritability and environment are obviously confounded, due to the psychological and environmental effects of depression and its vulnerabilities and risk factors for other family members. Quantitative genetic analyses in the form of twin studies provide methods of partitioning the variance contributed by genetic and environmental factors. In general, studies of adults report heritability estimates of around .4, with more variance accounted for by environmental factors, particularly that which is unique to individuals and not "shared" in family contexts (reviewed in Lau & Eley, 2010). When applied to children and adolescents, however, twin studies have provided more variable heritability estimates. Rice (2010) notes that heritability is nonsignificant in childhood samples (with high rates of environmental contribution), whereas heritability is significant among adolescents, similar to rates found in adult depression. The majority of twin studies of children and adolescents have been based on symptom measures of depression, with some differences depending on whether self-ratings or parental ratings are employed. Thus caution is warranted until further studies with more diagnostic-based ascertainment are conducted. The finding that adolescent but not childhood depression has a significant heritable component is consistent with several follow-up studies of depressed child patients into adulthood, which found relatively low rates of continuity of depression (although those who were not depressed as adults nonetheless had severe behavioral disorders and impaired functioning; see, e.g., Harrington et al., 1990; Weissman, Wolk, Wickramaratne, et al., 1999). It should be noted that although questions remain about heritability of depression across different ages, analyses of gender differences tend to find little evidence of different genetic contributions to males and females, despite the greater incidence of depressive disorders in females arising in adolescence (Franic, Middledorp, Dolan, Ligthart, & Boomsma, 2010).

Important developmental information has emerged from *longitudinal* twin studies. For example, Lau and Eley (2006) examined depressive experiences three times during adolescence and early adulthood in the G1219 study, finding evidence of "new" genetic and nonshared environmental influences emerging over time. The investigators speculated that such changes might contribute to the increasing rates of depression in adolescence, and that such changes might mutually influence each other (such as increasing selection into stressful situations, which themselves could trigger other genetically driven vulnerabilities toward depression). A longitudinal study of Swedish twins at four points between ages 8 and 20 by Kendler, Gardner, and Lichtenstein (2008) examined changes in genetic and environmental risk factors for mixed depression/anxiety symptoms. They found evidence for changes in genetic influences, with new influences coming "online," but also for attenuation of earlier influences on later symptoms. They conclude that genetic factors show a dynamic course over development, possibly contributing to the low continuity of symptoms from childhood to adolescence.

Although classical quantitative genetic analyses of twin samples permit the partition of variance in depression into genetic and environmental factors, newer methodologies have also yielded important leads. For example, the Children of Twins study of twin sets of parents and their children permits analysis of genetic effects separate from family (environmental) condi-

tions. Investigators Silberg, Maes, and Eaves (2010) examined whether genetic or family environmental factors (or both) provided the best explanation for the association between parent and offspring depression. The authors concluded that the best predictor of the associations between parent and offspring depression was family environment, whereas offspring conduct disorder was predicted by both genetic and environmental factors.

Research in psychopathology in general has increasingly developed techniques and devoted resources to the molecular genetic approaches to gene finding, including various studies of depression in adults. However, such strategies have not been applied to depressed child and adolescent samples, and probably need to be deferred until clearer resolution of age and developmental issues is attained. Nevertheless, there has been considerable interest in addressing the question of how genetic factors exert their effects—in both adult and child/adolescent depression—with increasing focus on candidate genes. Specifically, studies of gene–environment interactions (G×E), and to a lesser degree gene–environment correlations (*r*GE), have employed the same candidate genes as those studied in adult depression. It appears that, as in adults, depression in youth is associated with genetic risk for increased exposure to adverse environments (*r*GE) as well as greater reactivity to such environments (G×E). Notably, a polymorphism in 5-HTTLPR has been associated with adult depression, particularly under stressful conditions (reviewed in Karg, Burmeister, Shedden, & Sen, 2011). Several studies have found similar relevant patterns in depressed or "at risk" (due to maternal depression) children (e.g., Gibb, Uhrlass, Grassia, Benas, & McGeary, 2009; Hayden et al., 2008), and adolescent or mixed child/adolescent samples (Eley et al., 2004; Goodyer, Croudace, Dudbridge, Ban, & Herbert, 2010; see also Hankin, Jenness, Abela, & Smolen, 2011, for a longitudinal analysis). Other studies of candidate genes in adult depressed samples also have yielded evidence of gene–environment interactions (e.g., BDNF—Goodyer et al., 2010; Kaufman et al., 2006; dopamine D2 receptor gene—Hayden et al., 2010). Increasingly, investigators are integrating brain circuit activation with genetic analyses in youth samples. For example, as noted in the review of brain reactivity, Lau and colleagues (2010) found that adolescent depressed or anxiety patients who were BDNF Met carriers showed greater amygdala and hippocampal activations than those with Val/Val homozygotes, although many inconsistencies in findings across neuroimaging (and candidate gene–environment) studies are evident, suggesting needs for replication, larger and better-characterized or homogeneous samples, and measurement precision.

Studies of *r*GE are particularly needed for understanding risk for depression due to parental depression, as depression is strongly correlated with various environmental circumstances, such that children "inherit" not only genes but environments including dysfunctional parenting (a possible case of "passive" *r*GE). Evocative and active *r*GE may also occur, as when a child's heritable traits lead to behaviors that provoke reactions in others, which in turn contribute to depression (e.g., dependency may provoke rejection), or lead to selection into adverse environmental conditions (e.g., low self-esteem may contribute to the selection of dysfunctional romantic partners). *r*GE with respect to the occurrence of stressful life events is well known; Hammen (1991), for example, used the phrase "stress generation" to refer to the tendency of individuals with a history of depression (not just current depression) to contribute to the occurrence of stressful life events—a trend also observed in children with depression and children of depressed women. Starr, Hammen, Brennan, and Najman (2012) found that the presence of short alleles of 5-HTTLPR interacted with depression to predict stressful life events in a high-risk sample of adolescents. Lau and Eley (2008) applied quantitative genetic analyses to twins and siblings in the G1219 longitudinal study to test for different effects of *r*GE and G×E; they incorporated two measures of the environment—negative life events that had been at least partly caused by a participant, and participants' reports of maternal punitive discipline. The complex findings implicated both G×E and *r*GE on the two measures, and suggested that adolescent depression's genetic risks are due in part to exposure to these two adverse conditions, and that the adverse conditions themselves may activate genetic effects and increase the probability of depressive reactions. The authors call for further studies of the mechanisms by which genetic effects are mediated, including brain circuits such as amygdala reactivity, as well as cognitive and personality processes.

Although the future of genetic approaches to understanding depression in adults and youth will doubtless lead in exciting directions with the expansion and further development of traditional quantitative and molecular paradigms, *epigenetic* processes that determine the where, when, and how much of fundamental protein components of DNA will also increasingly expand our understanding of genetic mechanisms of behavior. As reviewed by Lau and Eley (2010), animal research on

how gene expression is affected by environmental experiences, such as maternal care, will invariably open up new findings and questions about the origins, developmental course, and stability of behavioral and emotional outcomes relevant to depression.

Summary

Undeniably, the past decade has seen a surge in interest and methodological advances in the study of biological characteristics associated with adult depression—and, by extension, child and adolescent depression. Considerable interest focuses on emerging evidence in depressed children and adolescents on dysfunctional neural circuits underlying emotional processing and their associations with brain regions and mechanisms of information processing and cognitive control, as well as the effects of dysregulated biological stress processes in the HPA axis, and their associations with neurocognitive mechanisms. Similarly, research has underscored the importance of genetically mediated influences. However, major questions remain about the origins and mechanisms of neural abnormalities, and the transactions among experiential and biological factors. Developmentally sensitive models, studied in longitudinal designs, are needed for the field to advance in the clarity of our understanding of depression as it appears in youth.

Emotional Vulnerability to Depression

Mood disruptions are fundamental to depression; consequently, developmental theory and research have sought to uncover the unique pathways through which emotional functioning contributes to risk for depression in youth. In addition to the biological and cognitive processes related to emotions reviewed in other sections of this chapter, investigations of emotional vulnerability to depression have explored stable, trait-like aspects of emotionality (i.e., temperament), and situational, state-like aspects of emotional processing, responses, and regulation.

Theoretical Models

One group of theoretical perspectives focuses on temperament, as reflected in stable individual differences in self-regulation and affect that are presumed to result from the interplay between biology and experience (Rothbart & Posner, 2006). Theorists have highlighted three dimensions of temperament with relevance to depression (for a review, see Rothbart & Posner, 2006): high negative emotionality (NE; a tendency toward experiencing frequent, intense, and lasting negative affect); low positive emotionality (PE; a tendency toward experiencing low levels of positive emotions such as joy and pleasure); and poor effortful control (EC; difficulty inhibiting undesired impulses and effectively regulating attention). According to the tripartite model, the combination of high NE and low PE differentiates depression from internalizing disorders such as anxiety (Clark & Watson, 1991). Together, NE, PE, and EC account for children's' dispositional emotionality and responsivity to emotionally evocative stimuli.

Theorists typically conceptualize temperament as a diathesis for depression (e.g., Hyde, Mezulis, & Abramson, 2008; Yap, Allen, & Sheeber, 2007). According to these models, temperament may serve as a vulnerability to depression directly, by fostering symptoms (e.g., depressed mood, anhedonia, irritability), or indirectly, by fostering emotional vulnerability (e.g., rumination, emotion dysregulation) or eliciting negative experiences (e.g., stress) that in turn contribute to depression. Temperament also may act as a moderator, shaping children's emotional reactivity to environmental risks for depression, consistent with broader developmental theories such as the biological sensitivity to context model (Boyce & Ellis, 2005). Importantly, these theoretical models predict that direct, indirect, and moderated pathways are complementary rather than mutually exclusive.

Other perspectives focus on individual differences in emotional responses, emotion regulation, and emotion processing as precursors to depression. Response style theory posits that individuals who tend to engage in unproductive emotion-related rumination sustain and amplify negative moods rather than resolve them, such that a ruminative response style contributes to the onset and maintenance of depression (for a review, see Rood, Roelefs, Bogels, Nolen-Hoeksema, & Schouten, 2009). Emotion regulation perspectives propose that a failure to effectively regulate emotional responses is fundamental to mood disorders including depression, and that poor emotion regulation early in development will set the stage for later symptoms (e.g., Compas, Jaser, & Benson, 2009). Building on emotion regulation perspectives, others have proposed that deficits in processing emotions (e.g., identifying and understanding emotions, regulating attention to emotions) may underlie emotion regulation difficulties, which in turn

are expected to heighten vulnerability to depression (e.g., Flynn & Rudolph, in press). Some aspects of executive functioning with relevance to emotion regulation, such as problem solving, response selection, and regulation of attention, could also play a role in shaping vulnerability to depression (e.g., McClintock, Husain, Greer, & Cullum, 2010), although research is needed in youth populations (see later discussion of cognitive vulnerabilities to depression). In recent years, emotion processing and regulation perspectives have increasingly focused on ways that developmental changes in emotional functioning, particularly related to biological maturation (e.g., puberty, neurological maturation), may contribute to the higher prevalence of depressive symptoms in adolescence (e.g., Forbes, Phillips, Ryan, & Dahl, 2011).

Empirical Evidence

TEMPERAMENT

Empirical investigations of temperament and depression generally support theoretical predictions. Prospective research supports direct associations between high NE and depressive symptoms in adolescence (e.g., Krueger, 1999). Furthermore, heightened rumination (Mezulis, Simonson, McCauley, & Vander Stoep, 2011) and generation of stressful life events (Barrocas & Hankin, 2011) mediate the prospective association between NE and depression in youth; emotion dysregulation mediates the prospective link between EC and depression (Zalewski, Lengua, Wilson, Trancik, & Bazinet, 2011). Temperament also moderates the impact of environmental factors on depression. In some cases, temperamental vulnerability (e.g., high NE, low EC) enhances the contribution of environmental factors—such as negative parenting (Kiff, Lengua, & Bush, 2011) and peer victimization (Sugimura & Rudolph, 2012)—to depression. However, temperament also may promote resilience; for example, Gartstein and Bateman (2008) found that low NE attenuated the link between maternal depression in infancy and depression-like symptoms in toddlerhood.

EMOTION PROCESSING

A number of emotion-processing deficits are associated with vulnerability to depression in youth. Depressive symptoms are correlated with youth's inaccurate identification of parents' emotions in parent–child interactions (Ehrmantrout, Allen, Leve, Davis, & Sheeber, 2011) and with perceptions of more anger and less joy in low-intensity facial stimuli (van Beek & Dubas, 2008). Regarding one's own emotions, low emotional clarity, or difficulty identifying and distinguishing between one's emotions, and perceptual asymmetry in processing of emotional faces (i.e., reduced posterior right-hemispheric bias) predict subsequent depressive symptoms in youth. Importantly, maladaptive responses to stress (e.g., low levels of engagement strategies, such as emotion regulation; high levels of dysregulated, automatic responses, such as rumination and emotional numbing) mediated these associations, supporting the idea that poor emotion regulation is a mechanism through which emotion-processing deficits increase vulnerability to depression (Flynn & Rudolph, 2010a, 2010b, in press).

EMOTION REGULATION

Depressed youth also exhibit compromised emotional responses and regulation. Depressive symptoms are correlated with parent and self-reports of poor emotion regulation (for a review, see Durbin & Shafir, 2008). Corroborating these findings, cross-sectional research indicates that compared to nondepressed youth, depressed youth exhibit more dysregulated expressions of negative affect as indexed by experience-sampling methods (Silk et al., 2011) and observations (Sheeber et al., 2009). Some longitudinal research supports the idea that poor emotional functioning sets the stage for later depression in youth. Consistent with response style theory, emotion-related rumination is a robust prospective predictor of heightened depressive symptoms, particularly among adolescents (for a meta-analysis, see Rood et al., 2009). Limited research reveals prospective links between aspects of poor emotion regulation and youth depression, including high emotional inertia (i.e., temporally persistent moods; Kuppens et al., 2011) and poor regulation of sadness and anger (Feng et al., 2009).

Origins and Development of Emotional Vulnerability

Both environmental and biological factors play a role in shaping the development of emotional vulnerability to depression in youth. Considerable evidence links early adversity (e.g., maltreatment, parent depression) to disruptions in emotional processing and regulation (at both biological and behavioral levels) among youth consid-

ered at risk for depression (for a review, see Abaied & Rudolph, 2014). Proximal environmental factors, such as maladaptive parent socialization of emotion regulation and coping, also contribute to deficits in emotional functioning and depression (e.g., Abaied & Rudolph, 2010b, 2011). However, additional research is needed to test directly whether youth emotional functioning accounts for prospective contributions of adversity and parent socialization to depression.

Developmental neuroscience research suggests that emotional vulnerability to depression also has neurological underpinnings. Researchers have proposed that reduced neural response to rewards may underlie the low levels of PE common to depression, and that biological maturation may exaggerate this pattern in adolescence (for a review, see Forbes & Dahl, 2012). Youth at risk for depression (e.g., daughters of depressed mothers) also show maladaptive patterns of neural activity during emotion regulation tasks (e.g., Joormann et al., 2012). These processes may be affected by endocrinological changes associated with pubertal maturation; Forbes and colleagues (2011) found that pubertal maturation rather than age predicted less activation in brain regions associated with emotion regulation in response to social threats. Outside the context of neuroscience research, Silk and colleagues (2011) found that depressed adolescents experienced higher levels of negative emotions than nondepressed adolescents, and that this difference was amplified among those with advanced pubertal status. These puberty-related changes in emotional vulnerability may help to explain the higher rates of depression onset in adolescence than in childhood.

Summary

Emotional vulnerability to depression operates though both state- and trait-like processes. Prospective designs provide ample empirical support for temperament models of depression and response style theory, such that youth's dispositional emotionality and style of emotional responses are implicated in the development of depression. Although research supports emotion processing and regulation deficits among depressed youth and youth at risk for depression (i.e., those exposed to early adversity), additional longitudinal investigations are needed to more clearly differentiate emotion regulation deficits as antecedents versus consequences of depression. Future research also should seek to elucidate the pathways though which multiple levels of emotional functioning (i.e., biological, cognitive, behavioral) combine and interact to shape vulnerability to depression.

Cognitive Vulnerability to Depression

Cognitive models implicate negative belief systems and maladaptive information processing in the onset and course of depression. According to these models, cognitive vulnerability serves as a stable predisposition that interacts with life stress to predict depression. This vulnerability is reflected in characteristic biases in attention, interpretation, and recall of information. More specifically, cognitive theories often suggest that a key determinant of depression is the *match* between a particular cognitive vulnerability and a particular stressor. That is, stressful events or circumstances would induce depression to the extent that they precipitate a loss of self-worth in an individual's specific area of cognitive vulnerability. In this regard, the most common distinction focuses on individual differences in the tendency to base one's self-worth either on success in interpersonal relationships (as reflected in sociotropy or dependency) or on individual achievement and independence (as reflected in autonomy or self-criticism) (Beck, 1987; Blatt & Zuroff, 1992; Coyne & Wiffen, 1995).

Theoretical Models

Beck's (1967, 1987) cognitive theory of depression elucidates three aspects of disrupted cognitive functioning in depression. First, depressed individuals possess core dysfunctional attitudes and negative cognitive schemas (characterized by themes of loss, failure, and inadequacy) that guide information processing. Second, these schemas drive systematic biases in thinking, which create idiosyncratic interpretations of events (e.g., negative automatic thoughts, cognitive errors). Third, depression is associated with the "negative cognitive triad," or a tendency to possess negative views of the self as worthless or inadequate, the world as mean or unfair, and the future as hopeless. The theory maintains that these cognitive styles heighten susceptibility to depression, especially when activated by external stressors. Because the rigid nature of cognitive schemas renders them highly resistant to change, depressed individuals may be vulnerable to persistent difficulties.

A second set of cognitive theories involves reformulations of Seligman's (1975) "learned helplessness" model. The original version posited that depression

stems from the experience of uncontrollable, noncontingent events. A revision of this model (Abramson, Seligman, & Teasdale, 1978) introduced the notion of a "depressive attributional style," or a predisposition to attribute negative outcomes to internal, global, and stable factors, and positive outcomes to external, specific, and unstable factors. In the most recent version of this model, Abramson, Metalsky, and Alloy (1989) described a subtype of "hopelessness" depression, which evolves from the interaction between exposure to negative events and a depressogenic inferential style involving pessimistic inferences about the causes, consequences, and self-implications of events.

Related self-regulatory theories (Rehm, 1977; Weisz, Sweeney, Proffitt, & Carr, 1994) suggest that one's expectations about outcomes (e.g., perceptions of control and competence, outcome contingencies) and one's personal investment in outcomes (e.g., goals, standards, values) jointly confer vulnerability to depression. Competence-based models focus in particular on the perceived competence aspect of self-regulation (Cole, Martin, & Powers, 1997). Appraisal-based models emphasize maladaptive appraisals about the meaning of events (a tendency to appraise challenging events as threatening, harmful, or stressful, rather than as opportunities for learning, mastery, and growth; Lazarus & Folkman, 1984).

Response style theory (Nolen-Hoeksema, 1991) proposes that depression arises from individual differences in self-focused attention. According to this theory, the tendency to "ruminate"—rather than distract oneself—in response to negative affect determines susceptibility to persistent and severe depression. Rumination involves perseverating on depressive symptoms and the possible causes and consequences of symptoms. More recent elaborations of this theory distinguish two dimensions of rumination (Treynor, Gonzalez, & Nolen-Hoeksema, 2003). Whereas "brooding" involves passively focusing on symptoms, "self-reflection" involves actively attempting to gain insight into one's problems. It is thought that brooding, but not self-reflection, serves as a specific vulnerability for depression.

Empirical Evidence

Over the past decade, researchers have increasingly used prospective designs to evaluate the etiological significance of cognitive vulnerability, as well as to test cognitive vulnerability–stress interactions. This research has yielded significant support for cognitive vulnerability–stress models of depression in youth, although there are exceptions, with some studies yielding qualified support (e.g., by age, type of outcome, interactions with other vulnerabilities) or no support for these models (for reviews, see Abela & Hankin, 2008; Gibb & Coles, 2005; Jacobs, Reinecke, Gollan, & Kane, 2008).

SELF-REPORTED BELIEFS AND STYLES

Most longitudinal research uses self-report questionnaires to examine explicit aspects of cognitive vulnerability, such as dysfunctional attitudes (e.g., perfectionism, need for social approval), negative automatic thoughts (e.g., catastrophization, overgeneralization), negative inferential style (e.g., stable, global attributions for failure), self-critical thoughts, low perceived control, and ruminative response styles. Overall, this research provides compelling evidence for the idea that self-reported cognitive vulnerability alone and, in particular, vulnerability–stress interactions prospectively contribute to subsequent depressive symptoms and disorders in youth.

Examining Beck's theory, a few studies provide partial or full support for the idea that dysfunctional attitudes prospectively interact with stress to predict depressive symptoms (e.g., Abela & Skitch, 2007; Hankin, Abramson, Miller, & Haeffel, 2004; Lewinsohn, Joiner, & Rhode, 2001). Examining the hopelessness theory, a growing number of studies reveal that depressive attributions about the causes of events interact with stress to predict depressive symptoms (e.g., Abela et al., 2011; Bohon, Stice, Burton, Fudell, & Nolen-Hoeksema, 2008; Carter & Garber, 2011; Hankin, 2008). A few studies provide partial or full support for the predictive contribution of depressogenic inferences about the consequences and self-implications of events (e.g., Abela, 2001, 2002). Building on these findings, Abela and colleagues (e.g., Abela & Sarin, 2002) have shown that it may be important to identify youth's "weakest link"—namely, their most negative cognitive style—in research examining cognitive vulnerability–stress interactions. Research also supports the predictive contribution of perceived competence (Tram & Cole, 2000) and control (Rudolph, Kurlakowsky, & Conley, 2001) to depressive symptoms. Finally, ruminative response style alone (Nolen-Hoeksema, Stice, Wade, & Bohon, 2007) and in interaction with stress (Abela & Hankin, 2011) predicts subsequent depression. When subtypes are distinguished, effects hold

for brooding rather than reflection; moreover, brooding accounts for stability in depressive symptoms in girls but not in boys (Burwell & Shirk, 2007). Despite evidence for cognitive vulnerability–stress models, it is noteworthy that some studies provide only partial or no support for these theories (for reviews, see Abela & Hankin 2008; Gibb & Coles, 2005; Jacobs et al., 2008); moreover, research often supports a reciprocal association wherein depressive symptoms predict subsequent maladaptive cognitions (e.g., LaGrange et al., 2011).

Less research has tested the validity of cognitive specificity models in youth. Some research supports self-criticism × achievement stress contributions (Abela, Sakellaropoulo, & Taxel, 2007) and dependency × interpersonal stress contributions (Little & Garber, 2000) to depressive symptoms over time; however, other research has not supported the predictive role of cognitive vulnerability–stress match (for a review, see Abela & Hankin, 2008). Research also reveals that depressogenic interpersonal beliefs and schemas (negative beliefs and biased processing about interpersonal relationships) confer vulnerability to depression in the face of interpersonal stress (Hammen et al., 1995; Shirk, Boergers, Eason, & Van Horn, 1998). These preliminary findings indicate the need for further pursuit of longitudinal research on domain-specific cognitive vulnerability and cognition–stressor match.

INFORMATION-PROCESSING BIASES

Researchers have used two approaches to examine the role of implicit information-processing biases in depression. The first approach involves experimental assessments of selective attention and memory. Relative to nondepressed youth, depressed youth show an attentional bias toward sad faces (Hankin, Gibb, Abela, & Flory, 2010) and idiosyncratic processing of self-referent (Hammen & Zupan, 1984; Neshat-Doost, Taghavi, Moradi, Yule, & Dalgleish, 1998) and other-referent (Rudolph, Hammen, & Burge, 1997) information. This research reveals that depressed youth show either more of a bias toward negative stimuli, or less of a bias toward positive stimuli, than do nondepressed youth, although there are exceptions (for a review, see Jacobs et al., 2008).

The second approach involves examining the accuracy of cognitive appraisals in depressed youth. Most investigations of cognitive vulnerability assess decontextualized belief systems (e.g., generalized dysfunctional attitudes) or interpretations of hypothetical events (e.g., negative inferential style), making it difficult to determine the accuracy of depressogenic cognitive styles. Although we might surmise that extreme negative beliefs (e.g., catastrophization) are at least somewhat biased, it is clear that depressed youth do, in fact, experience significant competence deficits and environmental adversity (for a review, see Rudolph, Hammen, & Daley, 2006). Thus characteristic negative cognitions could, at least in part, reflect realistic appraisals of such disturbances. To resolve this issue, a few studies have examined the accuracy of appraisals by assessing cognitions within the context of actual life experiences.

Examining self-appraisals of competence, research reveals that depressed youth underestimate their competence relative to objective ratings (e.g., Brendgen, Vitaro, Turgeon, & Poulin, 2002), supporting the presence of a depressive bias in self-appraisal. Examining appraisals of naturally occurring life events, one study confirms that depressed youth overestimate event stressfulness (the degree of negative impact associated with events) and event dependence (the extent to which the youth contributed to event occurrence) relative to objective ratings (Krackow & Rudolph, 2008), confirming the presence of a depressive bias in appraisals of event meaning, causes, and consequences.

Despite evidence for information-processing biases in depressed youth, this research is limited by several methodological constraints. First, studies of information processing primarily use concurrent designs, precluding strong conclusions regarding the temporal precedence of cognitive vulnerability. Indeed, a few studies (Cole, Martin, Peeke, Seroczynski, & Hoffman, 1998; McGrath & Repetti, 2002; Pomerantz & Rudolph, 2003) suggest that depressive symptoms foster biased self-appraisals (i.e., underestimations of competence) over time. Second, research reveals that depressed youth are sensitive to actual deficits in their competence (Rudolph & Clark, 2001), suggesting some realistic basis for negative appraisals and the need for future research to distinguish realistic versus distorted perceptions of reality. Third, much of this research overlooks the contextual component of cognitive theories—namely, that depressogenic cognitive schemas may remain latent until activated by negative mood states or events. To address this concern, future research needs to assess information-processing biases under conditions of cognitive activation, such as following negative mood induction (e.g., Taylor & Ingram, 1999), or as a diathesis that interacts with stressful life events to predict depression.

Origins and Development of Cognitive Vulnerability

For a full understanding of the role cognitive vulnerability plays in depression, it is important to elucidate how it emerges and develops over time. Original cognitive theories, developed in adults, view cognitive vulnerability as an early-emerging and persistent predisposition stemming from adverse experiences. This perspective assumes that cognitive vulnerability is a relatively stable, latent personality trait that is activated by mood-related or environmental triggers (Joormann, 2009). Prompted by research suggesting developmental differences in the stability and predictive validity of cognitive vulnerability (for a review, see Abela & Hankin, 2008), as well as research suggesting that depressive symptoms may leave a cognitive "scar" (Nolen-Hoeksema, Girgus, & Seligman, 1992; Pomerantz & Rudolph, 2003), the field of developmental psychopathology increasingly views cognitive vulnerability as a dynamic construct that crystallizes over the course of development, perhaps in response to maturational and experiential changes during the transition through adolescence.

INDIVIDUAL-DIFFERENCE ORIGINS

There is some evidence for a genetic liability to cognitive vulnerability, including negative attributional style (Lau, Rijsdijk, & Eley, 2006), information-processing biases (Beevers, Wells, Ellis, & McGeary, 2009; Pérez-Edgar et al., 2010) and rumination (Beevers, Wells, & McGeary, 2009). Research also has investigated the neural and biological basis of cognitive vulnerability. For example, differential patterns of brain activation (Monk et al., 2008) and heightened cortisol activation to stress (Rudolph, Troop-Gordon, & Granger, 2011) are linked to attentional biases and rumination, respectively. Temperament or personality traits may play a role in the development of cognitive vulnerability. One study revealed that low levels of positive emotionality in early childhood predicted subsequent information-processing biases (less recall of positive self-referent information; Hayden, Klein, Durbin, & Olino, 2006). Another study revealed that depressive personality traits were associated with girls' tendency to overestimate the stressfulness of events and their contribution to events, even after the researchers adjusted for lifetime history of depression (Rudolph & Klein, 2009). Increasing interest also has emerged in how core executive functions (cognitive processes that guide planning, decision making, and self-regulation) influence cognitive vulnerability to depression. For example, deficits in cognitive inhibition interfere with efficient updating of working memory (i.e., focusing attention on relevant information and ignoring irrelevant information), setting the stage for rumination, information-processing biases (e.g., elaboration of and difficulty disengaging from negative material), and other forms of cognitive vulnerability (for reviews, see Gotlib & Joormann, 2010; Joormann, 2009). Given these links, it is not surprising that executive function deficits are associated with depression in adults (for a review, see Gotlib & Joormann, 2010); research with youth is more limited and typically relies on adult reports of temperamental dimensions associated with executive functions, such as EC and attention regulation, rather than cognitive tasks (for a review, see Eisenberg, Smith, Sadovsky, & Spinrad, 2004).

SOCIAL-CONTEXTUAL ORIGINS

Several theories suggest that early exposure to chronic or severe adversity (e.g., trauma, family disruption, life stressors, maladaptive parent socialization) is internalized in the form of cognitive vulnerability (e.g., Gibb & Coles, 2005; Rose & Abramson, 1992). Consistent with this idea, mounting evidence reveals that such forms of adversity predict the emergence of cognitive vulnerability over time in youth (for reviews, see Abela & Hankin, 2008; Gibb & Coles, 2005). Research also documents information-processing biases in the offspring of depressed mothers. In one study, never-disordered daughters of depressed mothers selectively attended to negative emotional information, while never-disordered daughters of never-disordered mothers selectively attended to positive emotional information (Joormann, Talbot, & Gotlib, 2007). In another study, maternal depressive symptoms were associated with a negative bias in youth's processing of mother-relevant information (specifically for youth with heightened emotional reactivity to stress; Flynn & Rudolph, 2012). Offspring of mothers with a history of depression also show patterns of psychophysiological functioning suggestive of deficits in selective attention (Pérez-Edgar, Fox, Cohn, & Kovacs, 2006). Collectively, these studies support the idea that stressful life contexts foster the development of cognitive vulnerability, which may contribute to the intergenerational transmission of depression. Of course, it also is possible that childhood adversity and maternal depression reflect a genetic liability that is in-

stantiated in the form of cognitive vulnerability. Additional research is needed to determine the mechanisms through which adverse contexts and maternal depression heighten cognitive vulnerability.

DEVELOPMENTAL CHANGES

A quantitative review (Lakdawalla, Hankin, & Mermelstein, 2007) reveals that the cognitive vulnerability–depression link strengthens with age; this finding indicates the importance of understanding changes in the stability, consolidation, and predictive power of cognitive vulnerability across development. Several cognitive transformations during the adolescent transition may set the stage for increasing cognitive vulnerability (for reviews, see Abela & Hankin, 2008; Gibb & Coles, 2005; Jacobs et al., 2008). Cognitive vulnerability may emerge as children develop the capacity to engage in abstract reasoning, integrate information across situations and time, and make stable attributions about behavior. Cognitive processes also become more rigid across development, making it less likely that individuals will flexibly integrate schema-incongruent information; this rigidity may be intensified by normative increases in self-consciousness during adolescence. At the same time, a maturational gap emerges between emotional reactivity and cognitive regulatory capacity (Dahl, 2004), laying fertile ground for the cultivation of emotionally driven difficulties in regulatory focus (e.g., rumination) and unchecked negative inferences about stressful events. These maturational changes may intersect with increasing life stress during adolescence (Rudolph & Hammen, 1999) to set the stage for heightened cognitive vulnerability. Shifts also may occur in the association between cognitive vulnerability and stressors. Whereas cognitive vulnerability may emerge from stressors (Tram & Cole, 2000) or prior depressive symptoms (LaGrange et al., 2011; Pomerantz & Rudolph, 2003) earlier in development, it may interact with stressors later in development. Moreover, cognitive vulnerability contributes to the generation of stress (e.g., Eberhart, Auerbach, Bigda-Peyton, & Abela, 2011; Shih, Abela, & Starrs, 2009), highlighting the dynamic association between cognitions and stress.

Given evidence for distinct dimensions of cognitive vulnerability in youth (Ginsburg et al., 2009), it is possible that these dimensions coalesce into stable traits at different stages of development. Supporting this idea, research using an advanced quantitative modeling approach suggests that a reliable time-invariant (trait-like) component of negative attributional style does not emerge until early adolescence (Cole et al., 2008), whereas stable components of other negative cognitions (negative automatic thoughts, the negative cognitive triad) emerge during middle childhood (LaGrange et al., 2011). These findings underscore the need to distinguish various aspects of cognitive vulnerability, some of which may be more accessible and well developed earlier in childhood (and thus serve as predictors of depression), and others of which may involve more complex cognitive processes (e.g., making inferences about events) and do not stabilize until youth show certain cognitive advances during adolescence. Once the various components reach a certain level of stability (i.e., become trait-like), they may consolidate into a single set of interrelated vulnerabilities (Abela & Hankin, 2008).

Summary

Early research often failed to test key aspects of cognitive vulnerability models, such as the temporal precedence and stability of dysfunctional cognitive styles, the activation of cognitive vulnerability by negative mood states or stressors, and the accuracy of negative cognitions. Notable advances in the use of rigorous, prospective, multiwave, and experimental designs over the past decade address many of these limitations. As a result, the field has witnessed significant progress in addressing some of the ongoing controversies and affirming the position of cognitive theories as useful conceptual frameworks for understanding the etiology and persistence of depression. At the same time, recent advances illustrate the need to embed cognitive theories of depression within the context of dynamic developmental frameworks that explain the emergence, consolidation, and crystallization of cognitive vulnerability over time. Future efforts to refine and validate cognitive theories of depression must elucidate the independent, transactional, and interactive contributions of cognitive vulnerability and other risk factors (e.g., genetic, biological, emotion-regulating, and social processes) with the goal of developing integrative multilevel models.

Interpersonal Vulnerability to Depression

Interpersonal approaches to understanding depression posit that depression is fundamentally an interpersonal disorder (Coyne, 1976; Joiner & Timmons, 2009). Interpersonal difficulties are robust predictors and consequences of depression, and many other forms of vulnerability to depression (e.g., cognitive, emotional)

are expressed in interpersonal contexts. Furthermore, interpersonal vulnerability to depression may be of particular import for youth, whose relationships evolve dramatically over the course of childhood and adolescence. In recent years, substantial progress has been made in theory and research seeking to understand interpersonal vulnerability to depression in youth.

Theoretical Models

According to interpersonal theories of depression, originally developed to understand adult depression, depressed individuals both *react* and *contribute* to interpersonal difficulties. Specifically, impairment in social skills (e.g., excessive reassurance seeking, social withdrawal) and relationship disturbances (e.g., unsupportive or conflictual relationships, interpersonal stress) heighten vulnerability to depression. In turn, characteristics and behaviors of depressed individuals contribute to stress in relationships, aversive interpersonal encounters, and rejection, which maintain or promote depression over time (Coyne, 1976; Gotlib & Hammen, 1992; Joiner & Timmons, 2009). This cyclical process may help to explain high stability and recurrence of depression.

Extensions of these theories to youth provide developmentally sensitive accounts of the early origins of interpersonal disruption, as well as the continuously evolving interplay between interpersonal disruption and depression over time and across critical developmental stages (e.g., Cyranowski et al., 2000; Rudolph, Flynn, & Abaied, 2008). According to these models, early exposure to social adversity may set the stage for proximal interpersonal vulnerabilities in youth. These models take into account key developmental transitions, paying particular attention to ways in which biological (e.g., puberty, sex), cognitive (e.g., executive functioning, abstract reasoning), and social (e.g., increasing importance of peers and romance) development may exacerbate preexisting interpersonal vulnerability and contribute to the sharp increase in depression beginning in midadolescence. Finally, developmental perspectives on the interpersonal context of depression posit that interpersonal vulnerabilities may manifest themselves in a variety of relationship contexts, including family, peer, and romantic relationships.

Empirical Evidence

Longitudinal research supports both directions of influence—interpersonal impairments and problems predicting youth depression, and youth depression predicting incompetence and dysfunction in relationships—in multiple interpersonal domains. We first discuss research covering interpersonal stress across different domains and then focus on specific relationships, including those with family, peers, and romantic partners, focusing on links between proximal aspects of youth's relationships and depression.

INTERPERSONAL STRESS

Exposure to interpersonal stressors (pooled across multiple types of relationships) predicts subsequent depression in youth (e.g., Carter & Garber, 2011; Hankin, Mermelstein, & Roesch, 2007). Furthermore, the process of interpersonal stress generation, in which depressive characteristics and behaviors (e.g., excessive reassurance seeking, negative conceptions of relationships) disrupt relationships and create new interpersonal stressors, also contributes to the maintenance of depression over time (for a review, see Hammen, 2009a). Consistent with the idea that depression is particularly damaging to relationships, depressed youth are more likely to generate interpersonal than noninterpersonal stress (Hammen, 2009a; Rudolph, Flynn, Abaied, Groot, & Thompson, 2009).

FAMILY RELATIONSHIPS

Drawing from family systems (Cox & Paley, 1997) and attachment theory (Bowlby, 1969) perspectives, much of the research on interpersonal vulnerability to depression in youth focuses on the family context. Youth who are exposed to stressful and unsupportive family environments and maladaptive parenting are at heightened risk for developing depression. Families of depressed youth are more conflictual and less cohesive compared to families of nondepressed youth, and parents of depressed youth are more negative (i.e., unsupportive, hostile, or intrusive) in parent–child interactions compared to parents of nondepressed youth (for a review, see Abaied & Rudolph, 2014). Aspects of the family environment (e.g., high parent–child conflict, coercive and emotionally negative interactions among family members) and parenting behavior (e.g., low parental warmth, parent hostility, and psychological control) forecast subsequent depression in youth (e.g., Schwartz et al., 2011; Soenens et al., 2008; Stice, Ragan, & Randall, 2004), and a highly critical parenting style predicts the onset (Silk et al., 2009) and maintenance (McCleary & Sanford, 2002) of youth depression.

As predicted by interpersonal theories of depression, youth depressive symptoms also disrupt family environments. Youth depression predicts more stress in parent–child relationships (Raposa, Hammen, & Brennan, 2011), lower perceived family relationship quality (Lewinsohn, Rohde, et al., 2003), and lower perceived support from parents (Needham, 2007) over time. Furthermore, depressed youth perceive their parents as increasingly hostile, harsh, and inconsistent over time (Kim, Conger, Elder, & Lorenz, 2003). Observational research has revealed more negative interchanges, less positive reciprocity, and more negative reciprocity between depressed children and their parents than in nondepressed families (for a review, see Abaied & Rudolph, 2014). Thus depressed children's symptoms or dysfunctional behavior may evoke negative responses from their parents and perpetuate negative parent–child interactions over time. Providing some support for transactional associations, some research documents reciprocal effects between low perceived parent support and depressive symptoms (Allen et al., 2006; Branje, Hale, Frijns, & Meeus, 2010; cf. Stice et al., 2004). Therefore, substantial evidence supports problematic family relationships as both predictors and outcomes of youth depression.

PEER RELATIONSHIPS

Learning to build and maintain positive relationships with peers, with whom most youth spend a large portion of their time, is a key developmental task in childhood, and peer relationships become more central to self-worth and emotional well-being during the transition to adolescence (Laursen, 1996). Thus, in recent years, researchers have paid increasing attention to peer relationships as a context of vulnerability to depression. Building on early cross-sectional work identifying a variety of impairments in depressed children's relationships with peers (e.g., Rudolph & Clark, 2001; for a review, see Gotlib & Hammen, 1992), investigators have demonstrated that deficits in interpersonal behaviors within peer relationships, including excessive reassurance seeking, negative feedback seeking, social withdrawal, and ineffective responses to peer stressors contribute to subsequent depression (e.g., Agoston & Rudolph, 2011; Borelli & Prinstein, 2006; Prinstein et al., 2005). Furthermore, exposure to social difficulties such as peer rejection, exclusion, victimization, and poor-quality friendships predict heightened depressive symptoms over time (Burton, Stice, & Seely, 2004; Nolan, Flynn, & Garber, 2003; Rudolph, Troop-Gordon, Hessel, & Schmidt, 2011). Supporting early (Coyne, 1976) and updated (Joiner & Timmons, 2009) interpersonal theories of depression, depressive symptoms also are contagious within peer groups, such that depressive symptoms in one's peers predict increases in one's own depression over time, with stronger effects generally emerging for girls compared to boys (e.g., Conway, Rancourt, Adelman, Burk, & Prinstein, 2011; van Zalk, Kerr, Branje, Stattin, & Meeus, 2010). One mechanism of depression contagion may be "co-rumination" (i.e., extensively discussing problems and negative feelings). Co-rumination among friends, although associated with higher friendship quality, predicts subsequent heightened depressive symptoms among girls (Rose, 2002; Rose, Carlson, & Waller, 2007). Together, these findings indicate that impaired functioning within peer relationships constitutes a substantial risk factor for subsequent depression.

Depression also interferes with children's subsequent interpersonal functioning. Depressed children have difficulty negotiating peer conflicts, and they elicit negative affect and aversive responses from unfamiliar peers (e.g., Rudolph, Hammen, & Burge, 1994), suggesting that characteristics of depressed children undermine the quality of their interactions. Perhaps as a result, children with the highest levels of depressive symptoms are most likely to lose friends over time (van Zalk et al., 2010), and depressive symptoms prospectively predict less stable and poorer-quality friendships (Oppenheimer & Hankin, 2011; Prinstein, Borelli, Cheah, Simon, & Aikins, 2005). Providing insight into two pathways through which depression can undermine peer relationships in youth, Agoston and Rudolph (2013) found that socially helpless behavior (e.g., lack of social initiative and persistence in the face of social challenge) and aggressive behavior accounted for the prospective contribution of depressive symptoms to low social status over time. In sum, disruptions in peer relationships may be antecedents or consequences of depression in youth.

ROMANTIC RELATIONSHIPS

Despite the developmentally salient and normative nature of adolescent romantic attraction and involvement (Collins, 2003), a small but growing literature suggests that romantic involvement in adolescence represents a substantial risk factor for subsequent depression (Davila et al., 2009; Starr, Davila, et al., 2012). Davila (2008) proposes that many youth lack the resources

to cope effectively with the challenges associated with romance, leaving romantically involved youth vulnerable to depression; for example, romance often involves intense and potentially novel emotions (e.g., sexual attraction, passion, romantic love) and introduces a variety of stressors (e.g., rejection, breakups, initiation of sexual behavior).

Consistent with this view, stress in romantic relationships (Daley & Hammen, 2002), negative interactions with partners (La Greca & Harrison, 2005), and low levels of intimacy (Williams, Connolly, & Segal, 2001) are associated with vulnerability to depression above and beyond involvement in romance. Romantic breakups constitute a particularly robust predictor of depressive symptoms and the onset of depressive episodes (Joyner & Udry, 2000). Supportive, low-conflict family relationships protect romantically involved youth from depression (Steinberg & Davila, 2008), whereas excessive reassurance seeking (Starr & Davila, 2008) and a preoccupied relational style (Davila, Steinberg, Kachadourian, Cobb, & Fincham, 2004) exacerbate this association. Thus lack of access to social support for coping with romantic stress may help to explain the link between romance and depression. Some studies have found stronger links between romantic involvement and depression or internalizing symptoms among girls compared to boys, and among younger compared to older adolescents (e.g., Joyner & Udry, 2000; Zimmer-Gembeck, Siebenbruner, & Collins, 2001).

Depression also may foster dysfunction in romantic relationships. In adolescence, depression is associated with generation of subsequent stress in romantic relationships (Hankin et al., 2007) and with dysfunction in romantic relationships, such as partner relationship dissatisfaction and physical coercion (Rao, Hammen, & Daley, 1999). Similarly, Daley and Hammen (2002) found that late adolescent women's depressive symptoms predicted lower levels of emotional support from their partners over time. Thus preliminary evidence supports disruption in romantic relationships as not only an antecedent but also a consequence of depression.

Summary

Supporting interpersonal theories of depression, research indicates that functioning within multiple domains of relationships may both contribute to and result from depression in youth. Relevant aspects of interpersonal functioning include dysfunctional social behaviors, poor-quality or unsupportive relationships, negative interactions with others, and interpersonal stress. Despite the transactional nature of interpersonal theories of depression, the majority of longitudinal studies in this area have focused on unidirectional pathways, and those that have tested transactional pathways have yielded inconsistent results; some only found support for one direction of effect or the other (Agoston & Rudolph, 2013; Borelli & Prinstein, 2006; Oppenheimer & Hankin, 2011; Prinstein et al., 2005; Stice et al., 2004). Unexamined moderators known to contribute to depression (e.g., genetic risk, cognitive style, or pubertal development) may have masked transactional effects in these studies. Future efforts to uncover transactional pathways should focus on moderators that are highly relevant to the aspects of interpersonal vulnerability being studied. In addition, most research in this area focuses on one relationship, and research is needed to examine the relative impact of different interpersonal contexts on depression in youth. Finally, long-term longitudinal studies will provide much-needed empirical tests of the core predictions stemming from developmental theories of interpersonal vulnerability to depression, including the notion that proximal interpersonal vulnerability is a mechanism through which early social adversity sets the stage for depression in childhood and adolescence.

Early Social Adversity and Depression

Moving beyond the proximal interpersonal context, developmental psychopathology theories of depression increasingly consider the adverse long-term consequences of early social adversity. Both prospective and retrospective research implicates early exposure to adverse social environments—through parental depression, trauma, loss, maltreatment, insecure attachment, or family disruption—as a precursor to youth depression (e.g., Garber & Cole, 2010; Hazel, Hammen, Brennan, & Najman, 2008; for a review, see Goodman & Brand, 2009). To achieve a better understanding of the relevant explanatory mechanisms, recent efforts have focused on articulating how early adversity undermines youth development in ways that heighten subsequent risk for depression.

Models of Risk

Developmental scientists have proposed several nonspecific models of early risk with potential relevance for youth depression. O'Connor (2003) distinguishes

three models accounting for the long-term impact of early experience. Most relevant to understanding the effects of early adversity on depression are the "experience-adaptive" or "developmental programming" model and the "cumulative-effects" model. An experience-adaptive model holds that biological systems adapt to environment input, particularly during sensitive periods of development; moreover, this malleability is developmentally constrained, such that systems have difficulty readjusting to later changes in the environment (although they may be altered through direct intervention). A cumulative-effects model holds that early experiences have a long-term impact to the extent that these effects are reinforced or maintained by later events; this model includes both an additive-effects variant (the effects of later adversity add to the effects of earlier risks) and an interactive-effects variant (the effects of later adversity depend on the history of earlier risks). Boyce and Ellis's (2005) "biological sensitivity to context" model combines elements of the experience-adaptive and cumulative-effects models; specifically, this model suggests that early adversity calibrates the stress response system, such that youth exposed to stressful early social environments show heightened biological reactivity to later stress. In something of a departure from other risk models, this sensitivity is thought to exert risk-augmenting effects under subsequent stressful conditions, but risk-protective effects under subsequent supportive conditions.

Focusing more specifically on interpersonal processes and depression, Rudolph and colleagues (2008) present an integrative model wherein early family adversity (e.g., insecure parent–child attachment, parental depression) interferes with the development of adaptive interpersonal behaviors and fosters maladaptive interpersonal behaviors. These social-behavioral deficits cause youth to generate further disturbances in their relationships, which serve as proximal precursors of depression. Depressive symptoms further undermine interpersonal functioning, leading to the perpetuation or exacerbation of depression and risk for recurrence. More specific models of risk explain the contribution of particular forms of adversity, such as maternal depression (e.g., Hammen, 2009b) and maltreatment (Alink, Cicchetti, Kim, & Rogosch, 2009), to youth depression.

In recent years, efforts to understand long-term risk have considered how early adversity interacts with recent stress to confer vulnerability to depression (similar to the interactive cumulative-effects model). According to a "stress amplification" model, childhood adversity amplifies depressive reactions to recent stress; that is, youth with a history of adversity are presumed to demonstrate higher levels of depression than those without a history of adversity when exposed to severe but not mild recent stress. According to a "stress sensitization" model, childhood adversity reduces an individual's threshold for depressive reactions to recent stress; that is, youth with a history of adversity are presumed to require only mild stress to trigger depression, whereas youth without a history of adversity require more severe stress to trigger depression. Mounting evidence supports stress sensitization models, indicating that youth exposed to early adversity (e.g., parental abuse/neglect, multiple forms of family disruption) are more likely than those with no history of adversity to become depressed following exposure to mild or moderate levels of stress (e.g., Harkness, Bruce, & Lumley, 2006). One interesting study revealed stress amplification effects in prepubertal girls, but stress sensitization effects in girls progressing through puberty (Rudolph & Flynn, 2007), suggesting changes in sensitization across the adolescent transition. Of note, the stress sensitization effect (at least when declines in the strength of association between life stress and the onset of depression across episodes are examined) appears to be most pronounced in those at low genetic risk for depression, perhaps because those with high genetic risk are already sensitized to an initial onset of depression even in the presence of low levels of life stress (Kendler, Thornton, & Gardner, 2001).

Pathways of Risk

Building on research documenting stress sensitization and stress amplification effects, contemporary efforts have explored specific pathways through which these processes unfold (for a review, see Goodman & Brand, 2009). One line of research focuses on the idea that a history of prolonged or severe adversity sensitizes developing brain systems so as to create heightened reactivity to stress later in life (for a review, see Gunnar & Loman, 2011). Another line of research suggests that early adversity induces risk through exposure to maladaptive parent socialization patterns and stressful interpersonal contexts that undermine the normative development of sense of self, coping skills, and interpersonal competencies, leaving youth vulnerable in the face of future stress or even causing them to generate stressful events and circumstances (for reviews, see Hammen, 2009b; Rudolph et al., 2008).

Supporting biological risk pathways, exposure to early adversity predicts future dysregulation of the HPA axis (e.g., Cicchetti & Rogosch, 2012; Rao, Hammen, Ortiz, Chen, & Poland, 2008), deviant neural processing of emotional stimuli (Cicchetti & Curtis, 2005; Parker, Nelson, & The Bucharest Early Intervention Core Group, 2005), atypical patterns of frontal lobe activity (Dawson et al., 2003), and compromised immune system functioning (Shirtcliff, Coe, & Pollak, 2009). In addition to these functional variations, recent research reveals that lifetime exposure to adversity predicts differences in brain structure, specifically smaller volumes in specific regions of the PFC; moreover, reduced PFC volumes mediate the link between lifetime adversity and poorer executive function (spatial working memory) in adolescents (Hanson et al., 2012). In turn, individual differences in brain structure and function and poorer executive function are linked to depression, thereby supporting the idea that disruption in the systems underlying emotion regulation, stress reactivity, and cognitive self-regulation can serve as one mechanism through which early adversity contributes to future affective risk (for a review, see Forbes & Dahl, 2005).

Supporting psychosocial risk pathways, early adversity (e.g., maternal depression, maltreatment insecure attachment) exposes youth to several forms of interpersonal disruption, such as maladaptive socialization of emotion, problematic parent–child relationships, and stressful contexts (for reviews, see Abaied & Rudolph, 2014; Hammen, 2009b; Rudolph et al., 2008). For example, depressed, maltreating, and insecurely attached parents show less adaptive responses to their children's stress and expression of emotion (e.g., Abaied & Rudolph, 2010a; Edwards, Shipman, & Brown, 2005; Shaw et al., 2006) and engage in more hostile and less positive parenting (for a review, see Abaied & Rudolph, 2014). It is not surprising, therefore, that these youth suffer from a spectrum of functional deficits linked to depression, such as ineffective regulation and expression of emotion, social-behavioral deficits (e.g., seeking of negative feedback, avoidant responses to stress), relationship disturbances (e.g., poor friendships, peer victimization), and a tendency to generate interpersonal stress (for reviews, see Abaied & Rudolph, 2014; Rudolph et al., 2008). Providing explicit support for psychosocial pathways, research supports models in which disrupted parent–child relationships, heightened stress exposure, and social competence deficits mediate the contribution of early adversity, such as maternal depression, to subsequent youth depression (Garber & Cole, 2010; Hammen, Shih, & Brennan, 2004). However, because these studies have not used genetically informed designs, it is difficult to tease apart the extent to which the transmission of risk is due to socialization versus shared genetic vulnerability.

Resilience in the Face of Risk

Exposure to adverse conditions early in life, including parental depression, clearly does not uniformly disrupt the successful outcomes or healthy development of all children. Although studies of risk and vulnerability factors and processes predominate in studies of depression and dysfunctional outcomes, some research has examined predictors of resilient outcomes (including absence of depressive and other disorders), as well as protective processes. The classic study by Masten, Best, and Garmezy (1990) reported a resilience profile not specific to depression outcomes that generally has been replicated in studies of children of depressed mothers: "[They have] a positive relationship with a competent adult, they are good learners and problem-solvers, they are engaging to other people, and they have areas of competence and perceived efficacy valued by self or society" (p. 425). Masten and colleagues (2004) also found that along with parenting quality, IQ and positive personal characteristics and coping styles were predictive of resilient outcomes in a longitudinal study of high-risk youth. In a sample of youth at risk for depression due to maternal depression, Brennan, LeBrocque, and Hammen (2003) found that positive quality of parenting was a significant predictor of resilient outcomes by age 15. Pargas, Brennan, Hammen, and LeBrocque (2010) also found that positive maternal parenting, higher IQ, and personal qualities of high self-esteem and social competence with peers were protective factors in youth resilience at age 20. In the same high-risk sample, Hammen and colleagues (2008) found that youth with early-onset depression who "desisted" from further depression during the follow-up of 5 years to age 20 had significantly more positive peer and family relationships and higher self-esteem at age 15 than youth who had early-onset depression and also went on to have a recurrent/chronic course to age 20. Southwick, Vythilingam, and Charney (2005) reviewed a variety of positive personal traits and attributes, as well as genetic, neurobiological, and neuroendocrine factors also likely to play a role in protection against depression in the face of stressful experiences.

Summary

Emerging theory and research implicate early adversity as a pervasive and potent contributor to depression, propelling youth along a risky pathway characterized by significant intrapersonal and interpersonal disturbances that both heighten sensitivity to and increase the likelihood of future stressful experiences, thereby promoting risk for depression. These psychological, biological, and interpersonal disruptions may help explain the intergenerational transmission of risk. As noted, however, early adversity and consequent risks could, in part, reflect a shared genetic liability that accounts for vulnerability to depression. Understanding the intersection between genetic and environmental risks associated with early adversity will be a key direction for future research. Moreover, it will be important to determine whether the negative consequences of early social adversity depend on the timing of exposure, or whether they emerge during particular developmental stages. Given research implicating the adolescent transition as a pivotal interpersonal context of risk for depression (Rudolph, 2009; Rudolph et al., 2008), the long-term legacy of early adversity may be intensified during this stage, perhaps crystallizing into more severe and/or persistent forms of depression. Further research should build on initial studies of resilience to study both resistance to depression and deflection of the course of depression to less severe trajectories.

AN INTEGRATIVE DEVELOPMENTAL MODEL OF YOUTH DEPRESSION, AND DIRECTIONS FOR FURTHER STUDY

This chapter acknowledges the significant expansion of empirical research, using improved and innovative methodologies, in child and adolescent depression. There has been an increasing focus on developmentally sensitive models, although significant questions remain about the applicability of adult approaches to diagnosis and conceptualization, how childhood- and adolescent-onset depressions may differ, and especially, how development and experiences alter the neural and neuroendocrine systems relevant to depression. Because adolescent-onset depression is the "prototype" of most adult depression that is studied and treated, further understanding of developmental considerations will be fundamental to understanding recurrent adult depression—in short, a reversal of the typical "downward extension" models of adult depression applied to children. Three key methodological goals are encouraged for future studies:

1. Greater refinements in definitional issues of "depression" that address the challenges raised by heterogeneity, comorbidity, and the arbitrary lines between clinical and nonclinical depression, including transdiagnostic and endophenotype strategies. Such strategies also will assist in addressing the important question of the specificity of depressive outcomes, and tell us what is unique to the understanding and prediction of depression.
2. A greater emphasis on empirical studies with longitudinal designs, which will more precisely illuminate changes in vulnerabilities and clarify their mechanisms.
3. Further integrative studies that include multiple domains of vulnerabilities, to address the complex, transactional associations among biological, emotional, cognitive, and interpersonal processes. Such models are not difficult to construct, but are very challenging to test and validate through empirical investigations.

Figure 5.1 depicts one multidimensional developmental model of depression. The model is intended to highlight the complex and reciprocal interplay among diverse etiological influences on depression. Drawing from our empirical review, we have articulated a version of a model designed to encourage future directions. Temporally, the model commences with the genetic and environmental vulnerabilities the child faces from birth (or from prenatal life). Early life adversities may include traumatic experiences and severe abuse, but often include the more common problems of family instability; exposure to parental mental disorders and dysfunctional behavioral patterns; economic and social disadvantage; and harsh, insensitive parenting. Such adversities often occur early in life, but tend to be fairly chronic. These adversities shape individual vulnerabilities in biological, emotional, cognitive, and interpersonal functioning. Future research should increasingly and more precisely characterize the ways in which adversities exert maladaptive effects—and, ideally, define how particular adverse conditions operate at particular developmental stages to promote depression specifically.

Genetic factors have excited considerable attention throughout many aspects of human health and behav-

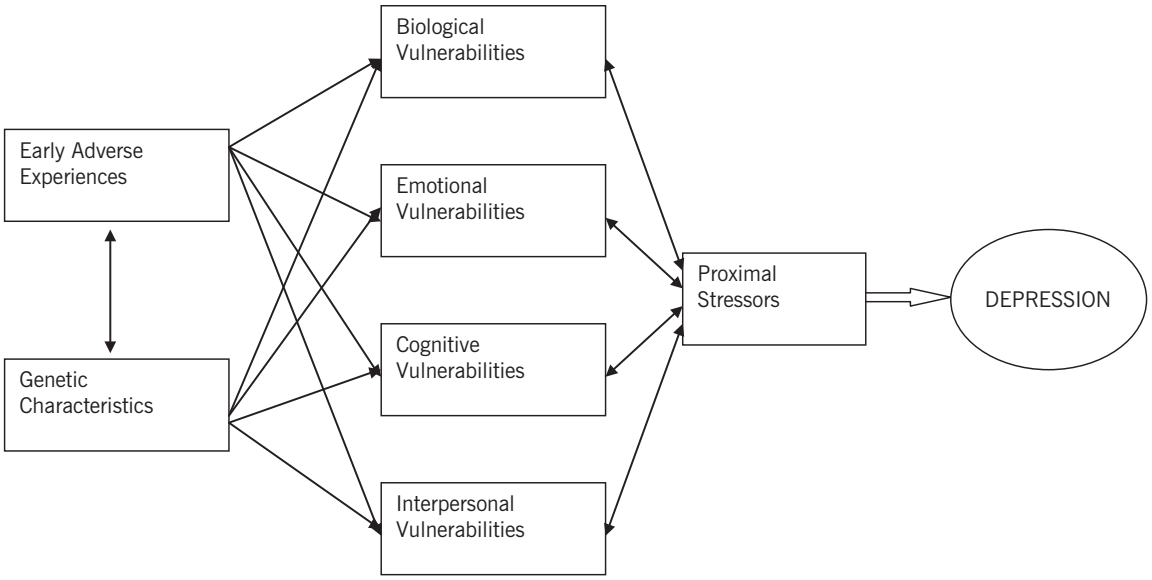

FIGURE 5.1. Multifactorial, transactional model of child and adolescent depression.

ior, and clearly represent a topic of obvious significance to our understanding of depression. There is substantial emerging evidence for heritable aspects of biological, emotional, cognitive, and interpersonal vulnerability. It is safe to predict that energetic efforts will be devoted to understanding the nature and mechanisms accounting for such genetic effects. In view of extensive evidence that the small effects of each of multiple genes are involved in human behavioral tendencies, the identification of candidate genes in youth depression along with the exploration of the various gene–environment interactions (and correlations) are likely to be of considerable interest to developmentally focused research.

The vulnerabilities depicted in Figure 5.1 are not meant to be exhaustive of possibilities for predicting risk for depression, but represent topics for which the literature so far has produced suggestive findings. Not shown in the figure because of their complexities are the multiple and bidirectional associations among the vulnerability factors themselves; nor is it easy to illustrate all the possible moderating and mediating pathways between the early adversity and genetic factors and the vulnerabilities to predict depression—although studies evaluating such complex pathways are clearly necessary.

In the model, the proximal predictor of depression consists of recent or ongoing stressful experiences, including both acute and chronic negative circumstances that typically trigger depression. Each of the vulnerability factors plays a role in how stress is construed or how it is processed at emotional and biological levels. Moreover, the vulnerability factors also play some role in the occurrence of stressors, not only in determining that an event is perceived as a stressor, but also in many cases contributing to maladaptive behaviors that cause stressors to occur. Also, individuals must deal with challenging circumstances but may lack the social, personal, biological, and cognitive resources needed to cope with or prevent stress effectively.

Depression is the outcome in the model, but it is also assumed that depression itself, as a commonly chronic or recurring condition, has deleterious effects on biological, emotional, cognitive, and interpersonal processes, thereby increasing or maintaining their likelihood for further negative impact on youth development. Imagine arrows issuing from depression back toward all the vulnerabilities, just as stress feeds both forward and backward. Indeed, a central question across levels of risk—including the biological substrate of depression—involves the effect of stress and prior

episodes of depression on the pathophysiology of depression. Depression is clearly a recurring problem for many sufferers, and perhaps depression experienced in adolescence represents a "degenerative" disorder that not only impedes normal developmental accomplishments but also heightens reactivity to future stressors.

The problem of depression in youth is a substantial one—not only because of its frequency and severity, but also because of the risk of a debilitating recurring disorder. Compounded with the impediments depression poses to achieving developmentally appropriate capabilities, depressed youth are likely to face their adulthood with impaired functioning in close relationships, parenting, and occupation, as well as emotional distress. We hope that further clarifications of etiological processes not only will serve the scientific goals of furthering the field's understanding of fundamental biological and psychosocial processes, but also will inform the interventions that are needed to interrupt the negative cycle.

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CHAPTER 6

Pediatric Bipolar Disorder

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Our understanding of pediatric bipolar disorder has changed rapidly in the last two decades. A bipolar disorder over the course of a lifetime is uncommon but not rare, and serious but treatable. As we will see, the roots of bipolar disorder run through the perinatal period, and first episodes often occur in childhood and adolescence. These early stages of development hold the keys to prevention, early identification and intervention, and ultimately better outcomes for people affected by bipolar disorder and their families. Although most of this chapter's focus is on childhood and adolescence, the presentation is set in a larger context of lifespan development. "Bipolar disorder" here refers to the adult range, or what has been confirmed to be consistent across age ranges, whereas "pediatric bipolar disorder" (hereafter abbreviated as PBD) denotes findings based on child and adolescent data.

BRIEF HISTORICAL CONTEXT

The modern conceptualization of manic–depression, now called bipolar disorder, goes back more than a century. Even older historical references and descriptions of presentations exist, although the thinking about etiology was necessarily different. Aretaeus of Cappadocia (now Turkey) provided one of the earliest clinical descriptions around 150 A.D., and Hippocrates and Aristotle also wrote about what to modern eyes looks like mania (Angst & Marneros, 2001; Glovinsky, 2002). Cases of mania in children and adolescents have been recognized for as long as there has been a diagnosis of bipolar disorder (Anthony & Scott, 1960). Researchers have identified case notes from an asylum describing a manic episode in a young girl in 18th-century Liverpool (Findling, Kowatch, & Post, 2003). Kraepelin (1921) documented instances of childhood onset in his comprehensive tome, *Manic–Depressive Insanity and Paranoia*.

The boundaries of bipolar disorder have always been unclear. Kraepelin (1921) strove to distinguish manic–depression from dementia praecox, foreshadowing the continued debate about the boundaries among bipolar disorder, schizophrenia, and schizoaffective disorder (Craddock & Owen, 2010). The boundary between bipolar disorder and unipolar depression also has been ambiguous and contentious. More recently, there has been heated discussion about the relationship between bipolar disorder and borderline personality disorder (Paris, Gunderson, & Weinberg, 2007; Perugi et al., 2013). All of these disorders can involve profoundly disrupted mood, raising the question of what would be unique to bipolar disorder (MacKinnon & Pies, 2006).

A recent historical change is a substantial increase in the frequency with which bipolar disorder is diagnosed in youth. Prior to the 1990s, there was a smat-

tering of published case reports. The 1990s ushered in a combination of research and popularization that made the diagnosis much more salient. The result was a dramatic rise in the rate of clinical diagnoses of PBD. The number of office visits billed under a diagnosis of a bipolar disorder rose 40-fold in the span of two decades (Moreno et al., 2007), and data from the Centers for Disease Control and Prevention indicated that more than 50% of psychiatrically hospitalized children under the age of 12 carried clinical diagnoses of bipolar disorders by 2003 (Blader & Carlson, 2007). It is still hotly debated whether these increases reflect corrections for past underdiagnosis, mislabeling of different entities as PBD, or a faddish overuse of what should be a rare diagnosis. Critics have raised the concern that the popularity of the PBD diagnosis might be influenced by pharmaceutical marketing or other extrinsic interests (Healy, 2006; Youngstrom, Van Meter, & Algorta, 2010). The debate has continued through the revisions to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) of the American Psychiatric Association (APA), with several position papers written to justify different approaches to the diagnosis in youth (Leibenluft, 2011; Youngstrom, 2009). DSM-5 (APA, 2013) advocates using a consistent set of criteria for children, adolescents, and adults, aligning with the recommendations of the International Society for Bipolar Disorders (Ghaemi et al., 2008; Youngstrom, Birmaher, & Findling, 2008). Although the idea of PBD is relatively new, the DSM definition has accrued considerable research investigating its validity; more than 9,000 peer-reviewed articles have been published at this writing, and more than 400 have been added to PubMed each year from 2008 onward. Some have also proposed creating a new diagnostic category for chronically irritable youth, in order to create a diagnostic alternative to expanding the concept of bipolar disorder (Leibenluft, 2011). DSM-5 has thus included a new diagnosis—disruptive mood dysregulation disorder (DMDD)—specifically to create an alternative to diagnosing PBD too often. Approaches to conceptualizing mood disturbance in youth are evolving rapidly.

DESCRIPTION OF THE DISORDER

Bipolar disorder is challenging to describe, due to its considerable heterogeneity. What does the clinical picture look like? Presentation runs the gamut from disinhibition and disorganization that are frankly psychotic, to periods of high energy associated with impetuousness but often large amounts of productivity, to episodes of severe and debilitating depression, as well as every permutation in between. Because of its episodic nature, it is also possible for a person to function within normal developmental limits during times of remission.

Definitional and Diagnostic Issues

The number of disorders DSM includes on the bipolar spectrum increased in DSM-III (APA, 1980), DSM-III-R (APA, 1987), and DSM-IV/DSM-IV-TR (APA, 2000), although DSM-5 (APA, 2013) stays with the same set of definitions as DSM-IV. The current nosology includes diagnoses of bipolar I, bipolar II, cyclothymic disorder, and other specified bipolar and related disorder (OS-BRD). The OS-BRD category subsumes the same prototypes that DSM-IV included under "bipolar disorder not otherwise specified" (BP-NOS), as well as adding a prototype of "short-duration cyclothymia." Both DSM-5 and DSM-IV also have designations for substance-induced manic symptoms and for manic symptoms due to another medical condition. However, unlike classification of most other disorders in DSM, correct classification of mood disorders (as we continue to call them, despite the fact that DSM-5 has dropped this category name) requires that the clinician first assess for the lifetime presence of mood episodes. Because mood disorders are episodic and often recurrent, the correct lifetime diagnosis may be tied to an index episode that occurred in the past. If a person seeks help for depression now, but had a manic episode years ago, then the depression is part of a bipolar illness, and the correct diagnosis would be "bipolar I, current episode depressed." Bipolar disorder is analogous to cancer, in that even when persons who are symptom-free are still labeled as having the disorder, albeit in remission. The nosology requires clinicians to evaluate lifetime history of depression, mania, hypomania, the potential for a mix of both poles of mood symptoms and periods of dysthymia in order to assemble the components for formal diagnosis of a mood disorder.

Bipolar disorder can lead to all possible mood states, whereas unipolar depression is distinguished by the absence of a lifetime history of hypomania or mania. Focusing solely on mania as the hallmark of bipolar disorder in general is problematic because (1) mania changes the lifetime diagnosis to bipolar I disorder, and thus, by definition, mania is not present in the other bipolar spectrum diagnoses; and (2) both youth and adults with

bipolar disorder tend to spend more time in depressed than in hypomanic or manic episodes (Axelson, Birmaher, Strober, et al., 2011; Judd et al., 2002). The burden of illness appears greater during the depressed phase in youth (Freeman et al., 2009) as well as adults (Judd et al., 2002), and people are more likely to seek help during periods of depression. Thus clinicians are more likely to see bipolar illness during states with pronounced depressive or mixed symptoms. Because this book has a separate chapter on depression (Hammen, Rudolph, & Abaied, Chapter 5, this volume), the diagnostic criteria for major depressive episode and dysthymia/persistent depressive disorder are not repeated here. It is crucial to remember that this organization of information does not reflect the clinical reality. Readers should approach Chapter 5 and the present chapter as a pair that need to be read together to have a comprehensive understanding of mood disorders—and depression and mania should not be compartmentalized in clinical practice or research. Similarly, it will also be valuable to consider persistent depressive disorder (APA, 2013), as dysthymic presentations often accompany depressive and bipolar disorders and are linked with substantial impairment.

Core Symptoms

The core symptoms of bipolar disorder involve dysregulation of mood and energy. Mood disturbance has been emphasized as a core feature of the illness, reflected in the "mood disorder" designation until DSM-5. However, the changes in energy and somatic aspects of the illness may be at least as important. Kraepelin (1921) described the disorder as influencing three major aspects of functioning, which he called "emotion" (now usually called "mood"), "intellect" (cognition), and "volition" (energy level). The DSM nosology has primarily focused on the affective component, with some acknowledgement of the cognitive and somatic symptoms. The DSM-5 revisions increase the emphasis on changes in energy, making them at least as salient as disturbance in mood. Energy changes are easier for individuals to observe in themselves, and are less prone to bias in retrospective recall (Angst et al., 2012). For these reasons, asking about changes in energy may be more sensitive to detecting hypomania than inquiries about mood. Increased focus on energy and activity also may reduce some aspects of cultural bias in assessment. Whereas framing in terms of "mood" is a very white, European, middle-class way of conceptualizing issues, other cultural groups often focus more on somatic elements of illness (Angst et al., 2010; Carpenter-Song, 2009).

Symptoms of Mania and Hypomania

The DSM-IV and DSM-5 criteria define a core set of diagnostic symptoms for mania and hypomania. Table 6.1 delineates the DSM-5 criteria for manic and hypomanic episodes. The distinction between hypomania and mania is primarily a matter of intensity, not quality. Hypomania is a clear change from a person's typical functioning, yet not so extreme as to cause marked impairment. If the behavior becomes severe enough to cause substantial problems, then it is considered mania instead of hypomania. Things are more ambiguous when mood is dysregulated but not causing impairment: If the person is able to function in school, and no one notices or is distressed by the intense emotional states, then it is less clear that it is pathological. A teen's raving to dance music for hours, or running alone pell-mell through the woods until exhausted, may not be evidence enough for hypomania or mania, despite its remarkable intensity in the moment.

A secondary distinction focuses on the duration of the mood state. The DSM-5 criteria specify that a manic episode is characterized by pronounced increase in energy and disturbance of mood much of the day, most days in a row, for at least a week. However, if the behavior is severe enough to warrant psychiatric hospitalization, then one need not have a week-long duration to establish the presence of a manic episode. Essentially, the minimum requirement is either a 1-week duration or hospitalization, whichever comes first. The criteria again become ambiguous in situations where hospitalization is not an option, due to factors such as the lack of access to a psychiatric facility. Then the behavior might be sufficiently disrupted to justify hospitalization, but results instead in arrest or no intervention at all.

For hypomania, the duration requirement is shorter, reflecting the general principle of hypomania being a diminution in degree of mania, rather than a qualitatively different state. The DSM-5 criteria have retained the durational threshold set at 4 days of clear change in mood or energy lasting much of the day, as previously operationalized in DSM-IV. Data from both clinical and epidemiological studies indicate that the modal episode length of hypomania is probably 2 days (Angst et al., 2011; Merikangas & Pato, 2009; Youngstrom, 2009). DSM-5 committees actively debated whether

TABLE 6.1. DSM-5 Diagnostic Criteria for Manic and Hypomanic Episodes

Manic Episode

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased goal-directed activity or energy, lasting at least 1 week and present most of the day, nearly every day (or any duration if hospitalization is necessary).

B. During the period of mood disturbance and increased energy or activity, three (or more) of the following symptoms (four if the mood is only irritable) are present to a significant degree and represent a noticeable change from usual behavior:

1. Inflated self-esteem or grandiosity.
2. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep).
3. More talkative than usual or pressure to keep talking.
4. Flight of ideas or subjective experience that thoughts are racing.
5. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.
6. Increased in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (i.e., purposeless non-goal-directed activity).
7. Excessive involvement in activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

C. The mood disturbance is sufficiently severe to cause marked impairment in social or occupational functioning or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

D. The episode is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication, other treatment) or to another medical condition.

Note: A full manic episode that emerges during antidepressant treatment (e.g., medication, electroconvulsive therapy) but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a manic episode and, therefore, a bipolar I diagnosis.

Note: Criteria A–D constitute a manic episode. At least one lifetime manic episode is required for the diagnosis of bipolar I disorder.

Hypomanic Episode

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least 4 consecutive days and present most of the day, nearly every day.

B. During the period of mood disturbance and increased energy or activity, three (or more) of the following symptoms (four if the mood is only irritable) have persisted, represent a noticeable change from usual behavior, and have been present to a significant degree:

1. Inflated self-esteem or grandiosity.
2. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep).
3. More talkative than usual or pressure to keep talking.
4. Flight of ideas or subjective experience that thoughts are racing.
5. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed.
6. Increased in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation.
7. Excessive involvement in activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the individual when not symptomatic.

D. The disturbance in mood and the change in functioning are observable by others.

E. The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization. If there are psychotic features, the episode is, by definition, manic.

F. The episode is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication, other treatment).

(continued)

TABLE 6.1. *(continued)*

Note: A full hypomanic episode that emerges during antidepressant treatment (e.g., medication, electroconvulsive therapy) but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a hypomanic episode diagnosis. However, caution is indicated so that one or two symptoms (particularly increased irritability, edginess, or agitation following antidepressant use) are not taken as sufficient for diagnosis of a hypomanic episode, nor necessarily indicative of a bipolar diathesis.

Note: Criteria A–F constitute a hypomanic episode. Hypomanic episodes are common in bipolar I disorder but are not required for the diagnosis of bipolar I disorder.

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DSM-5 has eliminated mixed episode as a distinct mood episode category. Instead, "with mixed features" is a specifier that can be used to modify any mood episode, including major depressive, manic, and hypomanic episodes. The mixed features specifier uses an algorithm that tries to focus on symptoms that are more specific to depressive or manic states, and exclude those that are potentially common to both mood polarities, when a clinician is determining whether the specifier should be used.

the duration should be shifted to 2 days instead of 4 days (cf. Towbin, Axelson, Leibenluft, & Birmaher, 2013). One point of view was that the 2-day duration risks inflating diagnostic rates of hypomania, and thus of some bipolar diagnoses. The contrasting position was that setting the threshold at 4 days reduces the sensitivity of the criteria, resulting in more false negatives that would be misclassified as having unipolar depression or some other condition. Duration criteria are directly relevant to issues of phenomenology in children and adolescents: One of the main reasons why many youth have been classified as having BP-NOS in several studies is the insufficient duration of the index mood episodes (Axelson et al., 2006; Findling et al., 2005; Youngstrom et al., 2008). Mood episodes in children sometimes are described as briefer than in adults, but the data indicate that adults frequently have 2-day episodes as well. The larger issue may be more that the 4-day or 7-day thresholds were not based on robust data (Dunner, Russek, Russek, & Fieve, 1982). Similarly, the scarcity of child psychiatric inpatient units means that severe behaviors often cannot lead to hospitalization, contributing both to misdiagnosis (Neighbors et al., 2007) and to the high rate of incarceration seen in adolescents with mood disorder (Pliszka, Sherman, Barrow, & Irick, 2000; Teplin, Abram, McClelland, Dulcan, & Mericle, 2002), particularly among ethnic minorities.

Symptoms of Depression and Dysthymia

Bipolar disorders usually involve periods of depressive symptoms—reaching the acuity of major depressive episodes in the case of bipolar I and bipolar II, or manifesting as "subthreshold" depression (due either to more mild or moderate severity, or to brevity of episode). Severe depressions lasting less than 2 weeks would fail to meet the durational criteria for a major depressive episode, for example. Again, we refer the reader to Chapter 5 of this volume to review the core symptoms and associated features of major depression, and to DSM-5 to review the criteria for persistent depressive disorder, as these symptoms also are central components of bipolar disorders. The DSM criteria for major depression and dysthymia (now called persistent depressive disorder in DSM-5) overlap, but are not identical. Hopelessness, for example, is considered a diagnostic symptom of dysthymia and not of major depression (APA, 2000, 2013). We suspect that this may have been an artifact of different measures being used in early studies, and that it then became reified in later definitions. The DSM bipolar definitions emphasize symptoms of depression (and do not specifically mention symptoms of dysthymia), but this also is probably an omission due to convention rather than driven by data. It is most likely to be problematic in the case of cyclothymic disorder, which in many respects is the bipolar analogue to dysthymic disorder (Van Meter, Youngstrom, & Findling, 2012).

The depressed phases of bipolar illnesses may show more "atypical" features (Goodwin & Jamison, 2007). Atypical depression is marked by hypersomnia instead of insomnia, increased appetite instead of decreased appetite, weight gain instead of loss, motor retardation or substantially decreased energy, and rejection sensitivity (APA, 2000, 2013). Rejection sensitivity may be a trait-like feature that is manifested regardless of current mood state (Davidson, 2007), whereas the other atypical features are limited to depressed states. At present,

no published data have specifically looked at whether atypical symptoms are more frequent in bipolar versus unipolar depression among youth with mood disorders. If this were the case, it would have considerable theoretical and clinical value. Conceptually, many of the atypical features cohere into a constellation of appetite, sleep, and energy-related symptoms that may indicate an "endophenotype," or an underlying set of features more closely tied to a biological process (Harvey, Mullin, & Hinshaw, 2006; Hasler, Drevets, Gould, Gottesman, & Manji, 2006). Clinically, atypical features might identify cases in which patients are seeking treatment for depression but are more likely to follow a bipolar course. Research addressing the atypical hypothesis would include (1) testing whether atypical symptoms are significantly more common among those with a history of hypomanic or manic episodes in addition to their depression; (2) testing whether atypical symptoms predict higher rates of "switching" to hypomania or mania in longitudinal studies or in acute treatment studies; and (3) examining whether atypical symptoms during depression correspond with contrasting disturbances during elevated mood states—such that increased appetite during depression corresponds with decreased appetite during mania, or depressive hypersomnia correlates with decreased need for sleep during mania. The first two research questions would have immediate ramifications for clinical assessment, whereas the third would help clarify mediational mechanisms by showing the extent to which atypical features are more linked to circadian sleep systems, appetite, or both.

Mixed Presentations

Mania and depression appear to be separate dimensions of mood functioning, not bipolar opposites along the same continuum. Mania is not "antidepression." Affective neuroscience indicates that positive affect and negative affect are virtually uncorrelated at the trait level, although the correlation may change at the state level (Carroll, Yik, Russell, & Barrett, 1999). It is possible for a person to experience high levels of positive affect, high levels of negative affect, elevations of neither ("euthymia," or functioning within normal limits), and high levels of both. Simultaneous elevation of positive and negative affect, or of manic and depressive symptoms, constitutes a "mixed state." It would be an oversimplification to reduce depression to high negative affect, or mania to elevated positive affect. Observers since Kraepelin have noted that mood disorders also involve changes in cognitive functioning, energy, and behavior, as well as mood. "Pure" depression would entail not just high negative affect, but also low positive affect, low energy, cognitive dulling and rumination, and low activity. Conversely, "pure" mania might involve high positive affect but low negative affect, high energy and activity, and the sense that cognition is accelerated. However, it is possible to have elevation or decrement on each component out of synchrony with the others, consistent with the moderate entrainment between cognitive, affective, and physiological systems (Izard, 1993). Kraepelin (1921) worked through the $2 \times 2 \times 2$ permutations implied by being clinically high or low on three facets; he thus described eight prototypical mood states, six of which would be mixed variants.

Clinical phenomenology confirms the prediction based on laboratory studies of affective systems: Blended states appear to be the rule, and pure presentations more of an exception (Van Meter et al., 2012). Many depressions involve high energy, often characterized as "agitated depression." Hypomania and mania often involve anger, frustration, or even rage—all negative in valence, although anger is an "approach"-oriented emotion in terms of cortical activity and behavioral correlates (Youngstrom, 2009).

There are two different temporal presentations that could produce mixed mood presentations. One involves the simultaneous occurrence of depressive and manic symptoms. This "dysphoric mania" often involves high energy coupled with negative valence. It is often volatile and can shift into other mood states quickly. Dysphoric mania is metaphorically like chocolate milk: The milk of mania and the chocolate of depression form a solution that is qualitatively different, and it is not clinically possible to separate components and say, "During this part of the day, John looked manic; and during this part of the evening, he looked depressed."

The alternate presentation is mood instability, oscillating between periods of relatively pure mania and depression. The metaphor in this instance would be fudge ripple ice cream, where the vanilla and fudge are co-mingled, but still distinct (Youngstrom et al., 2008). This conglomerate mood presentation often appears similar to the affective instability associated with borderline personality disorder, leading some to speculate that this personality disorder might be an extreme case on the bipolar spectrum with extremely brief mood episodes (MacKinnon & Pies, 2006).

Mixed presentations are clinically common in bipolar disorder generally, and may be even more frequent

in PBD (Algorta et al., 2011; Axelson et al., 2006; Duax, Youngstrom, Calabrese, & Findling, 2007; Kraepelin, 1921). They also are highly impairing, causing distress both to the affected persons and to the people around them. Mixed presentations carry great risk of suicide, as they pair the negativity and hopelessness of depression with the high energy and impulsivity that are more typical of mania (Algorta et al., 2011). Because they do not look like classic, "pure" depression or mania, they also are more difficult to recognize and diagnose correctly.

DSM-IV-TR criteria for a mixed episode (APA, 2000) required meeting full criteria for both mania and depression during the same episode (i.e., elated mood plus at least three B criteria, or irritable mood plus at least four B criteria for mania), along with at least five of nine depressive symptoms. The duration for a mixed episode followed the mania criteria: The episode needed to last 7 or more days, or to be severe enough to justify psychiatric hospitalization, rather than requiring 2 weeks for the depression. Concerns about the DSM criteria included that patients often showed mixed hypomanias, showing that the classification scheme was not exhaustive. In addition, DSM-IV(-TR) did little to describe mixed depressive presentations, and it also was vague about the number of hours in a day or the number of days in a week necessary to pass the threshold for diagnosing an episode.

DSM-5 has attempted to address these shortcomings by abolishing mixed episodes as a distinct episode type. Instead, "with mixed features" is a specifier that can be coded on top of a manic, hypomanic, depressed, or persistent depressive (previously "dysthymic") episode. If clinicians embrace the specifier, it could help to characterize mixed hypomanias more accurately, as well as to acknowledge the substantial portion of depression that involves mixed features. However, reviews of clinical diagnoses find that specifiers are rarely coded in practice (Garb, 1998). Thus the net result might be decreased clinical sensitivity to bipolar presentations. The DSM-5 algorithm for recognizing a mixed presentation tries to give more weight to symptoms specific to depression or mania. Irritable mood and poor concentration/distractibility do not count toward "with mixed features" in the DSM-5 framework (APA, 2013, pp. 149–150, 184–185) because they could appear in either pure depression or mania.

This approach faces several challenges: (1) It is more complex, making it less likely that clinicians will implement it consistently; (2) it was not tested against existing data to see whether the symptoms were in fact specific to one mood state; (3) nonspecific mood symptoms might actually be the most characteristic of mixed presentations; (4) the most impairing symptoms might be nonspecific (irritable mood is usually the top concern for parents and teachers initiating referrals); and (5) the algorithm ignores the possibility that a symptom might be qualitatively different during depression versus mania. Irritable mood or poor concentration could occur in both mania and depression, for example; but it is possible to distinguish manic from depressive presentations by the associated energy level and other contextual factors. Irritability during depression is a low-energy, grouchy, cranky presentation, possibly leading to lashing out if pushed; irritability during mania is high-energy and approach-oriented, and can lead to frustration when people set limits. Excluding irritability from consideration for "with mixed features" removes the potential to distinguish qualitatively different forms of irritability within each mood polarity. The complexity is made worse by having different criteria for the "with mixed features" specifier coded in the context of a manic or hypomanic episode (APA, 2013, pp. 149–150) versus a major depressive or persistent depressive episode (APA, 2013, pp. 184–185). The addition of a new "with anxious distress" specifier may further complicate the clinical description of mood presentations. Overall, empirical investigations of the new DSM-5 mixed features specifier (and other mood specifiers) will be crucial. Not only should this specifier's validity be examined, but how it is used in clinical practice should also be tracked.

Related Symptoms

A shortcoming of the DSM approach to diagnosis is that it privileges certain symptoms as part of the diagnostic criteria, and demotes the other symptoms or associated features. Bipolar disorders are associated with high levels of stress and anxiety (Wagner, 2006). The fact that many of these anxious symptoms are not included on the list of criteria for depression or mania draws an artificial division between them. When a substantial number of anxious symptoms are present, then the clinician needs to decide whether to diagnose a "comorbid" anxiety disorder, or whether to attribute the anxiety to the mood syndrome and perhaps code the "with anxious distress" specifier (APA, 2013, pp. 149, 184). The DSM criteria are hierarchical: A mood disorder takes precedence as the explanation for symptom

clusters unless the symptoms are clearly manifested outside the context of a mood episode as well. However, clinicians' implementation of this principle varies widely, resulting in significant differences in the rate of "comorbid" anxiety disorders labeled among cases with bipolar disorders across different research groups and clinics (Kowatch, Youngstrom, Danielyan, & Findling, 2005; Wagner, 2006). Similar problems arise with psychosis and the fuzzy lines among bipolar disorders, schizoaffective disorder, and schizophrenia (Barnett & Smoller, 2009), or between impulse-control disorders or antisocial behavior and mania (Bowring & Kovacs, 1992).

Types and Subtypes

DSM-5 retains the same broad set of bipolar disorders as in DSM-IV-TR, but with some modifications to criteria. We review those first, noting any modifications in DSM-5, and then briefly discuss alternate subtypes and nosologies. Because almost all published research reviewed here has used the DSM-IV criteria, they are presented as well. DSM-5 modifications currently have less of an evidence base than the DSM-IV definitions.

Bipolar I Disorder

DSM defines bipolar I disorder by the occurrence of at least one lifetime manic episode. Any and all of the other mood states described above are also possible in bipolar I, but the history of a manic episode defines the disorder as bipolar I. As noted earlier, if a person has had a previous manic episode but currently meets criteria for a pure major depressive episode, DSM would code this presentation as "bipolar I disorder, current episode depressed." This approach's strength is its recognition that the depression or other mood states may show a different response to treatment and follow a different course than would be expected if they did not occur in the context of a bipolar illness. An inherent challenge is that the definition subsumes tremendous heterogeneity. What does bipolar I look like? It may appear as florid mania, severe mixed mood, hypomania, depression, euthymia, or a blend of different aspects of each. The complexity increases when the element of time is added. Some people have long episodes, and some have frequent relapses; others have long periods of high functioning. Some may only experience a single manic episode in their lifetime; others have a predominance of depression; and some may have recurrent mania with no history of depression. At present, it is unclear whether these longitudinal courses reflect different subtypes of illness. It appears likely that they have different prognoses, but it is not well established that they show differential treatment response. The more distinct the mood episodes, and the better the functioning before or between episodes, the better the response may be to lithium (Alda, Grof, Rouleau, Turecki, & Young, 2005; Duffy et al., 2002).

DSM-IV also allowed bipolar I to be coded in the presence of a mixed episode. As discussed above, DSM-5 reclassifies such a mood episode as mania "with mixed features," while still assigning a lifetime diagnosis of bipolar I. The *International Classification of Diseases* (ICD) has required multiple episodes of mania to confirm a diagnosis of bipolar I. Faced with a single manic episode, ICD would indicate coding a "provisional" bipolar diagnosis (World Health Organization, 1992). This more conservative approach has probably contributed to lower rates of bipolar I disorder in studies using ICD instead of DSM criteria (Dubicka, Carlson, Vail, & Harrington, 2008).

Bipolar I is by far the most studied form of bipolar illness, and research on it comprises the bulk of the clinical trials addressing the bipolar spectrum. However, it only represents roughly a quarter of the cases meeting criteria for a bipolar disorder according to DSM criteria, and an even smaller portion if alternative criteria are used (Merikangas & Pato, 2009).

Bipolar II Disorder

From a clinical perspective, bipolar II disorder is best considered a form of depressive illness. To receive a bipolar II diagnosis, a person needs to have met full criteria for both a hypomanic episode and a major depressive episode. In DSM-5, either or both of the hypomanic and depressive episodes could also carry the "mixed specifier." The person is much more likely to seek treatment during the depressed phase of the illness, and the depression will generate much more impairment than the hypomania, by definition (Berk & Dodd, 2005). The person can also develop subthreshold mood problems, such as minor depression, brief hypomanias, or even persistent depressive dysthymia—corresponding to the "double depression" noted when dysthymia and major depression affect the same individual sequentially (Klein, Taylor, Harding, & Dickstein, 1988; Van Meter et al., 2012). The person cannot, however, display a full manic episode, or else the diagnosis must be changed to

bipolar I. Clinical observers note pronounced affective instability in many cases of bipolar II disorder (Berk & Dodd, 2005). The DSM-5 "with mixed features" specifier may help document this aspect of phenomenology.

Cyclothymic Disorder

DSM-5 retains the diagnosis of cyclothymic disorder from DSM-IV-TR. The definition specifies that the person shows pronounced hypomanic and depressive symptoms for an extended period of time—2 years or more in adults, and 1 year or more in youth, with the symptoms present more than half of the time and no more than 2 months symptom-free. DSM-5 has clarified that the hypomanic symptoms do not need to meet criteria for a hypomanic episode. The cyclothymic mood disturbance is associated with impairment. DSM is ambiguous about whether the mood presentation entails a distinct change from the person's typical functioning. There is conceptual debate about whether cyclothymia represents a distinct disorder, akin to dysthymic disorder, or would be better conceptualized as an affective temperament (Parker, McCraw, & Fletcher, 2012). The temperament model could suggest that cyclothymic traits constitute a diathesis for development of a full-blown mood disorder. Alternately, cyclothymia might represent a prodrome of bipolar illness.

Clinically, cyclothymic disorder is difficult to distinguish because by definition it excludes the most extreme and clear-cut presentations. The hypomanic symptoms cannot become too severe or pronounced, or else they form a manic episode (and the diagnosis must be changed to bipolar I). Similarly, the depressive symptoms cannot progress to a full-blown major depressive episode, or else the diagnosis must be changed to bipolar II or major depressive disorder with mixed features. The long duration of the index mood state also makes it difficult to discern from the person's typical functioning (Van Meter et al., 2012). Perhaps for these reasons, the diagnosis of cyclothymic disorder has rarely been used in youth (Youngstrom, Youngstrom, & Starr, 2005), although research studies suggest that it can be reliably identified and shows validity in terms of associated features, course, and family history (Van Meter, Youngstrom, Demeter, & Findling, 2013; Van Meter, Youngstrom, Youngstrom, Feeny, & Findling, 2011). Moreover, epidemiological studies suggest that it is prevalent and typically highly impairing (Merikangas et al., 2007, 2011; Van Meter, Moreira, & Youngstrom, 2011).

Other Specified Bipolar and Related Disorder or Bipolar Disorder Not Otherwise Specified

DSM-5 has renamed all of the DSM "not otherwise specified" (NOS) diagnoses as "other specified" (OS), even if none of the specific criteria were changed between DSM-IV and DSM-5. In the case of bipolar disorder, the definitions of OS-BRD and BP-NOS are similar, with the exceptions noted for the mood states (e.g., more emphasis on change in energy; making "with mixed features" a specifier instead of an episode definition) and clarifications about the number of hours required to meet the "much of the day" threshold. OS-BRD also adds major depressive episodes to the prototypes involving insufficient duration of hypomania or insufficient number of hypomanic symptoms. If interpreted as making major depression a required element, then the OS-BRD definition would focus on cases missing criteria for bipolar II disorder due to insufficient duration or symptom number. It would not include a large number of other cases that would meet other research or clinical definitions of BP-NOS used in DSM-IV (e.g., Axelson et al., 2006; Findling et al., 2005). OS-BRD also adds a new, fourth prototype of "short-duration cyclothymia" for presentations lasting less than 24 months in adults, and less than 12 months in youth.

In light of these shifts in criteria, which in some respects narrow and in other ways expand the scope of OS-BRD, we use "BP-NOS" when referring to research based on DSM-IV criteria—both to be consistent with the terminology used in the research base, and to help differentiate evidence from this research from evidence based on newer studies using the new DSM-5 criteria for OS-BRD. The APA intends OS-BRD (and previously intended BP-NOS) to be a diagnosis of last resort, employed only after a clinician has systematically considered the other bipolar disorders and has established that a case does not meet strict criteria for each of them. However, the opposite often occurs in practice, as both clinicians and researchers have been found to invoke a BP-NOS diagnosis without systematically checking whether criteria for another bipolar disorder would be met (Dubicka et al., 2008; Youngstrom, Youngstrom, & Starr, 2005). This is particularly common with cyclothymic disorder, which has been frequently lumped together with other NOS presentations and labeled as "mood disorder NOS," even in research studies. Many practicing clinicians have also used the NOS label when a young person might meet criteria for bipolar I

or bipolar II, believing that the NOS label might be less stigmatizing or more likely to be reevaluated when the youth is older.

DSM-5 has made two other noteworthy alterations to the "NOS" options from DSM-IV. One has been to eliminate "mood disorder NOS," which did not differentiate between bipolar and unipolar depressive spectrum illness. Practicing clinicians frequently used this as an even softer potential bipolar spectrum diagnosis (Youngstrom, Youngstrom, & Starr, 2005). The other has been to add "unspecified bipolar and related disorder" as a new residual option, for use when "the clinician chooses *not* to specify the reason that the criteria are not met for a specific bipolar and related disorder" (APA, 2013, p. 149; original emphasis). If practice and reimbursement trends stay similar over the next several years, the "unspecified bipolar and related disorder" diagnosis will probably become one of the most frequently used in practice.

BP-NOS and OS-BRD involve hypomanic and perhaps depressive symptoms. As with cyclothymic disorder, there can be no history of full-blown mania, or else the diagnosis must be changed to bipolar I; and no history of major depression, or else the diagnosis must become bipolar II (or perhaps major depression with mixed features in DSM-5). To qualify as a psychiatric disorder, the symptoms need to be associated with significant impairment in at least one setting.

DSM-IV-TR provided examples of prototypes for different BP-NOS presentations. These included recurrent hypomanic episodes without any lifetime history of mania or depression. DSM-5 allows coding the "with mixed features" specifier on the hypomania if clinically appropriate in bipolar II, but this specifier is not listed as an option for OS-BRD or unspecified bipolar and related disorder (APA, 2013, pp. 148–149). Nevertheless, people exhibiting this symptom course are present in epidemiological studies (Merikangas et al., 2012), family history studies (Hodgins, Faucher, Zarac, & Ellenbogen, 2002), and studies of subthreshold mood presentations (Kwapil et al., 2000). These people rarely seek clinical services because their functioning often is either normal or superior, and their fluctuations in mood and energy are not causing significant problems (Klein, Lewinsohn, & Seeley, 1996). Thus this variant of BP-NOS/OS-BRD is of more interest for research than clinical purposes, although it could be informative about factors related to resilience and good prognosis.

A second variant of BP-NOS/OS-BRD has an insufficient number of symptoms to meet full criteria for the index mood episode. The insufficient number of symptoms definition is most widely used in epidemiological studies, where it is straightforward to reanalyze data using alternative operational definitions, such as combining disturbance of mood with at least one other manic symptom, or examining liminal cases that fall one symptom short of the DSM threshold (Lewinsohn, Klein, & Seeley, 1995). These definitions automatically are more prevalent than definitions requiring a higher number of symptoms, but they still are associated with high degrees of impairment (Merikangas & Pato, 2009).

A third variant of BP-NOS/OS-BRD fails to satisfy the durational criteria for the index mood episode. The person might manifest all the symptoms of mania, but these do not last for a week or result in hospitalization. In like manner, the hypomania might not last 4 days, the depression might never have lasted 2 weeks or longer, or the cyclothymic/dysthymic period might only have lasted for less than a year. These subthreshold durations are not problematic if there has been a past episode that satisfied the full criteria; in that scenario, the current mood problems would be coded as "partial remission." However, if no past episode has met full criteria, and the current episode does not achieve the durational criteria, then the technically correct diagnosis would be OS-BRD in DSM-5 (and BP-NOS previously). The clinical and epidemiological data about the lengths of mood episodes are relevant to this scenario. Many youth with bipolar symptoms show a sufficient number of symptoms and considerable impairment, but the discrete mood episodes do not persist long enough to surpass the DSM duration thresholds (Youngstrom, 2009). Clinical data indicate that this is a frequent presentation among young people, and epidemiological and clinical data show that it is a common occurrence among adults as well (e.g., Judd & Akiskal, 2003). The DSM-5 stipulation that a hypomanic episode must last at least 4 days thus has the potential to shift many cases that would otherwise meet criteria for bipolar II into the OS-BRD category.

Substance-Induced Manic Symptoms

DSM-IV instructed that instances of manic symptoms coinciding with the use of street drugs or psychotropic medications should be classified as "substance-induced mood disorder with manic features," instead of being labeled as bipolar I or II. When a person develops mood and behavioral activation while taking a drug, it

is ambiguous whether the symptoms are features of the chemically induced "high," whether they are unintended side effects of the medication, or whether the medication is exposing a bipolar diathesis (Joseph, Youngstrom, & Soares, 2009). Many authorities suggest that behavioral activation while taking an antidepressant or stimulant might be a diagnostic indicator for a bipolar disorder (Akiskal et al., 2003; Ghaemi, Hsu, Soldani, & Goodwin, 2003). However, two reviews of the literature on antidepressant-induced "switching" into mania concluded that the evidence was most consistent with a "vigilance" hypothesis; that is, taking the medication was probably associated with better monitoring for potential hypomanic symptoms (Joseph et al., 2009; Licht, Gijsman, Nolen, & Angst, 2008). The appearance of high rates of treatment-emergent affective switching could be attributed to greater assessment sensitivity, as opposed to an underlying change in the rate of bipolarity. DSM-5 allows diagnosis of independent bipolar disorders in cases where the symptoms emerge during pharmacological treatment, particularly if mood symptoms precede the onset of substance/medication use, or if the symptoms persist for about a month after cessation of acute withdrawal or intoxication, or if there is other evidence consistent with an independent disorder (APA, 2013, p. 142). This would be consistent with a vigilance hypothesis, or with the idea that symptoms might be "breaking through" treatment. It also is consistent with the growing body of evidence that stimulants or antidepressants are not associated with higher rates of bipolar disorders or manic symptoms (Carlson, 2003; Pagano, Demeter, Faber, Calabrese, & Findling, 2008; Scheffer, Kowatch, Carmody, & Rush, 2005). However, the issue remains contentious (DelBello, Soutullo, et al., 2001), and it is possible that there may be a genetic predisposition associated with a subset of cases in which patients exhibit mood disinhibition when taking medication (Salvadore et al., 2010).

Narrow, Intermediate, and Broad Phenotypes of PBD

In response to the debate about the manifestations of bipolar disorder in children and adolescents, an influential paper delineated "narrow," "intermediate," and "broad" definitions of PBD (Leibenluft, Charney, Towbin, Bhangoo, & Pine, 2003). The DSM-IV criteria constituted the intermediate definition, and the narrow and broad definitions were departures from the DSM definitions. The narrow phenotype was largely based on the research operational definition used by Geller in her pioneering National Institutes of Health studies of PBD (Geller & Luby, 1997) at Washington University. The Washington University criteria required the presence of either elated mood or grandiosity in order to satisfy inclusion criteria for the bipolar group because irritable mood was nonspecific to PBD (Geller, Zimerman, Williams, DelBello, Bolhofner, et al., 2002). The Leibenluft and colleagues (2003) narrow criteria also adopted the focus on elated mood or grandiosity, along with requiring that the mood have clear episodic boundaries or fluctuations. Interestingly, the Washington University version of the Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS; Geller et al., 2001) makes it difficult to track episodes because it focuses on the onset and offset of discrete symptoms rather than orienting inquiry around distinct episodes (Galanter & Leibenluft, 2008). There is debate about how many of the youth in Geller and colleagues' data would meet the episodicity requirement for the narrow phenotype.

The narrow phenotype was originally envisioned as a research definition, not something intended for clinical use. Subsequent studies have found that many adults with bipolar disorders present with primarily irritable, not elated, mood, suggesting that the narrow phenotype might exclude a substantial portion of adult bipolar cases (Judd et al., 2002). Conversely, pediatric studies find that elated mood and grandiosity are endorsed in the majority of cases meeting criteria for DSM-IV bipolar diagnoses if the symptoms are assessed systematically via semistructured interviews or rating scales (Kowatch et al., 2005). Elated mood and grandiosity are not the most impairing symptoms, and for that reason they are rarely seen as the main presenting problems (Freeman, Youngstrom, Freeman, Youngstrom, & Findling, 2011; Hawley & Weisz, 2003). Families tend not to focus on these symptoms in their spontaneous descriptions of their children's situations (Carpenter-Song, 2009). There are few differences between cases with and cases without elated mood in terms of severity, associated features, or other correlates when systematically assessed (Hunt et al., 2009). Requiring elated mood or grandiosity might not have huge effects on diagnostic rates or validity if done systematically; however, relying on unstructured interviews that concentrate on initial descriptions of the presenting problem is likely to mislabel a substantial portion of bipolar cases (Galanter & Patel, 2005; Jenkins, Youngstrom, Washburn, & Youngstrom, 2011). In the British National Institute for Health and Care Excellence Guidelines (*www.nice.org.uk/nicemedia/live/10990/30193/30193.pdf*), the narrow definition

of PBD has been adopted as the core definition, without specifying a corresponding systematic approach to assessment. This combination of factors has probably contributed to the low rate of clinical diagnosis of PBD in the United Kingdom (see Dubicka et al., 2008, for an example of differences in interpretation of clinical vignettes).

The broad phenotype of PBD initially described a presentation in which mood might be mostly irritable, without clear periods of elated mood or grandiosity (Nottelmann et al., 2001). The hallmark of the broad phenotype, though, was considered to be the lack of clear episodes (Leibenluft et al., 2003). The onset of illness might be gradual and insidious, or the mood dysregulation could be chronic to the point that a parent might report it was present "from birth" or even *in utero* (Papolos & Papolos, 2002; Wozniak et al., 1995). The lack of definite episodes set the presentation apart from the DSM-IV(-TR) definitions of bipolar I and II, which clearly required that the mania, hypomania, or depression be a change from the person's typical functioning that was readily observed by others (APA, 2000). The broad definition also was at odds with Kraepelin's (1921) conceptualization of mood disorder as episodic or cyclical, which he used to separate manic–depression from schizophrenia and other entities that followed a more progressive and unremitting course. Several research groups focused on irritable mood as a core feature of PBD and argued that nonepisodic presentations also were common on the bipolar spectrum (Mick, Spencer, Wozniak, & Biederman, 2005; Wozniak et al., 2005). There was suspicion that many cases clinically diagnosed with PBD also fell into the broad definition rather than the intermediate or narrow one, based on the fact that irritable mood and aggression were often the features driving referral and treatment (Blader & Carlson, 2007; Leibenluft, 2011). However, the service databases that showed increasing rates of clinical diagnoses of PBD did not distinguish among bipolar subtypes; nor did they track symptom-level details to isolate whether cases fit a narrow, intermediate, or broad phenotype.

Disruptive Mood Dysregulation Disorder

The broad phenotype started as a general characterization of PBD diagnoses that did not require elated mood, grandiosity, or episodicity. Leibenluft and colleagues (2003) offered a more precise operational definition of "severe mood dysregulation" (SMD) as a way of trying to increase the reliability of research diagnoses. SMD initially excluded cases with diagnoses of schizophrenia, pervasive developmental disorder, substance use disorder, or posttraumatic stress disorder (PTSD), as well as any cases with bipolar disorder or episodic symptoms of elated mood. A series of secondary analyses used somewhat different operational definitions, relying on combinations of items extracted from diagnostic interviews to characterize the irritable mood and aggression as being more chronic or episodic (Brotman et al., 2006; Leibenluft, Cohen, Gorrindo, Brook, & Pine, 2006; Stringaris, Cohen, Pine, & Leibenluft, 2009). In parallel, a new KSADS module established more precise interview stems and probes to follow the SMD definition, and this module identified a cohort of youth who participated in several National Institute of Mental Health (NIMH) neurocognitive and imaging studies (Rich et al., 2010, 2011), as well as a lithium trial (Dickstein et al., 2009). The more specific definition of SMD identified a group of patients who appeared distinct from youth with PBD in terms of affective response, functional imaging, and family history. The group with SMD also did not fare significantly better on lithium than on placebo in the one clinical trial. The secondary analyses of the longitudinal data sets using the chronic aggression definition found high rates of depression, but not elevated rates of bipolar disorder (although the sensitivity of these studies to hypomania and bipolar II may have been low; two studies were outliers in terms of bipolar disorder rates at baseline, and all relied only on self-report at the long-term follow-up, which is known to be less sensitive to hypomania; Youngstrom, Findling, et al., 2005).

DSM-5 has added the diagnosis of DMDD based on the available research with various operationalizations of SMD, combined with concerns about the high rate of clinical diagnosis and pharmacological treatment of PBD. The proposed definition of DMDD was changed several times through the DSM-5 development process, morphing from SMD to "temper dysregulation disorder" and then to DMDD; it was also moved from the disruptive behavior disorders group to the mood disorders group, where it ultimately was placed at the beginning of the depressive disorders section (i.e., not in the DSM-5 section on bipolar and related disorders). The DMDD definition in DSM-5 departs from the original formulations of SMD in several important respects, such as having fewer exclusionary criteria and fewer required symptoms. Many experts were concerned about including DMDD as a new diagnosis for clinical use, in the absence of any data about prevalence, longitudinal course, treatment response, or delinea-

tion from other disorders such as oppositional defiant disorder (ODD), based on the actual criteria recommended in DSM-5 (Axelson, Birmaher, Findling, et al., 2011). The field trial examining the reliability of the DSM-5 criteria in clinical practice found a kappa of .25 (ranging from .06 to .49 across three sites; Regier et al., 2013), indicating that it will be difficult to use the criteria to reliably distinguish DMDD from other mood and behavioral problems in clinical practice. For now, it is reasonable to infer that certain youths with severe irritability and mood dysregulation do not meet criteria for a bipolar spectrum disorder; however, more research is needed quickly to establish whether DMDD is distinct from other externalizing behavior problems, as well as to chart an appropriate course of treatment (Axelson, Birmaher, Findling, et al., 2011; Towbin et al., 2013). Clinicians working with DMDD should refer to this volume's chapter on conduct disorder (CD) and ODD (Kimonis, Frick, & McMahon, Chapter 3) to get a sense of the developmental factors likely to be at work.

Dimensional Models

The authors of DSM-5 originally intended to shift to more dimensional approaches for describing bipolar disorders and other forms of psychopathology (Kraemer, 2007). In the end, the DSM-5 criteria conserved the categorical definitions of bipolar disorders from DSM-IV, suggesting the addition of a severity scale to describe quantitative degrees of difference. The Research Domain Criteria (RDoC) initiative of the NIMH also emphasizes dimensional models (Insel et al., 2010). Behavior checklists, rating scales, and interviews evaluating the severity of mood presentations provide a natural way of quantifying the features of bipolar disorders. Taxometric analyses of both depressive and manic symptoms find strong support for a dimensional aspect of presentation, and latent class models tend to find graded classes of greater severity (Haslam, Holland, & Kuppens, 2012; Prisciandaro & Roberts, 2009, 2011; Tijssen et al., 2010).

Using dimensional measures avoids false dichotomies between major and minor depression versus other distress, or between manic and hypomanic presentations versus milder fluctuations in mood and energy. Dimensional and factor mixture approaches have major statistical advantages in terms of greater psychometric precision and improved statistical power, as well as the virtue of better approximating the structure of the underlying latent variables (Nylund, Asparouhov, & Muthén, 2007). However, dimensional models need to accommodate some complex aspects of mood disorders, including the possibility that past mood levels might moderate the treatment response or prognosis of present symptoms (Youngstrom, 2010). Dimensional models also need to be adjusted to reflect the issues of duration and recurrence (Klein, 2008); these are not especially well handled by categorical methods at present, either. The point is that simply measuring current mood symptoms will not be adequate for a complete understanding of bipolar disorders.

ASSOCIATED CHARACTERISTICS

Negative Affect

PBD has associated characteristics that are consistent with what would be expected from the literature for bipolar disorder in adults. PBD is linked with high levels of negative affect and high emotional reactivity (Walsh, Royal, Brown, Barrantes-Vidal, & Kwapil, 2012), consistent with the tripartite model of depression and anxiety (Joiner & Lonigan, 2000; Watson et al., 1995), as well as findings that bipolar disorder in adults correlates with higher trait emotional instability and neuroticism (Barnett et al., 2011). The high negative affect could be a mechanism for the elevated stress and anxious symptoms frequently observed in conjunction with bipolar disorder. The degree of state negative affect obviously varies with the phase of bipolar illness, being highest during depression and mixed states, average during euthymia, and lowest during euphoric hypomania or mania. The high trait levels, and the adult finding of high trait neuroticism even between episodes, indicate a propensity to experience negative affect that could contribute to the greater rates of mixed presentations and the preponderance of depressed moods over the long term for many cases. The levels of trait negative affect and neuroticism are also significantly higher in females after adolescence, reinforcing the propensity toward mixed and depressive presentations for them (Cyranowski, Frank, Young, & Shear, 2000; Duax et al., 2007).

Behavioral Activation and Inhibition

Gray (Gray & McNaughton, 1996) identified three different motivational systems that appear evident in mammals and have distinct neural circuitry: the behavioral activation system (BAS), the behavioral inhibition system (BIS), and the fight–flight system.

These systems overlap with other conceptualizations of motivational systems underlying mood disorders. For example, the BAS appears highly similar to Depue's behavioral facilitation system (Depue & Lenzenweger, 2006). These models have proven fairly robust, with measurement extending from self-report (Carver & White, 1994) through performance measures in humans and animals, down to metabolic correlates, distinct brain circuits, and potential genetic correlates (Sanislow et al., 2010). The BAS and BIS in particular have been examined in conjunction with multiple disorders, including attention-deficit/hyperactivity disorder (ADHD), ODD, CD, and anxiety disorders, as well as mood disorders in youth (Alloy et al., 2008; Fowles, 1994; Quay, 1993).

The BAS is loosely similar to a "gas pedal," providing drive towards cues of reward and impelling approach behaviors (including fun seeking, but also appetitive aggression). Mania and hypomania are correlated with high scores on measures of BAS, consistent with high levels of energy and goal-oriented behavior, as well as positive affect and also irritability and anger. Depression is associated with low BAS scores, aligning with predictions from the tripartite model of depression and anxiety. High self-reported BAS scores predict later emotional instability and progression to bipolar disorder (Alloy et al., 2012). One theoretical model of bipolar disorder is the "BAS dysregulation hypothesis," which posits that bipolar disorder involves a tendency toward extremely high or low levels of BAS activity (Alloy et al., 2008), perhaps resulting from greater sensitivity to cues of reward or loss (Urosevic et al., 2010). Sensitivity to cues of threat would implicate the BIS, and also would be consistent with high levels of anxious symptoms associated with bipolar disorder. These models have been most extensively researched in emerging adulthood and later, but recent supporting data extend into childhood and adolescence (Gruber et al., 2013).

Neurocognitive Performance

PBD is associated with multiple deficits in cognitive performance, including poorer processing speed, executive functioning, and working memory compared to those of healthy controls, along with more focal deficits in emotion processing (Joseph, Frazier, Youngstrom, & Soares, 2008; Walshaw, Alloy, & Sabb, 2010). Most of these deficits are intermediate in degree between those associated with schizophrenia and intact functioning in healthy controls (DelBello & Kowatch, 2003; Frazier et al., 2012); again, this is consistent with findings in the adult literature (Phillips & Vieta, 2007). Many of these cognitive dysfunctions are not specific to bipolar disorder. In addition to overlapping with the patterns of functioning in schizophrenia, there also is much similarity to the patterns observed with ADHD (Walshaw et al., 2010). However, studies large enough to compare subgroups with PBD + ADHD versus PBD alone or ADHD alone find that the comorbid group has the most severe deficits; this suggests that each disorder may be linked with additive, incremental impairment (Henin et al., 2007). One of the largest decrements in performance that may be relatively specific to PBD is decreased planning, measured by tasks such as the Tower of London (Walshaw et al., 2010). Overall cognitive ability tends to be in the normal range for youth with PBD, although the lower average levels of planning, set shifting, processing speed, and verbal working memory can contribute to academic difficulties. Unfortunately, the medications used to treat PBD also can affect cognitive performance, and medication status and diagnosis are often confounded in the extant studies, making it difficult to disentangle what may be state effects on test performance from trait markers of illness or collateral effects of medication (Henin et al., 2007; Joseph et al., 2008).

In regard to structural abnormalities, PBD has been associated with more white matter hyperintensities (Adler et al., 2006), disrupted circuitry in diffusion tensor imaging (Gonenc, Frazier, Crowley, & Moore, 2010), increased ventricular volume, reduced anterior cingulate volume (Singh et al., 2012), and decreases in amygdalar volume (Blumberg et al., 2005). The pattern of findings again is highly consistent with the literature on morphological changes in adult bipolar disorder, with the exception of amygdalar volume (Schneider, DelBello, McNamara, Strakowski, & Adler, 2012). Several studies find decreased amygdalar volumes in youth with PBD, whereas adult studies find increased volumes. Some speculate that the amygdalar findings may reflect effects of medication exposure (Chang et al., 2005), but this remains to be confirmed by prospective analyses (Pavuluri, West, Hill, Jindal, & Sweeney, 2009).

Multiple studies find that emotional processing is disrupted in PBD, as indicated by increased amygdalar activation in response to emotional stimuli, and also dysregulated activity in the dorsolateral prefrontal cortex and anterior cingulate—regions implicated in emotion regulation (Garrett et al., 2012; Pavuluri, Passarotti, Harral, & Sweeney, 2009). A few studies

have compared youth with PBD to youth with ADHD or other disorders in imaging studies, and have found some degree of specificity in patterns of activation (Lopez-Larson et al., 2009, 2010). Again, it is challenging to separate state and trait effects of bipolar disorder from comorbidity and from medication effects. However, the accumulated evidence offers strong support for the validity of research diagnoses of bipolar disorder as having measurable associations with neurocognitive performance, changes in brain functioning, and changes in neural circuits and morphology.

Sleep Disruption

Decreased need for sleep is a symptom of mania presenting in more than two-thirds of youth with PBD (Kowatch et al., 2005). People with bipolar disorder are more likely to show "evening" versus "early morning" diurnal activity patterns, and may be prone to circadian reversal, in which they stay up all night and sleep during the day (Hasler et al., 2006; Salvatore et al., 2008). Recent studies using parent checklists (Meyers & Youngstrom, 2008) and actimetry (Mullin, Harvey, & Hinshaw, 2011) find evidence of poor sleep quality and disrupted sleep architecture in youth with PBD, replicating and extending findings in the adult literature (Harvey, 2008; Talbot, Hairston, Eidelman, Gruber, & Harvey, 2009). Sleep disturbance also has been associated with ADHD and depression. What may distinguish PBD is the combination of having less sleep but maintaining a high energy level during periods of hypomania or mania (Geller et al., 1998; Luby, Tandon, & Nicol, 2007; Youngstrom et al., 2008).

Disrupted Relationships with Family and Peers

PBD is also associated with substantial disruption of interpersonal relationships, both with peers and within the family of origin. Mirroring the findings with bipolar disorder in adults, families and youth with PBD show high levels of expressed negative emotion, poor communication skills, and high levels of conflict (Algorta et al., 2011; Coville, Miklowitz, Taylor, & Low, 2008; Du Rocher Schudlich, Youngstrom, Calabrese, & Findling, 2008; Geller, Tillman, Craney, & Bolhofner, 2004). Recent studies with youth find substantial decreases in quality of life in terms of family and peer relationships (Freeman et al., 2009; Siegel, La Greca, Freeman, & Youngstrom, 2014). Interestingly, PBD appears to be associated with more performance deficits than knowledge deficits about social skills (T. R. Goldstein, Miklowitz, & Mullen, 2006). There are many plausible reasons why PBD would be linked with poor interpersonal relationships, several of which we discuss below in the section on developmental pathways.

Increased Risk-Taking Behavior

PBD is correlated with high impulsivity, particularly during periods of high energy. Hypomanic and manic symptoms are associated with increased risky sexual behavior, greater thrill seeking, and higher rates of alcohol and substance use in adolescents (Geller, 1999; Stewart et al., 2012). It is unclear whether the strong correlation between bipolar disorder and substance use is driven more by "self-medication" or by sensation seeking, but the association begins in adolescence and remains pernicious. The higher rates of substance misuse contribute to the rule-breaking behavior associated with hypomania and mania, in turn adding to the risk of arrest and incarceration (Pliszka et al., 2000).

COMMON COMORBIDITIES

Several different conditions consistently show high odds of comorbidity with PBD. Some of the common comorbidities probably expose methodological issues with current diagnostic practices, but others may provide a window into the underlying processes shared by what are putatively distinct conditions. Comorbidity can result from several different circumstances. One is coincidence: An individual could have the misfortune to experience two different illnesses at the same time, even though they are uncorrelated in the general population. However, if the two disorders show a statistically significant association with each other, there are still many other possibilities about the nature of the association.

Caron and Rutter (1991) delineated several different mechanisms for what they termed "artifactual" and "true" comorbidity, and others have generally retained and elaborated on these two categories (Angold, Costello, & Erkanli, 1999; Lilienfeld, Waldman, & Israel, 1994; Youngstrom, Arnold, & Frazier, 2010). Artifactual comorbidity can result from (1) referral biases, or changes in detection of conditions due to biases in surveillance and assessment; (2) categorizing dimensions, or creating artificial distinctions where there are not qualitative differences in nature; (3) overlapping

diagnostic criteria, in which the same symptom may count toward multiple different diagnoses; (4) artificially subtyping what actually may be a homogeneous entity, including instances where a developmental process shows heterotypic continuity; and (5) one apparent disorder's actually being a part of the other. Mechanisms for true comorbidity can include (1) shared risk factors; (2) comorbidity as distinguishing a subtype that shows different trajectories or treatment response; (3) one disorder's moderating the risk for the other; or (4) one disorder's being a developmental precursor or prodrome for the other. We depart from Caron and Rutter (1991) in treating the "early manifestation" model of comorbidity as a form of true instead of artifactual comorbidity, consistent with developmental approaches to psychopathology. The framework is a helpful way of organizing a large volume of information, and we use it as the scaffolding for reviewing the evidence about comorbidity between PBD and depression, psychosis, ADHD, disruptive behavior disorders (ODD and CD), anxiety, pervasive developmental disorders/autism spectrum disorder, and substance use. As the literature on comorbidity in PBD comes more into focus, it is evident that the patterns of comorbidity are congruent between PBD and adult bipolar disorder, once again reinforcing the validity of the pediatric construct (Robins & Guze, 1970).

Depression

It might seem strange to conceptualize depression as "comorbid" with bipolar disorder. However, hypomania and mania may have risk factors and etiological mechanisms that only partially overlap with those for depression (Johnson, 2005; McGuffin et al., 2003). Surveillance and referral biases complicate our understanding of the relationship between depression and hypomania or mania. In clinical settings where people self-refer for treatment, depression is more likely to motivate treatment seeking. For that reason, it often would be clinically more useful to consider hypomania or mania as a potential comorbidity for depression (consistent with the DSM-5 use of "with mixed features" as a specifier). Failure to assess systematically for a history of hypomania, combined with limitations of self-report as a source of information about hypomanic symptoms, may add to the difficulty in recognizing bipolar II and cyclothymic disorder. However, when referrals for youth are initiated by parents or teachers, they usually are focused on externalizing behavior problems or irritability in particular, and it could be clinically useful to remember that depression is often an associated feature worth assessing directly. There is heuristic value in studying depression and mania separately, and then examining potential interaction effects when they manifest sequentially or co-occur.

Of the different artifactual contributions to comorbidity, categorizing dimensions is clearly relevant, as is artificial subdivision. Taxometric investigations of the latent structure of both depression and mania find strong evidence of a major dimensional component to both, with more inconsistent evidence of categorical subtypes (Haslam et al., 2012; Prisciandaro & Roberts, 2011).

Of the true mechanisms for comorbidity, the mechanism of shared risk factors is relevant, given the substantial overlap in genetic, biological, and environmental and social risk factors for unipolar depression and bipolar disorder (Tsuchiya, Byrne, & Mortensen, 2003). Less is known about whether the risk factors for hypomania or mania might be distinct from depression, but if they are, then the mechanism of comorbidity as subtype gains credence. Bipolar II disorder is an example: The co-occurrence of hypomania differentiates a subtype of depression that might follow a different natural course and show a distinct pattern of treatment response (Berk & Dodd, 2005). The developmental sequencing model of comorbidity has some support, as depressive episodes often come to clinical attention prior to hypomania or mania, and some longitudinal data identify depression first (Duffy, Alda, Hajek, Sherry, & Grof, 2010; Reichart et al., 2004). However, low insight and poor sensitivity of many assessment methods to hypomania contribute to potential referral bias and surveillance issues. The idea that either hypomania/mania or depression may moderate the risk of the other mood polarity has been studied least to date. Earlier-onset depression may be associated with later development of bipolar disorder (Shankman et al., 2009), but the evidence that hypomania and mania may increase the risk of depression is generally somewhat stronger than vice versa (Youngstrom & Van Meter, in press).

Psychosis

Psychotic symptoms can occur during manic or depressive episodes. Due to the rarity of early-onset schizophrenia (see Kuniyoshi & McClellan, Chapter 12, this volume), mood disorders are actually the more common

causes of psychotic features in children and adolescents. Estimates of the rates of psychosis in PBD range from 0 to 88% (Kowatch et al., 2005). Two major factors influencing the rate are the definition of PBD used, and the definition of psychotic features. If a sample with PBD includes cases with cyclothymic disorder or bipolar II, then there should not be psychotic features, based on the definition of hypomania as excluding psychotic features (APA, 2013). Bipolar II disorder could have psychotic features during the depressed phase of illness, but psychosis during what would otherwise be a hypomanic episode would upgrade the severity to mania, and thus change the diagnosis to bipolar I disorder. Conversely, if the delusions and hallucinations persist outside the context of a mood episode, then the person might meet criteria for schizoaffective disorder, bipolar type. Schizoaffective disorder can be conceptualized as a comorbidity of schizophrenia and mood disorder, or as the most severe expression along a continuum of psychotic illness (Malhi, Green, Fagiolini, Peselow, & Kumari, 2008).

Even within bipolar I disorder, differences in definitions of psychosis have large effects on estimates. Whereas many operational definitions concentrate on hallucinations and delusions, Geller and colleagues also include severe episodes of grandiosity or elated mood, arguing that in extreme instances the severity of the symptom involves a loss of contact with reality (Geller, Zimerman, Williams, DelBello, Bolhofner et al., 2002). In an earlier study, this group also counted a symptom as present if either the parent *or* child endorsed it, applying a disjunctive algorithm without reinterviewing the dyad or filtering with clinical judgment (Tillman et al., 2008). Disjunctive approaches maximize assessment sensitivity and yield the highest rates of endorsement, but risk lowering assessment specificity compared to using conjunctive (e.g., requiring both parent and youth to report the symptom for it to be counted) or compensatory (e.g., using the average of the informants' perspectives) strategies (Youngstrom, Findling, & Calabrese, 2003). The combination of multiple alternative definitions of psychosis and a disjunctive strategy may help explain why the rate of psychosis reported by Geller's group (76% of cases with bipolar I; Tillman et al., 2008) is an outlier compared to rates found by the rest of the field, which are typically closer to 20–35% among cases with bipolar I (Kowatch et al., 2005). Other studies have used a definition focused on delusions or hallucinations, and have often used clinical judgment or compensatory methods rather than a disjunctive approach to reconciling differences in informant perspectives (Birmaher et al., 2006; Findling et al., 2001).

Assessing psychotic features may be even more challenging in youth than in adults because normally developing children may have unusual beliefs, magical thinking, and nonscientific explanations for events, due to their stage of cognitive development (Piaget, 1954). Similarly, adolescents often believe that they are exceptional and less vulnerable to mistakes, accidents, and illness, due to their developmentally normative sense of their "personal fable" (Alberts, Elkind, & Ginsberg, 2006). Ideally, any assessment findings suggestive of psychosis should be followed by evaluation by a clinician who has extensive experience with both normal development and current cultural references, as well as exposure to instances of frank psychosis (Arnold et al., 2004). Given the complexity of evaluating psychosis and the high rates of potentially false-positive findings, it would be prudent to treat apparent psychotic features as a "yellow flag" triggering further inquiry, rather than using them as sufficient evidence to change a diagnosis from hypomania (cyclothymic or bipolar II) to mania (bipolar I) (Youngstrom, Jenkins, Jensen-Doss, & Youngstrom, 2012).

Epidemiological data suggest that referral and surveillance biases may contribute to the apparent overlap between psychotic features and mood disorders, inasmuch as there appear to be people who experience hallucinations or delusional beliefs without co-occurring mood or cognitive impairment, and who do not seek treatment (Bentall, 2003). Overlapping diagnostic criteria and categorizing of dimensions are unlikely to add to the apparent comorbidity of mood disorders and psychosis. However, the subdivision artifact might be relevant in the case of schizoaffective disorder, which does not appear to have firm boundaries with either bipolar disorder or schizophrenia, challenging Kraepelin's distinction between the two (Craddock & Owen, 2010).

Attention-Deficit/Hyperactivity Disorder

ADHD is probably the most common comorbidity recognized among youth diagnosed with PBD. The rates vary markedly across samples, ranging from 15 to 98% among cases diagnosed with PBD (Kowatch et al., 2005). However, rates of PBD appear much lower in most samples ascertained for ADHD (Galanter et al., 2003; Galanter & Leibenluft, 2008; cf. Wozniak et al., 1995), and epidemiological and clinical epidemiologi-

cal samples tend to find modest associations between ADHD and PBD (e.g., Merikangas et al., 2012; cf. Arnold et al., 2012). Among adults, ADHD is proving to be a common comorbidity (Nierenberg et al., 2005; Wilens et al., 2003); again, however, the rate of co-occurrence appears most influenced by the base rate of each condition in the clinical setting, rather than reflecting strong shared etiology (Galanter & Leibenluft, 2008; Youngstrom, Arnold, & Frazier, 2010). Referral and surveillance issues are definitely distorting the degree of co-occurrence observed in samples with different ascertainment patterns.

There are several symptoms that could occur in either ADHD or mania, consistent with the artifactual mechanism of overlapping criteria (Klein, Pine, & Klein, 1998). In diagnostic parlance, these symptoms are nonspecific to either condition. High energy or activity level, poor concentration and high distractibility, and talkativeness or pressured speech all can be ambiguous, being commonplace in both ADHD and mania (Klein et al., 1998). Similarly, irritability is frequent among youth with ADHD, as well as being a diagnostic symptom of mania (Geller et al., 1998). However, the high rates of comorbidity persist even when researchers exclude these potentially "shared" symptoms, and comorbid cases show greater average impairment and other features consistent with having additive effects from multiple diagnoses (Biederman et al., 2013; Faraone, Biederman, Mennin, Wozniak, & Spencer, 1997). Geller and colleagues' (1998) emphasis on elated mood and grandiosity as cardinal features of pediatric mania was a method to try to improve the specificity of the PBD diagnosis. Elated mood that is clinically unusual in terms of frequency, intensity, or duration does appear to be highly specific to PBD across multiple samples and interviews (Freeman et al., 2011; Geller, Zimerman, Williams, DelBello, Frazier, et al., 2002). Grandiosity appears moderately specific, although it can seem similar to the narcissism and entitlement often shown by youth with CD or antisocial tendencies (Youngstrom et al., 2008). Hypersexuality is another symptom that is more specific to a smaller subset of diagnostic entities; it is most strongly associated with sexual abuse, mania, or exposure to sexually graphic material. All of the symptoms that appear more specific to mania tend to be ones that are less intrinsically impairing or immediately distressing to others (Freeman et al., 2011), with the result that they are often not prominent in descriptions of the presenting problem (cf. Yeh & Weisz, 2001).

A different (but potentially complementary) strategy from concentrating on diagnostically specific symptoms for differentiating between ADHD and manic symptoms would be to probe whether the symptoms have followed a more episodic course, displaying clear changes from typical functioning for the youth and coinciding with other notable shifts in energy and mood. The emphasis on episodicity helps distinguish mood disorders—characterized by changes in functioning—from other more chronic conditions. Otherwise nonspecific symptoms may offer more contrast when viewed through the lens of chronic versus episodic presentations. Difficulty concentrating, for example, is more suggestive of mania when it is not typical of the person, but is manifested at the same time as the person shows decreased need for sleep or episodic changes in mood or energy. More persistent impairment in concentration would be consistent with ADHD, or perhaps with some other chronic syndrome, such as an anxiety disorder (Youngstrom, Arnold, & Frazier, 2010).

Other potential artifactual explanations appear unlikely to explain much of the covariation between ADHD and PBD. The greater prevalence of ADHD (Merikangas et al., 2010) makes it impossible that it is a subtype of bipolar disorder, and there are enough instances of PBD without ADHD that PBD is certainly not an ADHD subtype. The two conditions are not simple gradations along the same continuum, either: Mania is qualitatively different from severe attention problems, involving other mood features not commonly implicated in ADHD (Youngstrom, Arnold, & Frazier, 2010).

When bipolar and ADHD criteria are both met in the same case, it is likely to reflect a true comorbidity—particularly when the diagnostician has been careful to establish that the hyperactivity, impulsivity, and inattention persist outside the context of the mood episodes, or that there is pronounced worsening during a mood episode. ADHD and PBD share many risk factors, including overlapping genetic risks (Asherson & Gurling, 2012; Faraone, Glatt, & Tsuang, 2003; Mick & Faraone, 2009), pre- and perinatal risks (Tsuchiya et al., 2003), and possibly disrupted neurocognitive systems. ADHD and PBD show similarities in neurocognitive impairments, such as those in executive function and working memory (Walshaw et al., 2010) and several similar brain regions are implicated in morphological and functional imaging studies. Given that both ADHD and bipolar disorder are polygenic conditions, and that the environmental risk factors for both are nonspecific

and often overlap, one model of comorbidity is that of shared "building blocks" or shared mechanisms. It also is possible that specific constellations of symptoms might implicate a single underlying mechanism, and that this fundamental process might be disrupted in multiple disorders. Sleep, appetite, and energy are connected aspects of a circadian process with integrated hormonal and neurological regulatory systems, and disruption of this sleep–wake process may contribute to a broad variety of disorders. The model of shared "building blocks" offers a deeper conceptual explanation for comorbidity (Youngstrom, Arnold, & Frazier, 2010). In the case of ADHD and PBD, comorbidity is likely to reflect shared foundational components, but also to be the product of superficial methodological issues. If the assessment process does not discern whether the symptoms are episodic, or whether they co-occur primarily in conjunction with other mood and energy symptoms, then the rate of comorbidity will be spuriously increased. Conversely, failure to apply the hierarchical exclusionary criteria that DSM recommends (in which comorbid disorders are not diagnosed if the symptoms only occur in the context of a mood episode) also would inflate the apparent rate of comorbidity with ADHD, as a function of the nonspecific symptoms' getting counted toward both diagnoses.

Some believe that comorbid ADHD and PBD represents a distinct subtype (Biederman et al., 2013; Faraone et al., 1997). Data are inconclusive as to whether the co-occurrence represents simple additive effects, or whether it has firm diagnostic boundaries or a distinct treatment response or developmental trajectory. Similarly, there are not yet enough data to establish with confidence whether ADHD and PBD each moderate the risk for development of the other. Some have speculated that ADHD might be a prodrome for bipolar disorder (Tillman & Geller, 2006), but most longitudinal follow-ups of large ADHD cohorts have found that the vast majority of cases do not meet criteria for mania at long-term follow-up (Galanter & Leibenluft, 2008; Klein et al., 2012). It is likely that the ADHD studies may have missed some of the bipolar spectrum cases due to issues of forgetting, lack of insight, exclusive reliance on self-report, and other factors that contribute to poor sensitivity to hypomania (Angst et al., 2010); however, the Tillman and colleagues (2008) sample also may have had challenges in differentiating episodic from chronic symptoms, due to the structure of the interview—which could have blurred the boundary between the conditions (Galanter, Hundt, Goyal, Le, & Fisher, 2012). Overall, the data are consistent with a model of shared "building blocks," in which some of the risk factors and systems are implicated for both conditions, but other features may be distinct (Youngstrom et al., 2010).

Disruptive Behavior Disorders

Other disorders frequently comorbid with PBD are what were called the disruptive behavior disorders until the publication of DSM-5. ODD and CD are the two disruptive behavior diagnoses that have accumulated the most research, although clinicians have frequently used disruptive behavior disorder NOS and adjustment disorder with disturbance of conduct as billing diagnoses as well (Youngstrom, Youngstrom, & Starr, 2005). Less work has been done on genetic, physiological, or neurocognitive correlates of disruptive behavior disorders (although there has been investigation into antisocial personality disorder and psychopathy in adults; Blair, 2006).

Referral and surveillance biases probably play a large role in the pattern of comorbidity between disruptive behavior and mood disorders. Because externalizing behaviors frequently top the list of concerns motivating caregivers to seek services for children or adolescents (Garland, Lewczyk-Boxmeyer, Gabayan, & Hawley, 2004; Yeh & Weisz, 2001), youth with mood plus disruptive behavior issues are more likely to come to clinical attention than youth without apparent externalizing comorbidity. Consistent with the referral bias hypothesis, there appear to be adolescents and adults with histories of recurrent hypomania or even mania who do not have comorbid disruptive behavior disorders, and who do not seek services and may function well (APA, 2000; Cicero, Epler, & Sher, 2009; Merikangas et al., 2012).

Imposing artificial categories on underlying dimensions contributes to artificial comorbidity here as well, as shown by the research into the "bipolar profile" and externalizing scores on the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001). On the CBCL, groups of youth with PBD tend to score significantly higher on the Aggressive Behavior, Delinquent/Rule Breaking, Attention Problems, and Depressed/Anxious scales, along with the Externalizing Problems broad band, than comparison groups of healthy controls, youth with ADHD, and other youth receiving outpatient services (Mick, Biederman, Pandina, & Faraone, 2003). However, youth meeting criteria for ADHD, or

for ODD, CD, and other disruptive behavior disorders, tend to show moderate or clinical elevations on the same scales, as do youth with depression and comorbid ADHD (Diler et al., 2009; Meyer et al., 2009; Youngstrom et al., 2004; Youngstrom, Meyers, et al., 2005). Although bipolar diagnoses are associated with statistically significantly higher averages, there is a great deal of overlap in the distributions. Some clinicians and researchers may be focusing on extreme elevations of externalizing behaviors in assigning a bipolar diagnosis. Most clinically referred youth with PBD will have high parent-reported levels of externalizing problems, resulting in high diagnostic sensitivity of these scales (Youngstrom, Meyers, Youngstrom, Calabrese, & Findling, 2006); however, externalizing problems are linked with a wide variety of other socioemotional problems as well, leading to the low diagnostic specificity. To put this another way, externalizing problems are a developmental psychopathology outcome that can result from myriad different processes. Externalizing is the paragon of "equifinality" in developmental psychopathology, in which multiple developmental paths lead to similar behavior.

The scales and symptoms that show greater diagnostic specificity for PBD, discriminating it from disruptive behavior disorders and ADHD, indicate that PBD is not reducible to extreme externalizing (Youngstrom et al., 2006). Similarly, the differences in specific symptoms—such as decreased need for sleep, elated mood, and racing thoughts—show that PBD is not a type or subtype of disruptive behavior disorder. PBD possesses distinct features and follows a different longitudinal trajectory from that of ODD (Burke, Loeber, & Birmaher, 2002) or CD/psychopathy (Lynam et al., 2009). On the other hand, the critique of an artificial subdivision may apply to the new diagnosis of DMDD: The symptoms of DMDD overlap completely with ODD, and the difference in presentation may largely be a matter of severity and not qualitative differences (Axelson et al., 2012; Axelson, Birmaher, Findling, et al., 2011; Copeland, Angold, Costello, & Egger, 2013).

Equifinality creates much potential for confusion when clinicians are trying to assess bipolar versus disruptive behavior disorders. Irritability and aggression can be the product of dysregulated mood or of coercive interpersonal processes. Grandiosity can be a symptom of mania (Kowatch et al., 2005) or a reflection of a sense of entitlement/narcissism that is common among those with antisocial tendencies (Frick, Cornell, Barry, Bodin, & Dane, 2003). Disentangling these trajectories requires precision and careful thought about the context of the behavior. These issues shape differences in wording of checklists (Youngstrom, Meyers, et al., 2005) and variations in clinical training (Dubicka et al., 2008; Mackin, Targum, Kalali, Rom, & Young, 2006) that alter endorsement rates, inflating differences in diagnostic opinion and comorbidity rates (Kowatch et al., 2005).

Bipolar and disruptive behavior disorders may involve some true comorbidity. The conditions certainly share risk factors: Families with bipolar proband youths show elevated rates of antisocial behavior (Rende et al., 2007; Wozniak et al., 2010), and offspring of parents with bipolar disorder show higher rates of externalizing disorders, albeit the risk of mood disorder tends to be even higher (Birmaher et al., 2009, 2010; Hodgins et al., 2002). Mood disorder is a risk factor for externalizing behavior, too. Irritability is a more common presentation of depression than sad mood in young males (Poznanski & Mokros, 1994), and mood dysregulation directly perturbs interpersonal relationships, leading to peer rejection and contributing to increased familial conflict (Algorta et al., 2011; Du Rocher Schudlich et al., 2008). All of these in turn contribute to increased risk of aggressive and antisocial behavior (Dishion & Patterson, 2006). Intriguingly, the path could run in the opposite direction as well: Youth with high levels of externalizing behavior show elevated risk of depression at long-term follow-up (Brotman et al., 2006; Shankman et al., 2009; Stringaris et al., 2009). Our hypothesis is that if comorbidity here reflects a subtype, it is primarily a subtype defined by interpersonal processes, and less of a genetic nature.

Anxiety and Related Disorders

Youth with PBD tend to show high rates of generalized anxiety disorder, social phobia, separation anxiety disorder, panic disorder, and PTSD (Birmaher et al., 2002; Wagner, 2006). These are broadly consistent with results from adult clinical (McIntyre et al., 2006) and epidemiological studies, which also find high comorbidity among bipolar disorders, generalized anxiety disorder, and panic disorder (Merikangas & Pato, 2009). Estimates of the rates of comorbid anxiety within samples with PBD show extreme variation (Kowatch et al., 2005), again suggesting that methodological issues are at least partially confounding the findings. DSM-5 indicates that persons with bipolar disorders may have considerable stress and anxiety during hypo-

manic, manic, or depressive episodes, as well as during persistent depressive (dysthymia) or cyclothymic disorders. DSM-5 also stipulates a hierarchical approach to diagnosis, whereby a comorbid anxiety disorder should only be assigned if the anxious symptoms clearly persist outside the context of the mood episode (APA, 2013). DSM-5 has added the "with anxious distress" specifier to the mood disorder sections to provide a mechanism for coding the anxious features without adding otherwise unnecessary comorbid diagnoses. Differences in the extent to which clinicians and researchers enforce this hierarchical exclusion will lead to large swings in the apparent rates of comorbidity.

Referral and surveillance biases are likely to play a large role yet again. If adolescents are referring themselves for treatment, they are more likely to seek services when depressed and anxious; and if clinicians focus first on the anxious symptoms, then they are likely to diagnose an anxiety disorder and then "call off the search" for other diagnoses (the so-called "search-satisficing" cognitive heuristic; Garb, 1998). High anxiety levels are also associated with greater impairment in youth with PBD (Harpold et al., 2005; Sala et al., 2010; Wozniak, Biederman, Monuteaux, Richards, & Faraone, 2002), and so the anxious youth may be more likely to seek services (as observed in adult samples; Hamalainen, Isometsa, Sihvo, Pirkola, & Kiviruusu, 2008; Jacobi et al., 2004) and thus to be overrepresented in clinical samples (Berkson, 1946).

The mechanisms of categorizing dimensions and artificial subdivisions are also likely to be at work here. The tripartite model of depression and anxiety describes how the comorbidity between anxiety and depression reflects patterns on three underlying dimensions: negative affect, positive affect, and physiological hyperarousal (Clark & Watson, 1991). The negative affect dimension is shared across depression and anxiety disorders, representing a nonspecific component (Blumberg & Izard, 1986). Negative affect also is implicated in the depressed and mixed presentations of bipolar illness (Youngstrom & Izard, 2008). In the tripartite model, the diagnostically specific feature of unipolar depression is a low level of positive affect, corresponding to anhedonia (Chorpita, 2002). Bipolar depression also would have low positive affect, but hypomania and mania would be associated with elevations of positive affect. According to the tripartite model, the diagnostically specific dimension for anxiety disorders would be physiological hyperarousal (Clark & Watson, 1991). Subsequent work has found that physiological hyperarousal shows the strongest association with panic, with some phobias and obsessive–compulsive disorder showing greater associations with disgust instead (Davey, Forster, & Mayhew, 1993). However, dysregulation of positive affect and negative affect are clearly involved in both unipolar depression and bipolar disorders, and categorization of dimensions could contribute to the appearance of comorbidity with anxiety disorders (also entailing high negative affect). The possibility that bipolar disorders constitute a subset of anxiety disorders (or vice versa) appears unlikely, though: Each set of disorders involves additional dimensions of symptoms that are not central to the other. Bipolar disorders do not include physiological hyperarousal, disgust, or fear as core parts of their clinical presentation, for example (Youngstrom & Izard, 2008); and anxiety disorders do not include increased energy, decreased need for sleep, elevated positive affect, hypersexuality, or grandiosity as core features.

A developmental sequencing model of anxiety and bipolar comorbidity aligns with various sources of data. Studies of offspring of parents with bipolar disorders find high rates of anxiety disorders in the younger offspring (Birmaher et al., 2009; Hodgins et al., 2002). Longitudinal studies frequently find that generalized anxiety disorder precedes later major depressive episodes (Mineka, Watson, & Clark, 1998); and retrospective studies of bipolar disorders in adults find that many report meeting criteria for anxiety disorders prior to the onset of a full-blown mood episode (Kessler, Berglund, Demler, Jin, & Walters, 2005; Perlis et al., 2004).

Anxiety and bipolar disorders definitely share risk factors. Family studies find elevated rates of anxiety disorders in relatives of probands with bipolar disorders. Elevated trait negative affect, or trait neuroticism or emotional instability in a personality framework, are associated with both anxiety and bipolar disorders. The overlapping risk factors also extend to a more granular level. For example, the short allele of the serotonin transporter gene has been identified as a diathesis for both anxiety and mood disorders (Caspi, Hariri, Holmes, Uher, & Moffitt, 2010). Some have suggested that high trait negative affect, neuroticism, and generalized anxiety disorder may be different labels for the same presentation, and that this trait is a moderator that increases risk for developing other disorders. It is well established that anxiety disorders increase the risk of depression, and also the depressed phase of bipolar illness (Sala et al., 2012). Whether anxiety increases risk of mania is much less clear. The possibility that

comorbid anxiety denotes a distinct subtype of bipolar disorder is intriguing and as yet untested in the pediatric literature. Indirect evidence suggesting that it is possible comes from the adult literature on affective subtypes. Anxious temperament may be distinct from a hyperthymic temperament, with the latter showing a propensity for hypomania or mania but lower rates of anxiety disorders (Karam et al., 2010).

Pervasive Developmental Disorders/Autism Spectrum Disorder

A small number of studies report moderately elevated rates of comorbidity between pervasive developmental disorders (now redefined in DSM-5 as autism spectrum disorder or ASD) and PBD (DeLong & Nohria, 1994; Wozniak et al., 1997). These co-occurrences are unlikely to result from categorizing dimensions, or from artificial subdivisions being imposed on these dimensions. PBD is not associated with the same pronounced deficits in cognitive functioning as many cases of ASD are, or with major developmental delays in most aspects of social and emotional functioning. There is no evidence of a shared developmental sequence, where pervasive developmental disorders/ASD might be prodromes for mood disorders or vice versa. The most likely mechanism for apparent comorbidity is that pervasive developmental disorders/ASD are frequently associated with poor frustration tolerance, deficits in emotion recognition, and poor emotion regulation, all of which increase the risk of irritability and aggressive behavior. If clinicians give great weight to irritable mood and agitation in assigning a diagnosis of "mania," and they do not systematically assess other criteria, then it is likely that the resulting diagnosis of "PBD" will be a phenocopy that has superficially similar symptoms that result from a different etiology (Youngstrom, Arnold, & Frazier, 2010). However, there is some evidence that a shared etiological pathway could contribute to episodic mood dysregulation and other mood symptoms, in combination with cognitive disability and other symptoms of pervasive developmental disorder/ASD. The genetic microdeletion creating velocardiofacial syndrome (VCFS) results in mood dysregulation as well as cardiac problems, facial dysmorphia and cleft palate, and poorer cognitive functioning, for example (Papolos & Papolos, 2002), along with high rates of schizophrenia, ADHD, and autism (Gothelf et al., 2004; Kates et al., 2007; Murphy, 2002). Although the base rate of VCFS makes it unlikely to directly explain more than 5% of cases of PBD, it provides a potential example of how genetic or neurocognitive processes might contribute to multiple disruptions that create apparent comorbidity in subsets of cases (Youngstrom, Arnold, & Frazier, 2010). The prenatal teratogens and perinatal environmental risk factors that affect cognitive development are also shared across both disorders (Hack et al., 2002).

Obesity and Metabolic Syndrome

Cross-sectional studies find significant comorbidity between overweight status or obesity and PBD (Merikangas, Mendola, Pastor, Reuben, & Cleary, 2012). The relationship is complicated by the fact that many of the medications used to treat PBD are linked with rapid and profound weight gain (Correll, 2008b). However, studies of youth find that overweight status often precedes mood instability. Both obesity and bipolar disorder are correlated with the inflammatory cytokine response (Correll, 2008a; Correll, Frederickson, Kane, & Manu, 2008; Goldstein, Kemp, Soczynska, & McIntyre, 2009; Goldstein, Liu, Schaffer, Sala, & Blanco, 2013). Evidence is growing for a potential direct causal association, where greater abdominal fat leads to chronic inflammatory response that irritates blood vessels in the brain as well as the heart.

Obesity may have indirect effects on risk for mood disorders as well. Obesity decreases the age of onset for puberty (Biro, Khoury, & Morrison, 2006), which is as low as 8 years old for girls in the United States (Lee, Guo, & Kulin, 2001). The secular trend for earlier puberty means that the hormone cascade associated with puberty is happening at a younger age, out of synchrony with brain development. For example, the myelination of the prefrontal cortical regions happens in the late teens and is completed by the early 20s for most people (Shaw et al., 2008)—coinciding with the onset of menarche in societies with a non-Western diet (Parent et al., 2003). The earlier onset of puberty also brings with it changes in peer interactions that now may occur before the familial and community supports are ready (Ge, Conger, & Elder, 1996). In addition, obesity itself creates psychosocial stress, increasing the chances of teasing, peer rejection, and low self-esteem (Vander Wal & Mitchell, 2011). Unfortunately, the relationship is likely to be bidirectional, as some youth use eating as a coping mechanism, and social isolation may be associated with decreased participation in sports and with lower physical activity in general (Vander Wal & Mitchell, 2011).

Substance Misuse

PBD is associated with an elevated risk of substance misuse (Goldstein et al., 2008; Goldstein & Bukstein, 2010; Wilens et al., 2004, 2009). The association is not due to many of the usual potential artifacts: The diagnostic criteria for bipolar and substance use disorders are clearly distinct (APA, 2013). Substance use is not reducible to a dimension of mood dysregulation, and it is unlikely that all substance use is a subtype of bipolar disorder. The fact that many youth meet criteria for PBD before having any exposure to alcohol or drugs belies the possibility that PBD is a subtype of substance use disorder (Birmaher et al., 2006; Geller & Luby, 1997). Behavioral genetic studies also find that addictions have a heritable component that is independent of most other major psychiatric illnesses (Kendler, Davis, & Kessler, 1997).

Some of the other artifactual mechanisms identified by Caron and Rutter (1991) may still apply, however. Referral and surveillance probably distort the rates of comorbidity observed in different settings. Substance misuse may either worsen or mask underlying mood problems, increasing the rate of treatment seeking in some and delaying it for others (Jane-Llopis & Matytsina, 2006). There is evidence of gender differences in both substance use and treatment seeking in adults with mood disorders: Women are more likely to seek help, and men are more likely to drink and use other drugs (Potts, Burnam, & Wells, 1991). This is likely to contribute to the sex difference in rates of bipolar II disorder identified at clinics, as there is no evidence of sex linkage for bipolar II at a genetic level, yet it is recognized more often among women in clinical samples (Berk & Dodd, 2005). Furthermore, those with substance use issues but no associated mood problems are unlikely to present to a mental health setting, often encountering the substance treatment or forensic system instead. The extent to which these mechanisms play out in childhood and adolescence remains an important area for study.

The possibility that co-occurring substance use denotes a bipolar disorder subtype is plausible, but as yet there is no evidence of a clear boundary delineating it from other bipolar disorders. It also is unclear whether comorbid substance use should change the prescription for treatment: No studies have systematically examined comorbid substance use disorder as a moderator of outcome in adult—let alone pediatric—bipolar studies yet (Singh & Zarate, 2006), and a Cochrane Collaborative Systematic Review recommends initiating treatment of mood disorders whether or not adjunct treatment for substance use issues is available (Cleary, Hunt, Matheson, Siegfried, & Walter, 2008).

The most likely pattern of association is that PBD involves high levels of impulsivity and emotion dysregulation, which in turn increase the risk of experimentation with substance use. Problems with peer relations also may increase the chances of association with deviant peers, further raising the risk of substance misuse. There is the possibility of third-variable confounders as well: The high rate of ADHD among youth with PBD might be sufficient to explain much of the correlation between PBD and substance misuse, for example (Wilens et al., 2011). Even so, the large literature on mood disorders and substance use in adults indicates that mood disturbance contributes incrementally to increased substance use. Although the degree to which substance use increases mood disorder risk is less well established, reciprocal effects are likely once substance use starts, with misuse and addiction contributing to subsequent mood dysregulation and relational conflict (Wray, Simons, Dvorak, & Gaher, 2012).

DEVELOPMENTAL COURSE AND PROGNOSIS

There have been substantial advances in our understanding of the developmental course of PBD. As Figure 6.1 shows, there have been nine major prospective longitudinal studies to date, which have followed cases for periods from 2 to 22 years. Because of bipolar disorder's episodic nature, it is intrinsically hard to show developmental continuity in it. Cases with symptoms of hypomania or mania at early assessments consistently show high rates of depression, hypomania, and mania at later follow-ups. Eight-year follow-up data from Geller, Tillman, Bolhofner, and Zimerman (2008) found that more than 40% of youth showed a new episode of mania within the first 2 years after turning 18—a high incidence of "adult" mania early in follow-up.

Few epidemiological studies include prospective follow-up of PBD. This is an important gap in the literature because clinical samples may be focusing on more severe cases, and thus potentially biasing our estimates of recurrence risk or comorbidity. A secondary analysis of two large epidemiological samples in adults found evidence suggesting a possible group of cases that had manic episodes at the initial evaluation and no later episodes of depression or mania (Cicero et al.,

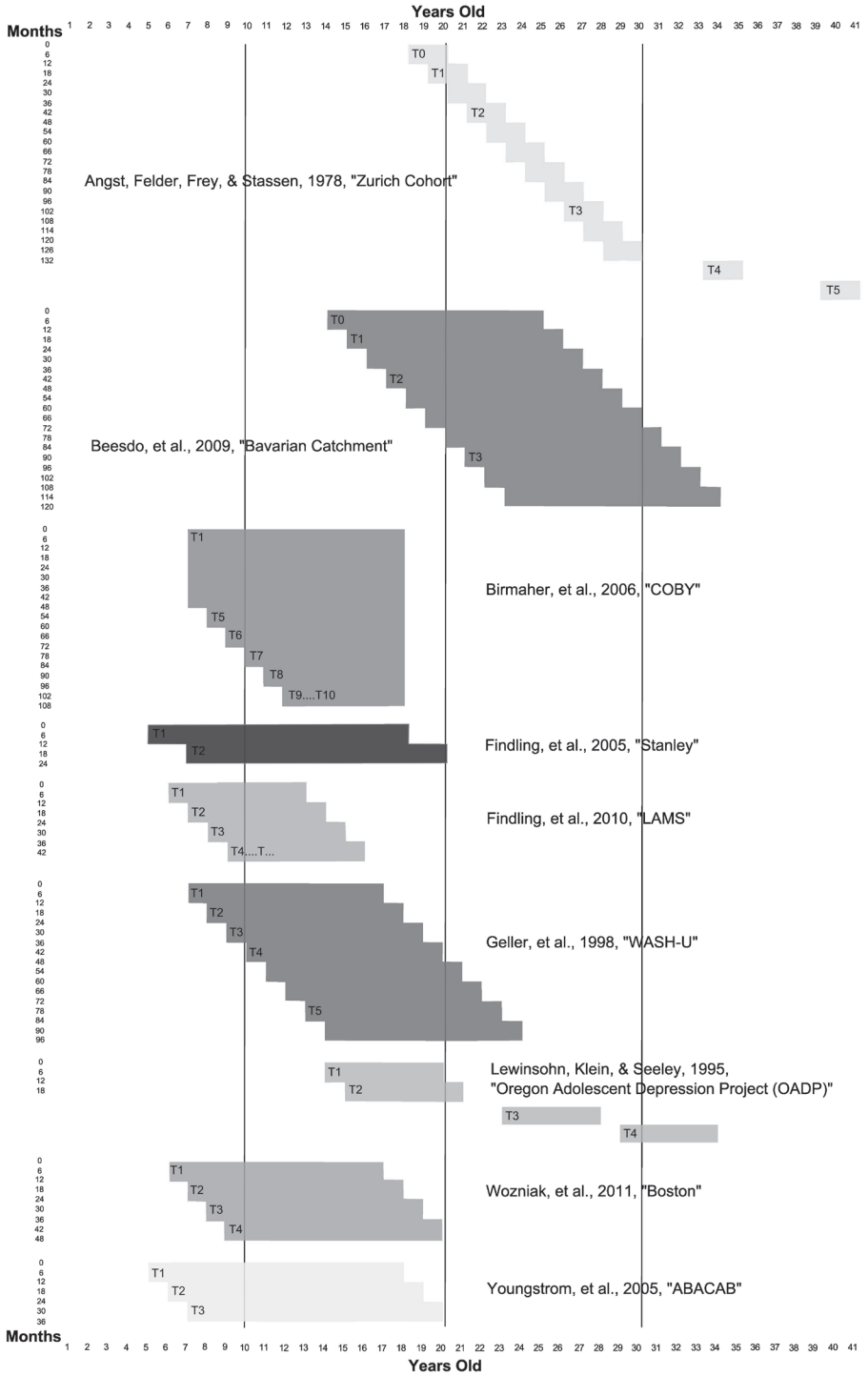

FIGURE 6.1. Prospective longitudinal studies of pediatric bipolar disorder.

2009). The pattern suggests the possibility of a "developmentally limited" form of bipolar disorder, in which affected persons might show mood lability or affective episodes as adolescents, and then grow out of the propensity to have severe mood issues as they develop better inhibitory mechanisms and emotion regulation (Cicero et al., 2009).

The "developmentally limited form" hypothesis inverts the traditional view that bipolar disorder is primarily an adult-onset illness. However, it is consistent with our growing understanding of neurocognitive development, including the tendency for affective regulation centers in the brain to myelinate fully in late adolescence and young adulthood (Gogtay et al., 2007; Shaw et al., 2008). The developmentally limited form hypothesis also is consistent with observations that hypomania and mania more commonly occur in younger age groups, whereas bipolar disorder in middle and later adulthood is primarily associated with depression, at least in clinical samples (Judd et al., 2002; Kraepelin, 1921). Epidemiological studies in adolescents identify some cases with histories of only mania or hypomania (Merikangas et al., 2012; Van Meter, Moreira, & Youngstrom, 2011). Prospective follow-up will be crucial to determine whether a significant portion of these cases show a benign prognosis. If so, then these developmentally limited cases often will not seek services, making them underrepresented in clinical samples. This in turn exaggerates our estimates of recurrence risk and poor prognosis, as we fail to gather data about those with a positive course and outcome. If there is a group that shows a good course, then this fundamentally alters our description of bipolar disorder from an incurable, recurrent, and potentially progressive illness to something in which we may be able to promote recovery by providing scaffolding to prevent severe problems until the emotion regulation systems reach full maturity. Strong analogies to other "developmental delay" models of pathology could offer innovative approaches to treatment.

Developmental Course in Clinical Samples

More data about developmental course are available from clinical samples (Axelson, Birmaher, Strober, et al., 2011; Geller et al., 2008). As noted above, naturalistic clinical samples may be biased toward exaggerating the risk of morbidity: Those who recover will not stay in treatment. This is an important caveat to consider when we review trajectories based on clinical samples. The child clinical data paint a picture similar to adult clinical data, suggesting high rates of relapse, continued service utilization, and possibly even a deteriorating course. It is unclear whether the recurrence and progression reflect changes in the environment, changes in the brain, or both. Neurological changes have gotten much attention in the form of "kindling" hypotheses, which posit that each mood episode changes synaptic connectivity in ways that increase susceptibility to future mood episodes, decrease the dependence on environmental triggers, and increase the resistance to treatment (Post & Leverich, 2006; Post & Weiss, 1997). An alternative hypothesis is that the neuropathy seen later in bipolar disorder may be the product of medication instead of the illness: It may be either the result of "self-medication" with street drugs and alcohol (which can induce cell death), or the effect of prescribed pharmacological agents on the developing nervous system (Schneider et al., 2012; cf. Hafeman, Chang, Garrett, Sanders, & Phillips, 2012). The pharmacotoxicity hypothesis argues that higher rates of substance use, including prescribed medications, may either trigger a bipolar diathesis or else cause neurological changes that create the potential for later mood dysregulation (Reichart & Nolen, 2004). Although some retrospective correlational data show an association between substance use (Post et al., 2010) or increased medication prescription (DelBello, Soutullo, et al., 2001) and earlier age of onset, other studies fail to find the same pattern (Pagano et al., 2008). There also are animal models demonstrating neuroprotective effects of lithium and other compounds (Manji, Moore, & Chen, 2000), leading some experts to argue for exploring prophylactic pharmacotherapy as a way of delaying or preventing the onset of full-blown mood episodes (Findling et al., 2007; Miklowitz & Chang, 2008). Prospective studies will be crucial to clarify the degree of evidence supporting each of these competing hypotheses, some of which are diametrically opposed, and all of which involve high stakes. More data about the risks and benefits of medication and other interventions will help people make better-informed choices about their treatment.

Age Differences in Phenomenology

There has been much discussion about whether bipolar disorder presents differently in children than it does in adults. Some have argued that earlier onset of illness is associated with increased mood lability, carbohydrate

craving, or oversensitivity to sensory input (e.g., Papolos & Papolos, 2002); other groups do not find significant associations between these variables and bipolar diagnoses. However, many of these speculative associations or differences have not had much investigation using semistructured diagnostic interviews to establish the criterion diagnoses.

More data are available testing the extent to which the DSM symptoms of mania are evident in youth meeting DSM criteria for a bipolar diagnosis. All of the DSM symptoms appear to manifest themselves in pediatric cases of hypomania and mania frequently (see Kowatch et al., 2005, for a meta-analysis), with relatively few symptoms appearing to show age-related effects in rate or association with the underlying mania factor. Manic symptoms appear to show a consistent factor structure, with a single major factor underlying symptoms in youth from age 5 through adolescence and adulthood (Frazier et al., 2007). In contrast, symptoms of depression appear to shift from a single global factor in children to a two-factor structure in adolescence (Frazier et al., 2007). Reliability for assessment of mood symptoms via semistructured interviews remained consistently high across the age segments studied.

In research testing for age cohort effects on the core depression and mania symptoms—as opposed to global severity scores—on several of the most widely used interviews, multiple symptoms showed significant effects of age even after investigators controlled for diagnosis and comorbid ADHD (Demeter et al., 2013). Age uniquely accounted for 2–4% of the variance in manic symptoms of motor activity, aggression, irritability, and bizarre thought content, and 8% of the variance in racing thoughts. The first three are likely to reflect normative developmental improvements in inhibitory control, and the other two reflect the higher rate of psychotic features in adolescent versus prepubertal samples. Age cohort uniquely explained variance in even more symptoms of depression, again reflecting a variety of developmental influences in addition to rates of depression and ADHD. Importantly, there were no significant age × diagnosis interactions for any of the 41 symptom ratings, indicating that the change in each symptom attributable to the presence or absence of mood disorder is stable across age ranges. Instead, the "background noise" contributing to elevations in symptoms for other reasons is what appears to change more with age.

Studies looking at parent reports on rating scales find that hypersexuality is more likely to be endorsed for adolescents than for younger children, and that problems with spending money impulsively are also more likely to be endorsed for older youth (Freeman et al., 2011). Both of these are highly face-valid observations. Item response theory analyses also indicate that irritable mood is one of the "easiest" items, requiring low levels of mania before parents are likely to endorse it, whereas psychotic symptoms require extremely high levels of mania (Freeman et al., 2011; Henry, Pavuluri, Youngstrom, & Birmaher, 2008). When adolescent and caregiver reports were compared, the underlying level of mania needed to be higher for the adolescents to endorse irritable mood in themselves, but teens were more likely to endorse hyperactivity or increased energy at lower levels of mania (Freeman et al., 2011).

Synthesizing all of the available information, we may conclude that younger clinical samples have higher overall levels of manic symptoms—partly due to higher rates of hypomania and mania, but also partly due to some symptoms' being inflated by other developmental factors (including, but not limited to, high rates of comorbid ADHD). Conversely, adolescent samples have higher rates of depressive symptoms—largely due to higher rates of depressive episodes, but also due to developmental changes' influencing the level of specific symptoms. However, the core symptoms associated with depression and mania appear consistent across age ranges, and they can be measured with good reliability via checklists and interviews. In the parlance of differential item functioning, mood symptoms do not show evidence of slope or factor loading bias due to age effects, but many mood symptoms do show modest age effects on averages after adjustment for mood diagnoses ("intercept bias"; Zumbo, 2007). The data indicate that there are not big developmental changes in the presentation of bipolar disorder within mood episodes, although some symptoms show age effects due to other factors. The biggest age effect on presentation of bipolar disorder is a shift in the propensity to experience episodes of mania versus depression.

EPIDEMIOLOGY

Prevalence/Incidence

Until recently, few epidemiological studies of children and adolescents systematically assessed symptoms of hypomania or mania. A meta-analysis found only 12 studies with usable data about rates of PBD, after re-

view of more than 1,500 titles and abstracts (Van Meter et al., 2011). However, more studies are adding mania modules to the diagnostic battery, and a consistent picture is emerging. The weighted average prevalence rate of bipolar spectrum disorder in youth averaged 1.8% across the 12 studies, which included 16,222 youth between the ages of 7 and 21 years ascertained during a period from 1985 to 2007. The rate of bipolar I disorder was 0.5%. The reporting of bipolar II, cyclothymic disorder, and BP-NOS was too patchy to allow estimation of separate rates. Intriguingly, the meta-analysis found no evidence of a secular trend for the rate of bipolar disorder to increase over the 22-year span covered by the included studies. The steady rate of bipolar spectrum illness in the community samples stands in sharp contrast to the marked rise in rates of clinical diagnoses over the same time period (Blader & Carlson, 2007; Moreno et al., 2007). Another unexpected finding was that the rates of bipolar spectrum disorder were equal in the United States versus the samples from other countries (Van Meter, Moreira, & Youngstrom, 2011). The data contradict the popular perception that PBD is isolated to the United States. Instead, the data fit the pattern of increased public awareness and clinical vigilance, consistent with what has been observed for ASD and other disorders (Joseph et al., 2009; Rutter, 2009). A more recent Canadian epidemiological sample corroborated the three major trends in the meta-analytic findings, with an overall rate of bipolar spectrum disorder of 2.1% among 15- to 18-year-olds (Kozloff et al., 2010).

It is difficult to disentangle meaningful signals about incidence versus prevalence in the current literature. Not all studies report incidence separately, and those that do use windows ranging from point prevalence to lifetime (Van Meter, Moreira, & Youngstrom, 2011). The heterogeneity in definitions of bipolar disorder and other design features swamp the differences attributable to shifts in index time period. However, across studies, several design features accounted for significant variance in the meta-analytic regressions: Studies including cyclothymic disorder or BP-NOS had significantly higher rates of bipolar spectrum disorder, and older participants had higher rates of bipolar disorder (Van Meter, Moreira, & Youngstrom, 2011). Rates of all bipolar spectrum disorders are higher in clinical settings than in the general community, and the rate of bipolar disorder tends to increase in more acute settings (see Figure 6.2).

Sex Differences

Studies in adults find no evidence of sex linkage for bipolar disorder, or evidence of differential prevalence rates, with the possible exception of bipolar II disorder's being more commonly diagnosed in women (Berk & Dodd, 2005). It is unclear whether the higher diagnosis rate among females is due to actual differences in incidence, or to patterns of treatment seeking or variations in diagnostic interviewing. Although there are plausible differences in psychosocial risk factors for depression, and possibly some hormonal mechanisms (Cyranowski et al., 2000), the poor sensitivity of unstructured clinical interviews to hypomania and the evidence that many people forget or discount past hypomania both contribute to misdiagnosis as unipolar depression.

Studies do find that men with bipolar disorder are more likely to experience mania, and that women are more likely to experience depressive and mixed episodes (Goodwin & Jamison, 2007). Pediatric data conform to this pattern, with younger males showing higher rates of mania, and adolescent females showing higher rates of depression; however, there are no overall significant sex differences in the rates of bipolar I disorder, cyclothymia, or BP-NOS (Axelson et al., 2006; Duax et al., 2007; Van Meter, Moreira, & Youngstrom, 2011). The cross-sectional data suggest a hypothesis that bipolar disorder may follow more of a recurrent depressive course in women, or that women show greater tendency toward an internalizing instead of an externalizing problem trajectory—but this remains to be confirmed with prospective data.

Socioeconomic Factors

Bipolar disorder shows a complicated relationship with socioeconomic status (SES). Older studies in adults originally found that bipolar disorder appeared more likely to occur among economically privileged groups, and schizophrenia more likely to occur among lower-SES groups (Goodwin & Jamison, 1990). More recent reviews conclude that much of this apparent association was due to diagnostic biases (Goodwin & Jamison, 2007), whereby ethnic minority and poorer individuals were more likely to be diagnosed with schizophrenia or antisocial behavior, and higher-SES individuals were more likely to be diagnosed with mood disorders (Strakowski et al., 1997). However, the data still do not find bipolar disorder overrepresented among the economi-

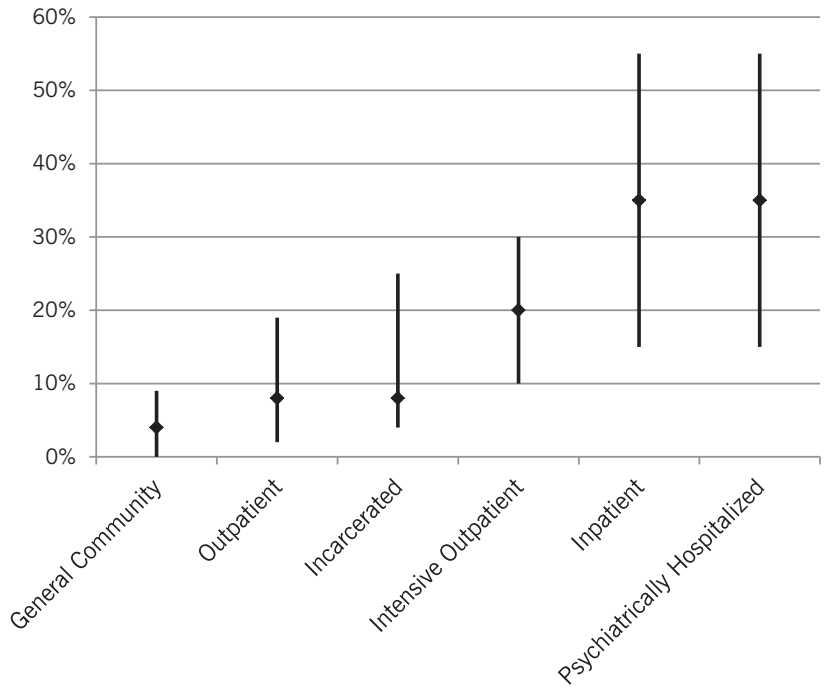

FIGURE 6.2. Median and range of prevalence rates for PBD in different clinical settings. Rates are based on prior reviews (Merikangas & Pato, 2009; Youngstrom, 2007; Youngstrom et al., 2009). Clinical settings are sorted into increasing intensity of services.

cally disadvantaged. It is possible that two opposing trends cancel each other out on average: Bipolar disorder appears linked to higher creativity and productivity, especially among family members of those affected (Johnson, Murray, et al., 2012). This would contribute to a positive association between bipolar disorder and SES. There is some evidence that professional or artistic success in a parent may be associated with mildly elevated risk of bipolar disorder in the offspring, consistent with this hypothesis (Tsuchiya, Agerbo, Byrne, & Mortensen, 2004). However, the devastating effects of the illness and the associated underemployment and unemployment often lead to poverty for the affected individual, and for families when a parent is affected (Lopez, Mathers, Ezzati, Jamison, & Murray, 2006).

The effects of SES are much more pronounced in clinical settings than in the epidemiological context. Consistent with findings in the adult literature, minority youth with bipolar disorder appear overrepresented in incarcerated samples when these are reassessed with semistructured interviews (Pliszka et al., 2000). African American and Hispanic youth with bipolar disorder are more likely to receive clinical diagnoses of CD or schizophrenia (DelBello, Lopez-Larson, Soutullo, & Strakowski, 2001). European American youth appear significantly more likely to receive medication than minority youths (dosReis et al., 2005), and more likely to receive prescriptions for mood stabilizers and atypical antipsychotics (Kowatch et al., 2013). These differences in diagnosis and service utilization may result from the interplay of cultural factors shaping beliefs about the causes of behavior and emotional problems, as well as differing views of what constitutes an "illness" for which medical treatment might be appropriate (Carpenter-Song, 2009; Yeh, Hough, McCabe, Lau, & Garland, 2004). Cultural differences in the description of the presenting problem may interact with a diagnostician's cognitive heuristics. When

an upper-SES family reports concerns about "mood swings," the initial clinical hypothesis may be a mood disorder. When a lower-SES family describes concerns about "behavior problems," then the starting hypothesis may be a conduct problem. Well-documented heuristics such as confirmation bias and search satisficing may then take over, generating the well-documented disparities in rates of clinical diagnoses (Garb, 1998; Jenkins, 2012).

Cultural Variations

Epidemiological studies in adults generally find similar rates of bipolar disorder across countries and within different racial and cultural groups within the United States. The Cross-National Collaborative Group study found lower rates of all psychiatric disorders in Asian countries, including lower rates of bipolar disorder (Merikangas, Jin, et al., 2011). This has been variously interpreted as being consistent with a greater focus on somatic aspects of illness than on emotional or cognitive components; as correlational evidence of the linkage between mood disorder and obesity or omega-3 fatty acids (in light of the substantially higher amount of seafood consumed in traditional Asian diets; Hibbeln, 1998); or as a consequence of heightened stigma towards mental illness (Hinshaw, 2006). Overall, the differences in rates are relatively modest.

Unipolar mania may be more common in some regions of the world, such as some Mediterranean regions (Yazici et al., 2002). There also are clear cultural differences in attitudes toward mental illness, treatment seeking, and specific behaviors. However, the few studies that have examined bias in specific measures or interviews, such as investigations of differential item functioning on measures of depression and mania, tend to find negligible evidence of bias. If people are left to seek services on their own, and then interviews concentrate on what people choose to volunteer and self-disclose, the effects of culture appear to be much larger than if people are systematically sampled and then complete a semistructured diagnostic interview or rating scale. When similar samples are asked the same questions, the differences in mood disorders appear much smaller than when culture guides the framing of the problems and the clinical encounters. Less is known about the extent to which these patterns prevail in child and adolescent age ranges, but the few investigations find consistent rates of bipolar disorder across African American, Hispanic, and European American youth when semistructured interviews are used in both epidemiological and clinical samples (Pendergast et al., 2014).

THEORETICAL FRAMEWORKS

Various theoretical frameworks have been proposed to explain bipolar disorder. Psychodynamic models posited mania as a defense mechanism against depression (Janowsky, Leff, & Epstein, 1970). Most researchers are not pursuing psychodynamic approaches actively at the moment, as biological models have become ascendant. Another notable omission is the lack of a behavioral/learning theory model of mania or bipolar disorder. Although behavioral interventions play a role in many psychotherapeutic packages, there has not been an overarching learning model or functional behavior analysis of mania. In general, bipolar treatment packages tend to comprise pragmatic assortments of techniques to reduce symptoms, and to improve coping and interpersonal functioning, rather than being organized around a major central theory.

At present, the majority of theoretical approaches toward bipolar disorder emphasize a strong biological component. Current theories avoid biological determinism, and articulate transactional models in which the biological and environmental factors interact and reciprocally influence each other to initiate and maintain dysregulated patterns of mood and energy; however, there is no model that fails to include some aspect of biology. Models emphasize different specific biological systems as core components of bipolar disorder. Some models emphasize the sleep system and circadian rhythm regulation (Harvey et al., 2006; Murray & Harvey, 2010). Others focus on basic motivational systems, such as Gray's BAS and BIS (Gray, 1986; Gray & McNaughton, 1996). Dysregulation of the BAS has been a particularly fruitful model, with accumulating evidence showing cross-sectional associations with mood symptoms in youth (Gruber et al., 2013), meaningful patterns of activation in imaging studies in adolescents and young adults (Nusslock et al., 2012; Urosevic et al., 2010), and longitudinal prediction of transition from at-risk to syndromal mood disorders (Alloy et al., 2008). Theoretical models also link BAS dysregulation with increased focus on cues of reward in bipolar disorder, and with increased emotional and behavioral activation following goal attainment, which may cascade into hypomanic or manic states (Johnson et al., 2000). Recent

work is also examining dysregulated positive affect as a core feature of bipolar disorder (Gruber, Eidelman, Johnson, Smith, & Harvey, 2011), as well as contributing to other mood and anxiety disorders (Carl, Soskin, Kerns, & Barlow, 2013).

Evolutionary psychology posits that depression may represent an adaptive mechanism to conserve resources and energy after an individual suffers a loss or rejection (Gilbert, Allan, & Trent, 1995). Emotion theorists have speculated that mania may represent a striving after goals that exploits initial opportunities or successes and attempts to amplify them, including greater interpersonal assertiveness and increased social dominance (Plutchik, 1980; Youngstrom & Izard, 2008). Depression may coincide with social rejection and loss of interpersonal influence (Gilbert & Allan, 1998). The emotional dimension of dominance may have a strong positive association with mood, with increased dominance coinciding with grandiosity and inflated self-esteem, as well as aggression toward challenges; in this view, decreases in dominance would coincide with depression (Demaree, Everhart, Youngstrom, & Harrison, 2005; Johnson, Leedom, & Muhtadie, 2012; Youngstrom & Izard, 2008). The emotion models extend prior work on the tripartite model of depression and anxiety (Clark & Watson, 1991), elaborating a greater role for positive affect in mania and mixed mood states. They also offer an organizational structure for integrating the RDoC with bipolar disorder, incorporating social dominance as well as the major domains of positive and negative affectivity (Sanislow et al., 2010). The BAS, sleep disruption (Mullin et al., 2011), and emotion models are each beginning to be investigated in PBD, with results that are so far consistent with expectations based on findings in the adult literature.

POSSIBLE DEVELOPMENTAL PATHWAYS

Bipolar disorder follows a developmental course. Even cases in which the first mood episode seems to appear from nowhere—an abrupt change from a previously high level of functioning—will have roots in biology and environmental factors that may be gleaned from family history or other sources. Cases with sharply defined episodes and good functioning between episodes also follow a developmental course. Mood episodes alter interpersonal relationships, often irreversibly; they may also lead to new biological set points and changes in neurocognitive functioning.

Our understanding of developmental pathways is similar to a partially completed jigsaw puzzle: There are several sets of variables that interlock, and we have assembled several groups of pieces, but we do not have the comprehensive picture solved. For example, neurological "kindling" has been advocated as a developmental model, in which each mood episode changes synaptic connectivity so that less environmental pressure is required to trigger subsequent episodes. The kindling model is consistent with evidence of progression, high rates of relapse in clinical samples, and decreased association between life events and triggering of subsequent episodes (Post, 2007). However, the kindling model does not yet integrate individual differences in temperament as risk or protective factors; nor does it comprehensively integrate models of normative psychosocial development or interpersonal interactions (Goodwin & Jamison, 2007).

Sleep dysregulation is another example of a cluster of related pieces. Only about 60% of youth meeting DSM criteria for any bipolar disorder show clear evidence of decreased need for sleep (Kowatch et al., 2005); for this subset, however, sleep disturbance is clearly linked with mood functioning. Genes related to circadian regulation are associated with bipolar disorder, and we also are learning about connections between sleep and metabolic functioning, which may exacerbate mood issues (Harvey, 2009). Sleep is linked to appetite regulation and weight gain, fitting cohesively with the patterns of symptoms seen in seasonal affective disorder and in atypical depression, which may be more common in bipolar depression in adults (Angst, Gamma, & Lewinsohn, 2002; Perugi, Fornaro, & Akiskal, 2011). Many of the brain regions implicated in sleep regulation also are regions of interest in bipolar disorder imaging studies (Harvey et al., 2006). Although many of the pieces are fitting together, we do not yet have a comprehensively elaborated model that connects the sleep system with other aspects of development.

A third cluster of pieces involves the relationship of psychosocial stressors, mood lability, stress generation, and substance use. Stress triggers mood, but mood lability and exaggerated emotional responses also tax interpersonal relationships and may lead to more rejection and stressful events (Rudolph et al., 2000). Mood and stress can thus create positive feedback loops. These loops appear to contribute to risk for substance misuse via multiple mechanisms. The "self-medication" hypothesis is a popular model clinically, suggesting that substance use may be a form of mood

regulation. Research support for this is moderate at present (Wray et al., 2012). A second developmental pathway for substance use would be via peer rejection's leading to association with more socially marginal or delinquent peers, who may provide increased opportunity for experimentation with substances. As reviewed in the section on comorbidity, shared third variables, such as impulsivity and poor executive function, add to the apparent correlation between mood and substance use.

A fourth cluster of pieces is accreting around motivation and interpersonal functioning. The BAS hypothesis (Alloy et al., 2008) and the social dominance model (Johnson, Leedom, & Muhtadie, 2012) both focus on how individuals prone to bipolar disorder may focus on cues of reward, or try to exert themselves socially, with successes feeding into a hypomanic spiral, and rejections or failures leading to intense emotional reactions and depression. The sensitivity to cues of rejection has also been noted in the context of atypical depression (APA, 2000).

As Table 6.2 shows, when we superimpose research on bipolar disorder with the epochs of typical development, we find that risk factors and correlates are present from conception through pregnancy and early infancy into adolescence and young adulthood, and that they continue to have reciprocal influences into late life. Juxtaposing the research with a developmental timeline reveals that bipolar disorder is not limited to a particular age range, defying the conventional separation of mental health research and services into "pediatric" and "adult" tracks. The table shows how the roots of what was previously been considered an "adult" illness stretch back before birth and into the prenatal environment. Comprehensive integration of a developmental psychopathology model will generate new and productive lines of inquiry with regard to bipolar disorder. Some possibilities include investigating the temperamental antecedents and moderators of risk for developing mood disorder in early childhood, or examining the role of androgens during the transition to adolescence and young adulthood. There are correlational data linking testosterone to social dominance (Bernhardt, 1997; Rowe, Maughan, Worthman, Costello, & Angold, 2004) and to mania (Ozcan & Banoglu, 2003; Pope, Kouri, & Hudson, 2000), raising the question of how much the higher androgen levels contribute to the greater rate of manic episodes in young males than in females. More work on the extent to which mania contributes to risk-taking behavior in adolescence, and triggers developmental "snares" such as pregnancy, traffic accidents, or other accidental injury, also looks promising (Stewart et al., 2012). Serious application of a developmental psychopathology framework will yield rapid progress filling in the gaps left by modern psychiatry's historic emphasis on biological models, adult manifestations, and tertiary intervention with acute illness.

RISK AND PROTECTIVE FACTORS

There are numerous nonspecific risk factors that produce small to moderate increases in the risk of developing bipolar disorder. These factors include genes of risk (which also are genes of interest for other disorders), poor maternal health during pregnancy, poor nutrition or substance use during pregnancy, stressful early environment, exposure to traumatic events, parental mood disorder, obesity, early onset of puberty, and early-onset depression (particularly with acute onset or psychotic features, disrupted sleep patterns, and adolescent substance use) (Goodwin & Jamison, 2007). There are correlations with peer rejection (Freeman et al., 2009; Siegel et al., 2014) and academic failure (Henin et al., 2007), which could represent risk factors, sequelae, or both. There are significant but weak associations with season of birth, leading to speculation about viral exposure or other mechanisms (Torrey & Miller, 2001). Low fish consumption is another factor that has prompted much interest. Omega-3 fatty acids are important in neural development, and higher rates of fish consumption during pregnancy are associated with lower rates of toddler and childhood aggression (Hibbeln et al., 2007). Later fish consumption correlates with lower rates of mood disorder and suicide at a global epidemiological level (Hibbeln, Ferguson, & Blasbalg, 2006). Effects appear modest at the level of current clinical trials, but the literature is changing rapidly (Freeman et al., 2006).

Family history of bipolar disorder appears to be the main exception to the general trend of nonspecific factors that contribute small to medium increases in risk (Tsuchiya et al., 2003). It is a robust predictor of pathology in general, but also shows further increases in the risk of developing bipolarity in particular. Reviews and meta-analyses conclude that there is at least a fivefold increase in risk of bipolar disorder when a first-degree

relative has bipolar disorder (Hodgins et al., 2002). These may be underestimates, as they are based on studies of offspring of parents with bipolar disorder, and the offspring had not been followed through the peak age of risk for onset of bipolar disorder. Conversely, the denominator of these risk estimates is derived from the rate of bipolar disorder in the general community; as epidemiological estimates rise, the size of the denominator increases, and the risk ratio or change in odds should decrease. One of the few studies looking at pedigrees with multiple family members affected found much larger estimates of risk (Gottesman, Laursen, Bertelsen, & Mortensen, 2010). The study was based on a Danish registry and hospitalization records. Thus the definition of bipolar disorder focused on severe cases and a relatively conservative definition, both of which may increase the strength of the signal.

Less is known about protective factors. Again, those that appear promising tend to be nonspecific. Greater cognitive ability in a youth or parent appears to be protective, possibly through compensation for difficulties and also through better navigation of health care systems (Gottfredson, 1997). Warmth and consistency in parenting, and better family communications, are likely to be protective, based on circumstantial evidence from longitudinal studies (Geller et al., 2008) and treatment studies where these are targets of intervention (Fristad, Verducci, Walters, & Young, 2009; Miklowitz, 2004). Healthy diet and regular exercise are also likely to be protective, based on the emerging evidence supporting the role of metabolic and inflammatory dysregulation in mood disorder. The "orchid" hypothesis is an interesting possibility, too: According to this model, the diathesis for mood sensitivity, coupled with a supportive environment, results in more positive outcomes—connoted by the delicate beauty of the orchid—rather than just the absence of pathology (Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2011). Thus research should investigate interactions in addition to testing main effects of risk and protective factors.

ETIOLOGIES

The field has made tremendous progress developing etiological models for bipolar disorder, yet a complete explanation remains tantalizingly beyond reach. Part of the challenge is that different models are focusing on different levels of analysis, and initiatives such as the NIH RDoC are seeking to foster synthesis across these different levels of genetic risk, cellular processes, neurophysiological systems, interpersonal interactions, and so forth (Cuthbert, 2005). A second issue, though, is that the DSM definitions of mood disorders are likely to capture heterogeneous groups with distinct etiologies, as experts now recognize for other polygenic conditions such as ADHD, ASD, and schizophrenia (see Youngstrom, Arnold, & Frazier, 2010, for discussion). Thus a single etiological model is probably an impossible goal, but making the connections between different models remains a worthwhile endeavor.

Genetics

Bipolar disorder has long been known as one of the most heritable major mental illnesses, with heritability estimates of 80% and higher; yet identification of specific genes has been frustratingly slow and prone to replication failures (Mick & Faraone, 2009; Smoller & Finn, 2003). Recent genome-wide association studies in adults find that many genes each contribute small amounts of risk for bipolar disorder (Wellcome Trust Case Control Consortium, 2007). Several genes that have accumulated some evidence tend to also be candidate genes for depression and anxiety (e.g., 5-HTTPLR), psychosis (COMT), ADHD (DRD4), or sleep disturbance (GRK3, CLOCK) (Mick & Faraone, 2009). The "case of the missing heritability," where studies of specific genes account for much less variance than implied by the heritability estimates, is not limited to bipolar disorder; it is endemic to psychiatric genetics (Mick & Faraone, 2009). Possible explanations include that the risk of bipolar disorder may be linked to differences in messenger RNA, not gene-coding DNA, or that large studies are mixing groups with distinct etiologies. Another issue is the poor reliability of clinical diagnoses of bipolar disorder: Most gene studies are relying on registries and clinical diagnoses to describe the phenotype. If the reliability of the phenotype definition hovers around a kappa of .1 to .4 (Regier et al., 2013; Rettew, Lynch, Achenbach, Dumenci, & Ivanova, 2009), then it will be difficult to detect effects. Research to date still strongly confirms that (1) genes play an etiological role in development of bipolar disorder; and (2) the genes identified in PBD are consistent with the genes of interest in adult samples, underscoring the validity of the pediatric diagnoses (Todd & Botteron, 2002).

TABLE 6.2. A Lifespan Developmental Framework for Bipolar Disorder

Epoch	Risk factors	Protective factors	Reciprocal influences	Sequelae	Age-typical issues
Conception	• Genetic factors • Poor maternal prenatal health	• Genetic factors • Good maternal prenatal health			
First trimester					
Second trimester	• Teratogens • Medication exposure	• Maternal diet and exercise			
Third trimester	• Very low birth weight • Prenatal complications • Microbiome	• Beneficial microbiome			
Infancy	• Diet deficient in micronutrients	• Secure attachment • Warm, responsive parenting • Good nutrition (vitamin D, omega-3 fatty acids)			
Toddlerhood	• Difficult temperament	• Warm, consistent parenting	• Mood disrupts parenting → increases conflict → more extreme mood . . .		
Preschool	• Transition into social settings outside home	• High-quality day care			
Elementary school	• Increased conflict in home			• Oppositionality	• High energy and impulsivity

Middle school	• Selecting more deviant peers • Puberty • More directly involved in conflicts	• Dominance and assertiveness may increase popularity (or provoke backlash)	• More conflicts with peers and family • Gender influencing peer relations	• Peer rejection	• Increased depressive symptoms • Risk of overweight
High school	• Sleep dysregulation • Weight gain as side effect of medication • Adolescent phase shift in circadian cycle • Increased androgen levels • Drug experimentation	• Positive social interactions • Academic attainment	• Overweight and poor sleep have positive feedback loop: Poor ghrelin and leptin levels → more eating, obesity → sleep apnea and poor sleep quality → disrupted ghrelin levels . . .	• Overweight + mood dysregulation + low self-esteem → eating disorder • Impulsivity → greater risk of addiction → precocious sexual activity	• Accumulated risk factors for suicidal ideation, behaviors
Early adulthood	• Possible developmental delay in emotion regulation centers (below) • Learned helplessness and hopelessness • Circadian rhythms	• Work: Entrains circadian rhythms (getting up, going to job), provides financial and social support • Normative myelination of emotion regulation circuits	• Greater independence = less structure • Diet (affecting mood and energy, influencing diet . . .)	• Potential downward drift: unemployment, teen pregnancy, other "snares"	
Middle adulthood	• Neurological "kindling" • Allostatic load: substance use, overweight, stress due to work and relational challenges	• Decreasing androgens	• Synaptic "kindling" • Neurological change due to substance use and trauma exposure	• Unmarried or divorced • Underemployed or unemployed	• More depression • Less mania and mixed mood features
Late life	• Cumulative nerve damage • Menopause	• Hormonal changes		• Premature death: heart disease, cancer, accident, suicide	• Accelerated memory loss • Depression • Increased suicide risk

Neurobiological Factors

The neurobiological factors involved in PBD overlap with the systems implicated in depression, schizophrenia, and ADHD. Neurotransmitters of interest include serotonin, dopamine, and (more recently) glutamate (Goodwin & Jamison, 2007). The atypical antipsychotics, which have large effect sizes for the reduction of acute mania, have dopaminergic mechanisms of action (Nandagopal, DelBello, & Kowatch, 2009). Dysregulation of the hypothalamic–pituitary–adrenocortical axis is linked to bipolar disorder, as it is to unipolar depression. There also is evidence for hormonal involvement, including probable androgen effects on mania (Ozcan & Banoglu, 2003), and other endocrinological processes in depression (Cyranowski et al., 2000).

Clinical observers and researchers have long considered bipolar disorder an affective disorder first and foremost, although it also involves disruptions in cognition, sleep, and energy. Consistent with the emphasis on emotional processes, the strongest evidence focuses on emotion regulation systems as being central to the development and progression of bipolar disorder (Strakowski et al., 2012). Specifically, multiple studies find that the amygdala's size and activation in response to emotional stimuli change in bipolar disorder (Chen, Suckling, Lennox, Ooi, & Bullmore, 2011). Two prefrontal cortical systems are responsible for modulating amygdalar activity: a ventrolateral prefrontal cortical system believed to process external emotional stimuli, such as affective facial expressions and cues of threat, and a ventromedial (orbitofrontal) cortical system believed to be responsible for monitoring internal feeling states. These two systems form feedback loops with the amygdala (Strakowski et al., 2012). Multiple studies now find evidence of decreased activity in the regulatory cortices, along with evidence of decreased connectivity between the amygdala and the emotion regulation regions (Blond, Fredericks, & Blumberg, 2012; Townsend & Altshuler, 2012). These neural tracts appear significantly disrupted in bipolar disorder, based on increased white matter hyperintensities in magnetic resonance imaging and higher fractional anisotropy in diffusion tensor imaging studies. A consensus model is emerging: In bipolar disorder, the amygdala appears to be more sensitive to emotional cues, and the cortical structures responsible for modulating fear and anger responses from amygdalar outputs are less connected and perhaps weaker. This creates a propensity for more extreme emotion responses, and for more dysregulation and shifting between mood states—leading to the mixed mood presentations and instability (Strakowski et al., 2012).

Changes in amygdala size and increases in tract disruption are correlated with length of illness, suggesting that successive episodes further damage and disrupt these affective circuits; however, this remains to be confirmed by prospective longitudinal imaging studies with strong designs (Blond et al., 2012; Townsend & Altshuler, 2012). There are fewer studies comparing persons with bipolar disorder to individuals with other conditions (such as ADHD or schizophrenia) instead of healthy controls, but the available evidence indicates that the disruptions of these two affect regulation systems are larger in bipolar disorder than in other conditions (Frazier et al., 2008; Whalley et al., 2012). It is not clear yet how much these differences represent diathesis versus results of illness, and some of the differences observed in adults with bipolar disorder may prove to be results of failure to follow normal adolescent development of these regions, rather than a deficit in preadolescent neurocognitive systems (Strakowski et al., 2012). Evidence suggests that these changes are less likely to be due to medication exposure than had been feared, as medication exposure tends to be associated with normalization of development and decreases in differences versus healthy controls (Hafeman et al., 2012). Overall, the available evidence reinforces the idea that bipolar disorder has a profound neurodevelopmental component.

Psychosocial Factors

Psychosocial factors also play an important role in bipolar disorder, although they have been less studied until recently. As mentioned above, increased conflict in the family and higher expressed negative emotion are tied to earlier age of onset, faster recurrence, and poorer response to treatment in pediatric samples (Geller et al., 2008; Keenan-Miller, Peris, Axelson, Kowatch, & Miklowitz, 2012) as well as adult samples (e.g., Hooley & Hiller, 2001). Although parental mood problems are difficult to disentangle from shared genetic effects between parent and child, such problems are associated with less parental monitoring, engagement, or control (Goodman & Gotlib, 1999). These are likely to exacerbate any underlying diathesis for mood disorder in the youth, although this remains to be demonstrated specifically in bipolar samples. Parental mood dysregulation is also likely to involve modeling of poor emotion

regulation and maladaptive metaemotion (Gottman, Katz, & Hooven, 1996), as well as contributing to higher amounts of stress within the family (Rudolph et al., 2000). Poor emotion regulation in the parent and child also increases the risk of abuse, and trauma and abuse are correlated with greater risk of developing syndromal bipolar disorder (Post & Leverich, 2006). There are hints that sexual abuse may particularly heighten the risk for general mood dysregulation in youth and for bipolar II in particular (Garno, Goldberg, Ramirez, & Ritzler, 2005), but this is partially confounded with the higher rate of sexual abuse among females, who also show higher rates of depression and bipolar II.

Familial Factors

Familial risk of bipolar disorder is well established, but it involves multiple different mechanisms. The genetic and interpersonal elements of familial risk were reviewed above. Familial risk involves other processes, too. One is diet. Choices about food (as well as family exercise patterns) play major roles in childhood obesity and shifts in pubertal onset, as well as influencing mood. There may also be important effects of micronutrients, such as vitamin D and omega-3 fatty acid, whose presence depends on family dietary patterns (Rucklidge & Kaplan, 2013). A more speculative but intriguing possibility is that the "microbiome," or differences in the microbes that live symbiotically in our bodies, may often cluster in families. Variations in the microbiome are showing large effects on obesity (Smith et al., 2013) and immune functioning (Maynard, Elson, Hatton, & Weaver, 2012), suggesting that the microbiome could be a candidate for explaining some of the heritability missing between the family-level and genetic-level estimates. The family is also where many of the environmental and cultural effects described next cluster.

Environmental/Cultural Factors

Culture is one of the most important determinants of diet, and thus it has indirect effects on risk of bipolar disorder through micronutrient consumption, risk of obesity, and the other processes described above. Culture also changes attitudes toward substance use, moderating the exposure of the youth to both opportunities to use substances and potential interpersonal conflict. Culture is associated with differences in attitudes toward women, as well as risk of abuse; in addition, it powerfully affects beliefs about the causes of emotional and behavioral problems, as well as attitudes toward disclosure and treatment seeking (Hinshaw, 2004). Stigma toward mental illness appears present across all cultures, but the degree of this stigma and how it affects behavior are culture-bound (Hinshaw, 2006). There also are mesosystem factors that shape the environment and impinge on the family, such as poverty and exposure to violence in neighborhoods; these also moderate risk of developing internalizing and externalizing problems (Rutter, 2000), and thus are likely to alter risk for bipolar disorder specifically.

More subtly, environmental factors influencing the development of bipolar disorder could include such factors as electricity and changes in ambient lighting. Artificial lighting has considerably changed sleep patterns, and television and the Internet further intrude on our sleep. These electronic influences may be contributing to secular trends in the rise of obesity, as well as to sleep-related impairments in executive function and emotion regulation, and thus plausibly to bipolar disorder (Harvey, 2009). These hypotheses have additional indirect support from clinical interventions that focus on reducing electronic stimulation and improving sleep hygiene (Fristad et al., 2009; Hlastala & Frank, 2006), as well as strong support from chronotherapy trials in adults (Goodwin & Jamison, 2007). Finally, social media on the Internet may create a combustible accelerant to any spark of mood dysregulation, given the way that impulsive statements and pictures can get broadcast widely and cannot be deleted.

CURRENT ISSUES

As the chapter to this point has made clear, there are numerous current issues pertaining to PBD. However, with the recent revision of the DSM nosology, three topics seem notably salient: (1) clarifying diagnostic boundaries with conditions that share features or underlying dimensions; (2) improving assessment to increase the reliability and validity of the evidence base; and (3) improving treatment options, particularly for the bipolar spectrum diagnoses.

Diagnostic Boundaries

As discussed above in the "Dimensional Approaches" section, it is not clear whether bipolar disorder constitutes a "natural category" that is qualitatively different

from other disorders or from the absence of pathology. Several studies suggest that many of the core aspects of bipolar disorder—such as the symptoms of depression or mania, or deficits in impulse control and executive function—are likely to be continua. As others have noted, imposing categorical definitions on phenomena that vary in degree rather than type is a recipe for artificial comorbidity. The regions of the underlying dimension could be claimed by multiple categorical definitions, much as high negative affect defines an area of functioning that is part of anxiety disorders as well as unipolar and bipolar mood disorders (Clark & Watson, 1991).

There also are specific dyads of diagnoses that are important to clarifying the diagnostic boundaries of bipolar disorder. Should these prove to be natural categories or taxa, then research should refine the criteria and guide differential diagnosis. If the substrates are dimensional, or a mixture of categories and continua, then research will help chart the fundamental shared systems and processes, similar to the guiding vision of the RDoC and other dimensional approaches.

Many of the key boundary issues have been discussed in the "Comorbidity" section. Some additional boundaries that will be vital to probe include the differentiation of cyclothymic disorder from BP-NOS/OS-BRD (Van Meter et al., 2012). Inconsistency about lumping these together makes it difficult to compare research samples and contributes to uncertainty about definitions of diatheses, episode length, and other major aspects of phenomenology. Future research also needs to clarify whether cyclothymia is best conceptualized as a temperament, a prodrome, an acute mood disorder in its own right, or a personality disorder (along the lines of an Axis II diagnosis in the DSM-IV nosology) (Parker et al., 2012; Van Meter et al., 2012). In a related vein, there has long been debate about the amount of overlap or connection between borderline personality disorder and bipolar disorder in adults. Personality disorders do not magically appear at one's 18th birthday. They have roots in adolescence, and aspects of them may have antecedents in even earlier biology and experience (Shiner, Tellegen, & Masten, 2001; see Shiner & Tackett, Chapter 18, this volume). Some are beginning to speculate that the BP-NOS/OS-BRD presentations associated with persistent emotion dysregulation may in fact be the pediatric precursors of what would be diagnosed as borderline personality disorder in adults (Zimmerman, Ruggero, Chelminski, & Young, 2010). Finally, the addition of the DMDD diagnosis in DSM-5 creates a new boundary condition that will need to be mapped carefully in distinction to cyclothymic disorder, as well as other depressive and disruptive behavior disorders (Axelson, Birmaher, Findling, et al., 2011).

Improving Assessment and Diagnostic Accuracy

Reliability is a necessary condition for measurements to have validity. Our understanding of PBD languished for decades because researchers and clinicians did not even consider the diagnosis or measure relevant traits, as shown by the fact that only 1% of the epidemiological studies in youth included data about bipolar spectrum disorders (Van Meter, Moreira, & Youngstrom, 2011). Now that the concept of PBD has been popularized, there has been a sharp rise in attention and in rates of diagnoses, but they are too often based on the use of unstructured clinical interviews (with an average kappa of < .10 when compared to semistructured diagnoses of bipolar disorders; Rettew et al., 2009) or of rating scales and definitions that are untested or have shown poor specificity to bipolar disorder (such as the various permutations of CBCL scales; Diler et al., 2009). Inconsistency and imprecision in the definitions of disorders, as well as the definitions of phenomena such as mixed mood features or "rapid cycling" versus mood instability (Youngstrom, 2009), also impede progress. First, samples of "bipolar" cases often include a large portion of cases not actually on the bipolar spectrum, consistent with fears about overdiagnosis of PBD. Second, there is ambiguity about the subtyping within bipolar samples, which complicates identification of meaningful differences in trajectory and treatment response. Third, many actual cases of PBD go undiagnosed, or they are misdiagnosed as something else. As reviewed above, longitudinal data suggest that perhaps a third of cases of adolescent depression ultimately follow a bipolar course; bipolar disorders are also frequently misdiagnosed as conduct problems or psychosis, especially in minority groups. Systematic evaluation of hypomanic symptoms, lifetime history of mania or hypomania, and family history of bipolar disorder would all rapidly, incrementally improve our classifications. The current definitions of disorders are imperfect, and it is likely that many cases with homogeneous clinical presentations will have distinct etiologies. However, improving the accuracy of our assessment and achieving greater consistency in diagnosis are crucial next steps. Upgrading clinical training to include the current data

about prevalence of bipolar spectrum disorders and to teach evidence-based assessment strategies will accelerate progress here (Youngstrom, Freeman, & Jenkins, 2009).

Improving Treatment Options

Although treatment is outside the scope of this chapter and this volume, treatment research also is informative about longitudinal course and underlying mechanisms. There is a troublesome mismatch between the current knowledge base and the epidemiology of PBD. Most treatment research has concentrated on bipolar I disorder, which represents roughly a quarter of the bipolar spectrum in epidemiological studies (Merikangas & Pato, 2009), and most studies use pharmacological interventions. There is a huge unmet need for investigations of prevention, targeted interventions to delay or prevent progression to full manic or depressive episodes, and approaches that target the environmental moderators of risk. The lack of psychosocial interventions has stunted our understanding of PBD because research has not engaged as deeply and thoughtfully with the less biological aspects of the condition. The relative lack of availability of psychosocial interventions also contributes to "upcoding" of diagnoses or misdiagnosing bipolar spectrum disorders as other conditions. Happily there has been progress in developing psychosocial interventions, so that there are now some "probably efficacious" interventions, and several more that show promise (Fristad & Algorta, 2013).

FUTURE DIRECTIONS

The past decade has seen rapid progress in expanding the evidence base about the validity, developmental course, and underlying mechanisms involved in PBD. There are several major conceptual themes that would be profitable areas for investigation. We assume that research into genetic and neurocognitive functioning will continue to advance incrementally yet swiftly. We focus here on three conceptual topics that may offer promise.

Mapping Bipolar Disorder onto the RDoC

As described above, bipolar disorder intersects with most, if not all, of the dimensions articulated so far in the RDoC (Sanislow et al., 2010). We do not advocate an "imperialism of bipolar disorder," in which the definition of bipolar disorder expands to annex all other conditions that share the symptoms or functional dimensions. Instead, we believe that the RDoC vision is likely to prove productive as a way of identifying dimensions that cut across diagnostic categories. This could clarify many instances of what others have called "artifactual" comorbidity (Angold et al., 1999; Caron & Rutter, 1991).

Despite the obvious connections with RDoC dimensions, bipolar disorder also will present some constructive challenges for the RDoC approach. These include the current lack of a good animal model for mania, which hinders integration of some basic science work with human clinical studies. Full understanding of bipolar disorder will require advances in the developmental aspects of the RDoC. Bipolar disorder also is likely to be characterized by instability and fluctuations, rather than simple mean differences in RDoC dimensions, requiring the development of models that look at differences in variance or other measures of within-person change rather than traditional main-effects models testing group means.

Integrating Models of Affective Temperament with Developmental Psychopathology

Several different models of affective temperament have been developed in adults, and they have garnered evidence of validity as correlates of both mood diagnoses and some biological variables (and even genes) of interest (e.g., Akiskal et al., 2005; Cloninger, Svrakic, & Przybeck, 1993). However, they have not been examined in much depth in pediatric samples, and they have not assimilated a developmental psychopathology framework. Affective temperaments are presumed to be stable and are treated as static variables, whereas a developmental psychopathology model would strive to connect models of temperament in infancy and early childhood with temperament and personality constructs in adolescence and adulthood (Cicchetti, 2010). The developmental psychopathology approach also offers sophisticated transactional models of biological and environmental effects, which are only beginning to be applied to adult affective temperament. Better integration of these approaches will help clarify the developmental continuities, as well as improving our understanding of what constitutes temperamental diathesis versus early-stage illness. Cyclothymic temperament has rarely been studied in youth, but clearly overlaps with aspects

of difficult temperament, for example. Cyclothymia also illustrates the ambiguity about conceptualizing a constellation of behaviors as "temperament" versus more chronic disorder. A variety of measures have accrued evidence of cross-sectional validity (Akiskal et al., 2005; Cloninger et al., 1993; Luby, Svrakic, McCallum, Przybeck, & Cloninger, 1999; Rothbart & Posner, 2006). The next steps will be to collect "linking samples" that pair "adult" and "youth" temperament measures in the same participants, to establish when the same underlying construct has been given different labels by each test author; and then to repeat administration prospectively, to be able to track what changes occur in the course of typical development versus presaging poorer outcomes.

Reconceptualizing Bipolar Disorder as a Systemic and Developmental Disorder

Our last proposal for a future direction is the most ambitious: We believe that the future of bipolar disorder lies in reconceptualizing it as a systemic condition that needs to be understood developmentally in order to be prevented or managed appropriately. We look to the changes in thinking about heart disease as a source of inspiration and ideas. Like heart disease, bipolar disorder does not involve a single organ. Instead, the risk of illness is tied to immune functioning, diet, sleep, exercise, metabolic functioning, and social and interpersonal factors such as stress. These same factors are showing complex yet compelling associations with heart disease. A simplistic analogy would be to conceptualize bipolar disorder as a "systemic brain disease," with severe mood episodes as being analogous to heart attacks. Unpacking this analogy reveals a wide variety of parallels and shared mechanisms, including strong correspondence between how each episode/attack can cause lasting harm even if an individual survives it. The symmetry also implies that a holistic approach to conceptualization and treatment is likely to have greatest impact. Early identification and intervention may shift to management of risk factors and mechanisms, much as prevention of heart disease involves management of blood pressure, glycemic index, and weight in order to delay or prevent the first infarct. Such a reconceptualization opens up a broad range of topics for psychological study and intervention. It also offers a structure to organize the rapid influx of data that is revolutionizing our understanding of PBD.

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CHAPTER 7

Suicidal and Nonsuicidal Self-Injurious Thoughts and Behaviors

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Self-injurious thoughts and behaviors (SITBs) represent a collection of maladaptive and life-threatening outcomes. SITBs range from nonsuicidal self-injury (NSSI; e.g., self-cutting) to suicide. Suicide is particularly concerning, as it is the second leading cause of death among adolescents and young adults, resulting in approximately 4,600 deaths per year (Centers for Disease Control and Prevention [CDC], 2013). Discussion of SITBs is especially timely in light of the newly proposed diagnoses of NSSI and suicidal behavior disorder that appear in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association [APA], 2013) as "Conditions for Further Study" in Section III.

This chapter reviews current knowledge about these perplexing behavior problems. Existing work should be viewed as preliminary steps toward better understanding SITBs. Although recent years have yielded nearly a doubling of research articles on the topic of SITBs (Cardinal, 2008), they have been disproportionately understudied. There still remain key challenges that the field is only now beginning to address. These include defining and classifying SITBs consistently, establishing reliable prevalence rates of all SITBs, empirically testing the interaction of relevant risk factors, and accurately predicting future SITB risk. Through these ongoing efforts, both current and future research can be expected to produce more precise and generalizable findings.

HISTORICAL CONTEXT

History reveals much societal rejection and stigma surrounding SITBs such as suicide and NSSI. Most past records pertain to suicide, and later ones include NSSI. A glance at specific historical views may help explain the relatively delayed emergence of this field of research.

Suicide has been a particularly controversial topic, as the inherent life-or-death nature of this phenomenon has challenged many philosophical, religious, and legal principles. Records go back to the classical period. While Stoics and Epicureans expressed tolerance for suicide during this time, some Greek philosophers, such as Aristotle and Pythagoras, viewed suicide attempt as a cowardly act (Minois, 1999; Williams, 1997).

Early religious authorities, including those of the Roman Catholic, Jewish, and Islamic faiths, also condemned suicide as a sin; in many cases, these condemnations directly influenced the law's treatment of suicide as a crime. For example, England in the Middle

Ages considered "self-murder" as an offense against nature, God, and the King (Williams, 1997). During this time, the moral and legal acceptability of suicide was critically dependent on *why* a person killed him- or herself. A suicide death with the *felo de se* (i.e., "felon of himself") verdict implied that the individual exercised free will when killing him- or herself and was therefore fully responsible for this crime. A suicide death with the *non compos mentis* verdict pointed toward an "unsound mind" as the primary reason for suicide. In the 16th and 17th centuries, people's interpretations of an unsound mind were based on either religion (e.g., the devil had taken possession of a person's soul) or psychology (e.g., the person had a mental illness). These deterministic explanations assumed that the individual could not be held accountable for his or her actions and therefore did not warrant posthumous punishment.

The gradual decrease in *felo de se* cases over time reflects the eventual decriminalization of suicide in many countries. The American colonies began decriminalizing suicide in the early 1700s. The term "suicide" began replacing the term "self-murder." After years of endorsing public shaming of suicide, France had its last documented case of *felo de se* in 1791 (Williams, 1997). Other European countries such as Germany, the Netherlands, and Norway decriminalized suicide between the mid-18th and 19th centuries (Neeleman, 1996). Although it was known for its rigid policies against suicide (Williams, 1997), even England witnessed fewer *felo de se* verdicts, more *non compos mentis* verdicts, and removal of religious and secular punishments for suicide by the late 1800s. However, it was not until 1961 that Parliament passed the Suicide Act, officially decriminalizing suicide in England and Wales (Neeleman, 1996).

This gradual process of decriminalization across time has led to a drastic shift in the way society now approaches the topic of suicide. In many countries, suicide has become a problem to understand and solve. Moving away from earlier religious interpretations of *non compos mentis*, research in psychology, medicine, and sociology has begun to elucidate ways in which to prevent (rather than punish) suicide. More precise measurement and greater attention toward suicide may also help explain some suicide trends over time. For example, increased efforts to classify a death appropriately as suicide may have contributed to the documented rise in adolescent and young adult suicide rates during the 1950s (Jamison, 1999). Other factors contributing to this increase may have included earlier and increased access to lethal means, younger age of alcohol use, and increased psychopathology among youth.

Up until the 20th century, most historical accounts relevant to NSSI pertained to culturally sanctioned body modification. Such body modification methods were deemed acceptable by societies at different points in time for various purposes: physical healing (e.g., trephination, in which holes were cut into the skull to relieve epilepsy), spirituality (e.g., spilling human blood to anoint Aztec idols), and social orderliness (e.g., scarification of pubescent girls among the Tiv people) (Favazza, 1987).

Documentation and commentary on culturally deviant NSSI behavior, as defined in the current chapter, emerged in the psychoanalytic literature toward the mid-1900s. These early interpretations considered NSSI to represent an unconscious attack on bodily parts representing genitalia (Menninger, 1938). Researchers and clinicians began profiling "wrist cutters" as typically young, intelligent, attractive women with particular psychological characteristics (e.g., history of drug use, lack of connection with others, feelings of relief from cutting) (e.g., Graff & Mallin, 1967). The greater number of publications and more frequent media coverage on the topic of NSSI have elucidated a more nuanced understanding of this behavior (Miller & Brock, 2010), as detailed in this chapter.

There are multiple reasons why nonsuicidal SITBs have not been as closely documented or discussed as suicidal SITBs until recently. First, behaviors such as NSSI are inherently less life-threatening and less visible than suicide. Second, until the mid-1990s NSSI was considered unworthy of research (see Favazza, 2009). This was likely a reflection of social norms, which deemed this to be an inappropriate behavior to acknowledge as a society. NSSI was similarly considered unworthy of treatment, as earlier efforts to establish a formal diagnosis around this behavior (e.g., "deliberate self-harm syndrome," "repetitive self-mutilation syndrome"; Favazza & Rosenthal, 1993; Kahan & Pattison, 1984) did not gain recognition in the DSM until its most recent edition (APA, 2013). Third, NSSI rates may have in fact been lower in the past, so that there was less to study until now. This possibility is based on a reportedly large increase in self-injury rates between 1985 and 1995 (Hawton, Fagg, Simkin, Bale, & Bond, 1997). This increase should be interpreted with caution, however, as those statistics include both suicidal and nonsuicidal self-injurious behaviors (Heath, Schaub, Holly, & Nixon, 2009).

The growing dialogue and concern around SITBs are prompting more research and treatment efforts now more than ever before. The quality of research is becoming increasingly refined and specific to subpopulations, such as youth. The remainder of this chapter discusses the current state of SITB research among this particularly vulnerable age group.

CLASSIFICATION AND DEFINITIONS

In order to study SITBs properly, a necessary first step is to classify and define them. There are currently two groups of SITBs: nonsuicidal and suicidal. Nonsuicidal SITBs include NSSI thoughts, NSSI behavior, and NSSI as a disorder (as newly defined by DSM-5). Suicidal SITBs include suicide ideation, suicide plan, suicide gestures, suicide attempt, suicide death, and suicidal behavior disorder (as defined by DSM-5).

NSSI Thoughts and Behavior

The term "NSSI thoughts" refers to serious consideration of or desire to engage in NSSI. These thoughts typically occur when a person is alone and experiencing negative thoughts (e.g., anger, aversive memory), and last for 1–30 minutes (Nock, Prinstein, & Sterba, 2009). Adolescents who think about NSSI experience these thoughts approximately five times per week.

"NSSI behavior" is defined as direct and deliberate physical harm to oneself in the absence of intent to die. Although most persons who injure themselves report little or no pain, NSSI episodes typically result in moderate to severe tissue damage (Nock & Prinstein, 2005; Whitlock, Muehlenkamp, & Eckenrode, 2008). Common forms of NSSI among youth include cutting, scratching, burning, biting, and hitting parts of the body (e.g., Laye-Gindhu & Schonert-Reichl, 2005; Lloyd-Richardson, Perrine, Dierker, & Kelley, 2007; Nock & Prinstein, 2004). Most adolescents use more than one method for NSSI, and perceive the behavior to induce more pain when a greater number of methods are used (e.g., Nock, Joiner, Gordon, Lloyd-Richardson, & Prinstein, 2006). Commonly targeted areas of the body for NSSI include hands, wrists, arms, and thighs (Whitlock, Eckenrode, & Silverman, 2006). The current definition of NSSI excludes culturally sanctioned self-injury (e.g., tattoos, body piercings), less severe forms of self-injury (e.g., picking wounds, nail biting), and other risky behaviors (e.g., gambling, substance misuse).

Youth report engaging in NSSI more frequently than adults do. Compared to young adults, who most often report engaging in NSSI fewer than 10 times in their lives (Whitlock et al., 2008), adolescents report doing so as frequently as 50 times a year or 1–2 times each week (Nock & Prinstein, 2004; Nock, Prinstein, & Sterba, 2009). Although substance and alcohol use is more common among self-injuring adolescents, the NSSI episodes themselves typically occur when adolescents are not using drugs or alcohol (Nock & Prinstein, 2005).

NSSI as a Disorder

Starting with DSM-5, the field now recognizes NSSI as potentially a disorder warranting its own clinical diagnosis (APA, 2013; see Table 7.1). The core feature of the newly proposed NSSI diagnosis is repeated NSSI behavior with clear intent to self-injure. Specifically, a person must have engaged in NSSI for at least 5 days over 1 year (Criterion A). This 5-day minimum is intended to capture those who intentionally engage in this behavior repeatedly, rather than those engaging only in isolated instances of experimentation. There must also be a clear lack of suicidal intent during the NSSI episodes. This may be determined either through explicit indication (e.g., patient report) or repetitively engaging in a behavior that the patient believes will not cause death. This feature emphasizes the similar but critically distinct phenomenology of suicidal and nonsuicidal behaviors.

The proposed criteria for NSSI as a disorder also require engaging in NSSI with the expectation that this behavior will serve a specific function (Criterion B). Examples of such expectations are that NSSI will reduce internal distress or increase pleasure. Moreover, there are three possible associated features of NSSI disorder (Criterion C): immediate psychological precipitants (e.g., tension, anger, distress); preoccupation with NSSI that is hard to resist; and frequent thoughts about self-injuring even in the absence of action. At least one out of these three must be endorsed to meet this criterion.

To be clear, self-injurious behaviors outlined by DSM-5 do not include those that are sanctioned by society or by the person's culture or religion (Criterion D). They also do not include those that are restricted to nail biting or picking at wounds. These DSM-5 exclusion criteria reflect the same ones discussed in this chapter for NSSI behavior.

TABLE 7.1. DSM-5 Proposed Criteria for Nonsuicidal Self-Injury

A. In the last year, the individual has, on 5 or more days, engaged in intentional self-inflicted damage to the surface of his or her body of a sort likely to induce bleeding, bruising, or pain (e.g., cutting, burning, stabbing, hitting, excessive rubbing), with the expectation that the injury will lead to only minor or moderate physical harm (i.e., there is no suicidal intent).
   Note: The absence of suicidal intent has either been stated by the individual or can be inferred by the individual's repeated engagement in a behavior that the individual knows, or has learned, is not likely to result in death.
B. The individual engages in the self-injurious behavior with one or more of the following expectations:
   1. To obtain relief from a negative feeling or cognitive state.
   2. To resolve an interpersonal difficulty.
   3. To induce a positive feeling state.
      Note: The desired relief or response is experienced during or shortly after the self-injury, and the individual may display patterns of behavior suggesting a dependence on repeatedly engaging in it.
C. The intentional self-injury is associated with at least one of the following:
   1. Interpersonal difficulties or negative feelings or thoughts, such as depression, anxiety, tension, anger, generalized distress, or self-criticism, occurring in the period immediately prior to the self-injurious act.
   2. Prior to engaging in the act, a period of preoccupation with the intended behavior that is difficult to control.
   3. Thinking about self-injury that occurs frequently, even when it is not acted upon.
D. The behavior is not socially sanctioned (e.g., body piercing, tattooing, part of a religious or cultural ritual) and is not restricted to picking a scab or nail biting.
E. The behavior or its consequences cause clinically significant distress or interference in interpersonal, academic, or other important areas of functioning.
F. The behavior does not occur exclusively during psychotic episodes, delirium, substance intoxication, or substance withdrawal. In individuals with a neurodevelopmental disorder, the behavior is not part of a pattern of repetitive stereotypies. The behavior is not better explained by another mental disorder or medical condition (e.g., psychotic disorder, autism spectrum disorder, intellectual disability, Lesch-Nyhan syndrome, stereotypic movement disorder with self-injury, trichotillomania [hair-pulling disorder], excoriation [skin-picking] disorder).

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To count toward a diagnosis of NSSI as a disorder, NSSI or its effects must also result in functional impairment (Criterion E)—that is, clinically important distress or disturbance in interpersonal, academic, or other major areas of functioning.

The final criterion details what NSSI as a disorder excludes (Criterion F). In order to ensure clear intent to self-injure, the definition does not include self-injury in the context of delirium, substance intoxication/withdrawal, or psychosis. NSSI as a disorder also excludes other forms of self-injurious behaviors, including those that are compulsive, impulsive, and stereotypic in nature (Favazza, 1987). These include repetitive stereotypies or those accounted for by other mental disorders (e.g., trichotillomania, various developmental disabilities, Lesch–Nyhan syndrome).

Proponents of this new diagnostic category argue that the NSSI diagnosis will enhance both research and practice (e.g., Muehlenkamp, 2005). In research, this proposed DSM-5 disorder will more clearly delineate nonsuicidal from suicidal behaviors, whose definitions have been often confused and treated interchangeably in past research (see below). These definitional inconsistencies have yielded unreliable prevalence rates and etiological findings. Definitional clarifications will facilitate accurate advancement in knowledge about both nonsuicidal and suicidal behaviors, potentially informing policy change (Shaffer & Jacobson, 2009).

Clinically, the establishment of NSSI as a disorder may improve the quality of assessments and individual patient care. A current problem is that individuals who engage in NSSI are often assumed to be suicidal. As many as 88% of adolescent inpatients report having their nonsuicidal cutting behaviors misinterpreted as suicide attempts (Kumar, Pepe, & Steer, 2004), potentially leading to unnecessarily restrictive and burdensome management methods such as inpatient hospitalization (Shaffer & Jacobson, 2009). Clinicians often

misdiagnose self-injuring patients with borderline personality disorder (BPD)—a label that is especially concerning when applied to children and adolescents, whose personalities are still developing (APA, 2000; Wilkinson & Goodyer, 2011). The criteria for NSSI as a disorder allow patients who self-injure to be represented as a distinct group, calling attention to the development of treatment approaches more specific to this concerning behavior outcome (Shaffer & Jacobson, 2009).

Notably, the introduction of NSSI as a disorder does not resolve the aforementioned problem of misdiagnosis. Those participating in the DSM-5 field trials found poor interrater reliability for the NSSI diagnosis (Freedman et al., 2013), highlighting the need for further study. The inclusion of NSSI in Section III of DSM-5 allows recognition of this new diagnosis, but does not permit reimbursement for existing treatment approaches.

Not all individuals support DSM-5 inclusion of NSSI as a disorder. Leading up to the DSM-5 release, concerned opponents of this diagnosis argued that the current state of research provides inadequate justification for diagnostic criteria (see DeLeo, 2011). Adding to this concern is the degree of stigma that may come to surround this mental disorder label—stigma perceived by both the general public and the diagnosed individuals themselves. Opponents claimed that the cost of such stigma may outweigh the benefits of establishing this diagnosis. Placement of NSSI in Section III of DSM-5, which highlights the novel and still tentative nature of this diagnosis, potentially tempers these opposing views.

Suicide Ideation and Plan

"Suicidal ideation" refers to serious thoughts about suicide or desire to kill oneself. One study with community-based adolescents revealed that those with suicidal ideation typically experience a suicidal thought once per week (Nock, Prinstein, & Sterba, 2009). Compared to NSSI thoughts, suicidal ideation typically lasts longer and leads to self-injurious actions less frequently. Beyond thoughts, a "suicide plan" is defined as serious consideration of how one would kill oneself. Making suicide plans and taking preparatory actions toward suicide (e.g., accessing lethal means) are more strongly associated with suicidal intent and behaviors than is suicidal ideation among adolescents (Pettit et al., 2009).

Suicide Gesture

"Suicide gestures" are defined as actions people take to make others believe that they want to kill themselves when they in fact have no intention of doing so. A gesture is also sometimes referred to as a "suicide threat." Adolescents typically report doing this in the presence of peers, and those who engage in this behavior do so an average of four or five times during their lives (Nock, Holmberg, Photos, & Michel, 2007). Notably, suicide gestures are less reliably reported behaviors across time, since adolescents who initially report this outcome often do not report it again when assessed later.

Suicide Attempt

A "suicide attempt" is defined as engagement in a self-injurious behavior with at least some (i.e., nonzero) intent to die. More than half of first-time suicide attempts are planned in advance, leaving approximately 40% who make unplanned attempts (Nock et al., 2013). Compared to adults, adolescents tend to use more over-the-counter medicines, are less certain of the lethality of their attempt, and are more frequently hospitalized for attempts (Parellada et al., 2008). Other methods of attempt include using firearms, hanging/suffocation, and jumping.

Suicide Death

"Suicide death," alternatively referred to in this chapter simply as "suicide," is a fatality that directly results from a suicide attempt. One common misperception is that the outcomes of suicide attempt and death are analogous with one another. Those who die by suicide represent only a portion of those who attempt it, and reflect distinct prevalence rates and sociodemographic characteristics (Moskos, Achilles, & Gray, 2004). Researchers have called for development of distinct prevention approaches and outcome measures for suicide attempt and death.

Suicidal Behavior Disorder

DSM-5 (APA, 2013) includes a new suicidal behavior disorder diagnosis (see Table 7.2). Its core feature is having engaged in a behavior within the past 24 months that was intended to end the patient's life (Criterion A). Although it is possible for a person to have engaged in NSSI separately, the self-injurious behavior required

TABLE 7.2. DSM-5 Proposed Criteria for Suicidal Behavior Disorder

A. Within the last 24 months, the individual has made a suicide attempt.
Note: A suicide attempt is a self-initiated sequence of behaviors by an individual who, at the time of initiation, expected that the set of actions would lead to his or her own death. The "time of initiation" is the time when a behavior took place that involved applying the method.)

B. The act does not meet criteria for nonsuicidal self-injury—that is, it does not involve self-injury directed to the surface of the body undertaken to induce relief from a negative feeling/cognitive state or to achieve a positive mood state.

C. The diagnosis is not applied to suicidal ideation or to preparatory acts.

D. The act was not initiated during a state of delirium or confusion.

E. The act was not undertaken solely for a political or religious objective.

Specify if:
Current: Not more than 12 months since the last attempt.
In early remission: 12–24 months since the last attempt.

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to qualify for the suicidal behavior disorder diagnosis *must* be paired with suicidal intent (Criterion B). Behavior counting toward this diagnosis does not include suicidal ideation or preparatory acts (Criterion C); nor can it have been initiated in a confused or delirious state (Criterion D) or solely for religious or political reasons (Criterion E). Along with NSSI disorder, suicidal behavior disorder has been placed in Section III of DSM-5 as a new diagnosis requiring further study.

DEFINITIONAL ISSUES

Research and clinical work on SITBs have been plagued by the use of vague and inconsistent terms and definitions for the aforementioned behaviors, preventing reliable comparison of NSSI-related findings across studies. The most concerning point of confusion is that between nonsuicidal and suicidal SITBs. Researchers in the United States have equated the term "deliberate self-harm" with NSSI, whereas those in the United Kingdom have used this and other terms (e.g., "parasuicide") to include *both* nonsuicidal and suicidal SITBs (e.g., Claes & Vandereycken, 2007). Some studies that have examined NSSI behavior, as defined in this chapter, have used other terms such as "self-mutilation," "cutting," "self-harm," or "self-inflicted injury." Researchers have called for a resolution of such inconsistencies (e.g., Nock & Kessler, 2006), and the field has increasingly used the definition and term "NSSI" as presented above (Nock, 2010).

Some findings regarding suicidal SITBs must be interpreted with caution due to definitional issues. For example, respondents themselves may have varied interpretations of the term "suicide attempt." According to one large-scale study, more than 40% of people who reported making a suicide attempt subsequently indicated that they actually did not want to die as a result of their behavior (Nock & Kessler, 2006). Also worth considering is the distinction between suicide attempt resulting in physical injury, and an attempt from which a person does not sustain injury because he or she changed their mind or was stopped (i.e., an aborted or interrupted suicide attempt; Barber, Marzuk, Leon, & Portera, 1998; Posner et al., 2011). Researchers are making greater efforts to establish consistency in suicidal SITB nomenclature and definitions, for the benefit of both researchers and clinicians.

EPIDEMIOLOGY

Prevalence/Incidence

Not surprisingly, more adolescents think about NSSI than engage in it. One community-based study reports that 42% of high school students experience NSSI ideation, and 9% experience more severe NSSI preoccupation (Laye-Gindhu & Schonert-Reichl, 2005). This is higher than the rate of NSSI thoughts reported among young adults (16.7%; Martin, Bureau, Cloutier, & Lafontaine, 2011).

Adolescents more often engage in self-injurious acts in the absence (vs. presence) of suicidal intent. Lifetime NSSI prevalence rates for community-based adolescents typically range between 15 and 20% (see Heath et al., 2009). Although cross-national work is limited, initial studies demonstrate relatively consistent prevalence rates across countries including the United States, the Netherlands, and Italy (Giletta, Scholte, Engels, Ciairano, & Prinstein, 2012). Factors such as NSSI definitions and assessment methods contribute to the range of prevalence rates. For example, research studies that include less severe forms of NSSI behavior (e.g., nail biting, wound picking) or use a checklist self-report to measure NSSI are more likely to report higher prevalence. Rates in clinical settings are much higher and have an even wider range: Some 40–82% of adolescent patients report past-year NSSI (e.g., Guertin, Lloyd-Richardson, Spirito, Donaldson, & Boergers, 2001; Nock & Prinstein, 2004). Adolescents generally report NSSI much more often than adults, who report 5.9% lifetime prevalence in the community, and approximately 30% in clinical settings (Jacobson, Muehlenkamp, Miller, & Turner, 2008; Klonsky, 2011). Researchers have begun to explore the prevalence of NSSI as a disorder as well, reporting 6.7% of community-based Swedish adolescents meeting the proposed criteria (Zetterqvist, Lundh, Dahlström, & Svedin, 2013).

Adolescents are most likely to engage in suicidal ideation out of all suicidal SITBs. A nationally representative U.S. study (the National Comorbidity Study Replication—Adolescent Supplement, or NCS-A) recently reported that 12.1% of community-based adolescents have seriously thought about committing suicide at least once in their lives (Nock et al., 2013). Other epidemiological studies of youth report somewhat higher U.S. (19.8–24.0%) and cross-national (21.7–37.9%) lifetime rates of suicidal ideation (Nock, Borges, Bromet, Cha, et al., 2008).

Suicide plan and attempt occur less frequently. Four percent of community-based adolescents have made a suicide plan, and that the same proportion has attempted suicide (Nock et al., 2013). Some epidemiological studies report slightly higher lifetime prevalence rates of suicide attempt among youth, ranging from 3.1 to 9.7% (Evans, Hawton, Rodham, & Deeks, 2005; Nock, Borges, Bromet, Cha, et al., 2008). As expected, hospital-based studies also report higher rates (e.g., 47.5% past-year history; Prinstein et al., 2008). Rates of these suicidal SITBs tend to be higher among youth than among adults. In fact, adults' lifetime prevalence rates for suicidal ideation, plan, and attempt are lower than the corresponding 12-month prevalence rates for adolescents (see Nock, Borges, Bromet, Cha, et al., 2008). One potential explanation is that suicidal behaviors may be increasing over time. Another, more likely explanation is that adults underreport their history of suicidal SITBs.

Suicide gestures also seem to be prevalent among youth. More than 20% of community-based adolescents and young adults (12–19 years) have engaged in a suicide gesture at least once in their lives (Nock et al., 2007). The same study reported relatively high past-year and past-month prevalence rates of suicide gestures (12.8% and 2.1%, respectively). Adult samples, by contrast, report a 1.9% rate of gestures (Nock & Kessler, 2006).

Adding to the gravity of SITBs, suicide is a common cause of death among youth. In the United States, data from the CDC (2013) reveal that an average of 3.9–4.5 suicide deaths per 100,000 children and adolescents occur each year between 2005 and 2010. The most common forms of suicide death in recent years have been suffocation (47.8%), firearms (38.8%), and poisoning (6.3%). When broken down further, the same data set reveals higher incidence rates among older adolescents (15–19 years; 6.7–7.5 per 100,000) than among children and younger adolescents (10–14 years; 0.9–1.3 per 100,000). Cross-national data on youth (<15 years) are comparable and range from 0.04 (England and Wales) through 1.32 (Russian Federation) per 100,000 (DeLeo & Evans, 2003). Rates of suicide death increase into adulthood, with an average incidence rate of 12.7–14.3 per 100,000 youth and adults (10–85+ years; CDC, 2013).

Sex Differences

There remains some debate about sex differences related to NSSI. Earlier profiles and theories about NSSI depict individuals who self-injure as typically being female (e.g., Graff & Mallin, 1967). Research with adolescents often supports this claim, with many studies reporting that girls are at least twice as likely to engage in NSSI as boys (e.g., Laye-Gindhu & Schonert-Reichl, 2005; Nixon, Cloutier, & Jansson, 2008). This is also the case for NSSI as a diagnosis (Zetterqvist et al., 2013). One possible explanation for this sex difference is the particularly strong effect of late-stage puberty among female adolescents, which increases risk of nonsuicidal and suicidal SITBs among girls even

after age and grade level are controlled for (Patton et al., 2007). This is especially the case for self-laceration and self-poisoning. The link between late-stage puberty and SITBs is at least in part explained by depressive symptoms, substance use, and sexual activity reported by girls during this time period. These may serve as stressful precipitants of SITBs. Another possible explanation is that all of these outcomes result from earlier social stressors, such as childhood sexual abuse or family dysfunction.

A notable inconsistency across empirical studies that may directly affect findings related to sex differences is in the definition of NSSI behavior. Some researchers argue that most samples demonstrating sex differences include a broader range of NSSI methods, such as medication abuse in the absence of suicidal intent (Heath et al., 2009). Other studies have found sex differences among more common NSSI methods, such that girls are more likely to cut themselves, whereas boys tend to hit themselves (Laye-Gindhu & Schonert-Reichl, 2005). Such inconsistent findings similarly exist for adults, perhaps due to the same NSSI method-related issues (see Muehlenkamp, 2005).

Research on sex differences for suicidal SITBs yields more conclusive findings. Nock and colleagues (2013) demonstrated that adolescent girls experience suicidal ideation nearly twice as often as boys, and attempt suicide nearly three times as often. This sex difference persists into adulthood (Kessler, Berglund, Borges, Nock, & Wang, 2005), and generalizes to Mexico, China, and European countries (Borges, Benjet, Medina-Mora, Orozco, & Nock, 2007; Hesketh, Ding, & Jenkins, 2002; Kokkevi, Rotsika, Arapaki, & Richardson, 2012). There is no sex difference when it comes to which adolescents who experience suicidal ideation go on to make a suicide plan (Nock et al., 2013).

Although girls are more likely to attempt suicide, boys are more likely to die by suicide. Boys have a higher incidence of suicide death in the United States and in most countries (see Berman, Jobes, & Silverman, 2007). Recent CDC data reflect similar patterns, with rates of 6.1–6.9 per 100,000 for boys and 1.5–2.0 per 100,000 for girls (CDC, 2013). Most cross-national data on youth and adult suicide deaths feature at least a 2:1 male–female ratio. An exception is China, whose selected rural and urban regions feature more frequent female suicide deaths (see Nock, Borges, Bromet, Cha, et al., 2008; World Health Organization [WHO], 2013). India had also been an exception, as it demonstrated a 1.3:1 male–female ratio (see Nock, Borges, Bromet, Cha, et al., 2008), but more recent data on India reveal a more typical 1:0.6 ratio of suicide deaths (WHO, 2013). Several factors may account for these differences, such as more frequent accessibility and selection of lethal means, greater degree of aggressiveness, and stronger suicidal intent characterizing male suicide deaths (Beautrais, 2002).

Sociodemographic Correlates

Both nonsuicidal and suicidal SITBs occur at different rates among those of different races and ethnicities. Broadly speaking, community-based European American youth are more likely to engage in moderate/severe NSSI than are African American or Asian American youth (Lloyd-Richardson et al., 2007). Similar patterns emerge for nonfatal suicidal SITBs (Nock et al., 2013). Native Americans represent an especially concerning demographic group, as they are more likely to die by suicide than any other racial group during adolescence (Nock, Borges, Bromet, Cha, et al., 2008). This is confirmed by recent suicide incidence rates among Native American adolescent boys (14.6 per 100,000) that are twice as high as those for girls (7.2 per 100,000) (CDC, 2013). Data on Hispanic/Latino youth are mixed, with some studies reporting more risk of SITBs (e.g., CDC, 2012) and some reporting less risk (e.g., Evans et al., 2005; Muehlenkamp, Cowles, & Gutierrez, 2010).

Aside from specific racial or ethnic characteristics, minority group status may be especially important to consider. That is, the racial/ethnic composition of an individual's immediate surroundings may be just as important to consider as the race/ethnicity of that individual. An example of this is Neeleman and Wessely's (1999) examination of suicide deaths throughout London. Afro-Caribbean and Asian individuals throughout London were found to be at greater risk of suicide, *unless* they were from geographical areas with greater populations of Afro-Caribbean and Asian individuals.

Further emphasizing the impact of minority group status, research has begun to suggest that SITBs present differently among sexual minority youth. College-based studies have found that students who identify their sexual orientation as homosexual, bisexual, or questioning are more likely to engage in NSSI (Gratz, 2006; Whitlock et al., 2006). Similar results were found for community-based adolescents endorsing nonheterosexual orientation (homosexual, bisexual, other; Deliberto & Nock, 2008). Sexual minority youth also are at greater risk of suicidal ideation and attempt (Fer-

gusson, Horwood, & Beautrais, 1999), as they report suicidal ideation nearly twice as often as heterosexual youth, and suicide attempt more than three times as often (Marshal et al., 2011).

There are mixed findings on the connection between nonsuicidal SITBs and socioeconomic status (SES) as defined by education or family income. On the one hand, some studies have found no differences in NSSI rates from sociodemographically distinct settings (e.g., urban vs. suburban high school comparison; Ross & Heath, 2002). And those examining variation within a single sample have not detected associations between NSSI and adolescents' SES or parental education (e.g., Laye-Gindhu & Schonert-Reichl, 2005; Lloyd-Richardson et al., 2007). On the other hand, some studies have reported alarmingly high rates of NSSI among privileged youth, with more than a third of a community-based sample reporting NSSI behaviors (Yates, Tracy, & Luthar, 2008). This unexpected prominence of NSSI may be due to achievement-oriented pressures combined with reduced familial closeness among this sociodemographic group (Luthar & Becker, 2002).

Although lower SES is associated with adults' suicidal SITBs, including suicide death (Qin, Agerbo, & Mortensen, 2003), it remains questionable whether education and income have an impact on suicide rates among youth. A recent cross-national study demonstrated that lower educational attainment increases risk of suicide-related outcomes in adulthood, but *decreases* such risk among youth (4–19 years) (Nock et al., 2012). This is especially the case in low- and middle-income countries. Regarding the other SES factor of family income, economic hardship during childhood can be among the array of early adversities that increase the likelihood of early-onset suicidal behaviors, especially in high-income countries (Bruffaerts et al., 2010). Revisiting the impact of minority status, it may be especially important to consider the role of individuals' SES in comparison to the surrounding economic climate.

AGE OF ONSET, COURSE, AND PROGNOSIS

Age of Onset

Nonsuicidal SITBs typically begin at adolescence. Researchers consistently report NSSI onset at early adolescence, with ages ranging from 12 to 15 years (Heath et al., 2009; Klonsky, 2007). Studies have also reported earlier instances of self-injury (presence of suicidal intent unknown) as young as eight years old (Hawton, Fagg, & Simkin, 1996). NSSI behavior may emerge during adolescence for a variety of reasons, such as learning about NSSI from peers, generating the idea of NSSI themselves, or learning about it from the media (Deliberto & Nock, 2008).

Suicidal SITBs also tend to emerge during adolescence. Risk of first-time suicidal ideation increases around the age of 12 years, peaks at approximately 16 years, and remains heightened into young adulthood (Nock, Borges, Bromet, Cha, et al., 2008). Though suicidal ideation and attempt have been recorded at ages as early as 4–5 years (see Pfeffer, 1997; Tishler, Reiss, & Rhodes, 2007), some researchers question young children's capacity for suicidal intent. Specifically, prepubertal youth may not yet understand the finality of death or be able to accurately predict the lethal consequences of their actions (Cuddy-Casey & Orvaschel, 1997; Pfeffer, 1997). Risk factors such as parental absence or childhood maltreatment may help account for earlier onsets of suicide-related outcomes (Bolger, Downey, Walker, & Steininger, 1989; Roy, 2004). Suicide gesture and attempt have similar ages of onset—approximately 13–14 years (Nock et al., 2007).

Course and Recurrence

Clinicians and experts in the field have noted that NSSI behavior typically persists for 10–15 years (e.g., Favazza, 1998). More than half of self-injuring adolescents stop engaging in NSSI and other self-injuring behaviors on their own by adulthood (Moran et al., 2012). Most adolescents engaging in NSSI report wanting to stop this behavior for the following reasons (listed in descending order by popularity): judgment that it is an unhealthy behavior, unwanted attention from others, scarring, feelings of shame, and family/friends' distress over their NSSI (Deliberto & Nock, 2008).

The prognosis of NSSI is concerning, since it increases risk of engaging in suicidal SITBs. At least among clinical samples, adolescents engage in NSSI for longer periods of time, use a greater number of methods, and report less pain from NSSI are more likely to attempt suicide in the future (Nock et al., 2006; Zlotnick, Donaldson, Spirito, & Pearlstein, 1997). NSSI is a strong indicator of later suicide attempt, to the point where it can predict attempt above and beyond history of suicidal behaviors (Wilkinson, Kelvin, Roberts, Dubicka, & Goodyer, 2011). Notably, among a minority

of self-injuring individuals, NSSI may prevent both suicidal ideation and attempt by providing an immediate, alternative coping mechanism (*antisuicide model*; Klonsky, 2007; Suyemoto, 1998).

Adolescent suicidal ideation typically persists and increases the likelihood of future psychopathology and suicidal behaviors. Approximately half of youth with suicide ideation continue experiencing such thoughts after their initial age of onset (Kessler et al., 2012). An important factor to consider is exactly *when* people first think about suicide. Earlier onset of suicidal ideation is associated with greater persistence of this outcome (Kessler et al., 2012), further highlighting the importance of interviewing early. Persistence of such thoughts is particularly cyclical for clinical patients. After an initial decline in adolescents' suicidal ideation following hospital discharge, such thoughts typically reemerge 9 and 18 months later (Prinstein et al., 2008). Factors that hinder remission of suicidal ideation include higher adolescent-reported depressive symptoms, higher NSSI frequency, and lower parent-reported externalizing symptoms.

According to several longitudinal studies, suicidal ideation can increase risk of subsequent psychopathology. Adolescent ideators may experience increased depressive, substance use, and anxiety disorders (Fergusson, Horwood, Ridder, & Beautrais, 2005; Garrison, Addy, Jackson, McKeown, & Waller, 1991). They also experience a decline in general behavioral and emotional functioning, interpersonal relationships, and self-esteem, and an increase in psychopathology, following ideation onset (Reinherz et al., 1995). It is possible that suicidal ideation has only a short-term impact on psychopathology, however, since examination of longer-term effects yields mixed findings (e.g., Dhossche, Ferdinand, van der Ende, Hofstra, & Verhulst, 2002).

Most notably, suicidal ideation increases the likelihood of more severe outcomes, such as suicide plan or attempt. In addition to the *presence* of suicidal ideation, *specific changes* in thoughts over time predict suicide attempt (Prinstein et al., 2008). That is, the rate at which suicidal thoughts subside or recur is strongly linked with subsequent suicide attempts. Suicidal ideation can also help predict when a person will act on their thoughts. Cross-national findings consistently report that 60% of adults with suicidal ideation transition to suicide plans or attempts within the first year of experiencing suicidal thoughts (Nock, Borges, Bromet, Alonso, et al., 2008). Future work needs to test whether this is the case among adolescents.

Although by definition a suicide gesture occurs *without* intent to kill oneself, it can still have implications for subsequent suicidal behaviors. One prospective study demonstrated that adolescent inpatients with histories of suicide gestures/threats are more likely to attempt suicide following discharge (Prinstein et al., 2008). More specific details regarding the duration or course of other nonsuicidal SITBs (e.g., the transition from NSSI thoughts to NSSI) remain unknown.

In addition to its immediately life-threatening nature, a suicide attempt indicates a poor longer-term prognosis. Adolescents who attempt suicide often reattempt. Nearly a quarter of adolescent attempters reattempt within 1 year, and nearly half reattempt within 10 years (Grøholt & Ekeberg, 2009; Hultén et al., 2001). This relationship between past and future suicidal behaviors has been rigorously tested and found to exist even when accounting for individuals' hopelessness and related psychopathology (e.g., Joiner et al., 2009). Suicide researchers have attributed reattempt to heightened aggression, cognitive sensitization (i.e., heightened accessibility to suicidal thoughts), and opponent processes (i.e., enhanced calming, pain-relieving effects from attempts) (Joiner, 2005; Stein, Apter, Ratzoni, Har-Even, & Avidan, 1998). As expected, a suicide attempt can also result in suicide death. Specifically, one-third of adolescents who die by suicide have made at least one prior suicide attempt (Marttunen, Aro, & Lönnqvist, 1992).

DIAGNOSTIC CORRELATES

With the exception of the proposed DSM-5 diagnoses of NSSI and suicidal behavior disorder, SITBs are not clinical diagnoses. Instead, the present section reviews common co-occurrences between SITBs and existing DSM-IV diagnoses. As such, these represent diagnostic correlates rather than comorbidities.

Nonsuicidal SITBs

Researchers and clinicians often observe NSSI behavior co-occurring with borderline personality disorder (BPD). This is not surprising, as the DSM-IV-TR criteria for BPD include NSSI as a symptom (APA, 2000). Approximately 50–60% of self-injuring adolescent

inpatients meet criteria for BPD (Ferrara, Terrinoni, & Williams, 2012; Nock et al., 2006). In some cases, NSSI may mark the emergence of BPD characteristics during adolescence. Crowell and colleagues (2012) found that self-injuring adolescents exhibited more BPD symptoms (e.g., avoidant behavior, self-damaging impulsivity) than depressed and noninjuring adolescents did. The combination of NSSI with suicidal behaviors may further increase co-occurrence or severity of BPD symptoms (Muehlenkamp, Ertelt, Miller, & Claes, 2011).

Despite their frequent co-occurrence, NSSI and BPD can be viewed as clinically distinct entities. Initial studies have directly compared BPD with the proposed diagnosis of NSSI as a disorder among adolescents and adults, and have found that self-injuring patients without BPD demonstrate a comparable (if not greater) degree of functional impairment as those diagnosed with BPD (Glenn & Klonsky, 2013; Selby, Bender, Gordon, Nock, & Joiner, 2012). NSSI behavior is also linked to other personality disorders, such as avoidant and paranoid personality disorders (Nock et al., 2006).

Adolescents who engage in NSSI behavior also meet criteria for several other disorders. Generally, the diagnoses most commonly co-occurring with NSSI behavior include substance use disorder, major depressive disorder, and impulse-control disorders. Adolescent inpatients with a history of NSSI most typically meet criteria for substance use disorder (59.6%), conduct disorder (49.4%), oppositional defiant disorder (44.9%), major depressive disorder (41.6%), and posttraumatic stress disorder (PTSD; 23.6%; Nock et al., 2006).

Suicidal SITBs

Approximately 90% of adolescents who have experienced suicide ideation or made suicide plans have a lifetime history of at least one DSM-IV diagnosis (Nock et al., 2013). The most commonly endorsed group of mental disorders among those with suicide ideation is depression/dysthymia (56.8%). Other commonly co-occurring diagnoses include disruptive behavior disorders (intermittent explosive disorder, 29.4%; oppositional defiant disorder, 34.4%; conduct disorder, 20.0%), substance use disorders (illicit drug abuse, 27.4%; alcohol abuse, 18.4%), and specific phobia (36.8%). Adolescents with ideation who go on to make plans are also especially likely to have a history of depression/dysthymia.

The connection between depression and suicide attempt varies depending on age. Among adults, depression appears to be associated with suicide attempts only through its strong and more direct association with suicidal ideation and plans (Nock, Hwang, Sampson, & Kessler, 2010). When controlling for suicidal ideation, depression no longer predicts suicide attempts; instead, disorders characterized by agitation and poor impulse control predict which of these adults will make a suicide attempt (Nock, Hwang, et al., 2009; Nock et al., 2010). Among adolescents, however, depression is more specifically and closely associated with suicide attempts (Nock et al., 2013). Specifically, a wide array of diagnoses ranging from depression/dysthymia to impulse-control disorders (e.g., intermittent explosive disorder, conduct disorder) and other diagnoses (e.g., eating disorders, attention-deficit/hyperactivity disorder) predict which adolescents experiencing suicidal ideation will also attempt suicide.

THEORETICAL FRAMEWORK

There are numerous theoretical approaches to both studying and treating SITBs. The theories most relevant to today's research and evidence-based practice are reviewed below. These theoretical frameworks could be applied to both youth and adults.

Theories on NSSI Behavior

Several theories explain what combinations of long-term factors contribute to NSSI behavior, such as why people choose this behavior over others and what maintains the behavior once it starts. Theories with the broadest of scopes (e.g., Nock, 2010) propose that temporally distal vulnerability factors at least partially account for NSSI behavior. These distal vulnerability factors could be environmental (e.g., childhood sexual abuse, dysfunctional family dynamics), biological (e.g., increased physiological response to stress, decreased prefrontal cortex activity), or psychological (e.g., poor communication skills, high self-criticism) in nature. Nock's (2010) integrative model assumes that a *combination* of these vulnerabilities is what increases the likelihood of NSSI. For example, rather than focusing solely on one environmental stressor (parental criticism) or psychological vulnerability (self-critical thinking), Wedig and Nock (2007) demonstrated that

the *interaction* of these two factors is especially predictive of SITBs, including NSSI. That is, parental criticism is especially deleterious for adolescents who think very self-critically. This model also assumes that temporally proximal risk factors (e.g., physiological hyperarousal to stress) further increase the likelihood of NSSI behavior.

A similar developmental multivariate view is Linehan's (1993) *biosocial theory*, which proposes that distal vulnerabilities increase risk of both NSSI and suicidal behaviors. Linehan specifies that "affective instability" (i.e., the tendency for emotional reactions to be more immediate, more intense, and longer-lasting) is a core biological deficit among self-injurious individuals—particularly those with BPD. It is not affective instability alone, but instead its combination with an "invalidating environment" (e.g., childhood trauma, family dysfunction), that increases SITB risk. Supporting studies have demonstrated that the quality of emotion regulation plays a central role in explaining adolescent NSSI behavior, and that this psychological risk factor mediates the effects of family- and peer-based stressors (e.g., Adrian, Zeman, Erdley, Lisa, & Sim, 2011).

Several theories focus more on the outcome of NSSI, and argue why at-risk adolescents specifically choose NSSI over other maladaptive behaviors have been proposed (Nock, 2009b). According to the *pragmatic hypothesis*, individuals choose NSSI because it can serve its purpose especially quickly and effectively. This behavior typically does not require much time, money, or energy, and is thereby a lower-maintenance activity than other maladaptive behaviors, such as substance use or binge eating. Another possibility is the *implicit identification hypothesis*, in which people may choose NSSI because they identify with their perceived concept as "self-injurers." This is supported by recent studies in which self-injuring adolescents demonstrated stronger implicit associations between the concepts of "self" and "cutting" on a behavioral task (i.e., *Implicit Association Test*; Nock & Banaji, 2007). In addition, the *self-punishment hypothesis* proposes that people may choose NSSI because it represents self-directed abuse, similar to what they have received in the past. Studies indeed demonstrate a history of parental criticism (Wedig & Nock, 2007) and child maltreatment (e.g., Glassman, Weierich, Hooley, Deliberto, & Nock, 2007) among adolescents who self-injure.

The following hypotheses describe how immediate interpersonal functioning may affect the decision to choose NSSI over other maladaptive behaviors. The *social signaling hypothesis* (Nock, 2008) states that NSSI is a means to communicate with others when more normative (i.e., less intense) efforts to communicate have failed. NSSI may in fact be an especially effective signal because of its clearly harmful and costly nature. Adolescents who self-injure demonstrate poor verbal communication skills (e.g., Hilt, Cha, & Nolen-Hoeksema, 2008), highlighting circumstances in which NSSI behavior may indeed serve a social function. Finally, according to the *social learning hypothesis*, some individuals engage in NSSI as a result of observing this behavior in others. This hypothesis is applicable to nearly half of self-injuring adolescents, who report learning about NSSI through their peers or media sources (Deliberto & Nock, 2008).

Once individuals select NSSI as a maladaptive behavior, the *four-function model of NSSI* (Nock & Prinstein, 2004) helps explain what maintains it over time. The primary assumption of this theory is that NSSI persists because of events immediately preceding and following an NSSI episode. According to this theory, there are two dimensions along which individuals are motivated to continue engaging in NSSI. The first dimension pertains to whether adolescents self-injure for reasons pertaining to themselves (i.e., automatic) or others (i.e., social). The second dimension indicates whether the NSSI behavior is followed by removal of an aversive stimulus (i.e., negative reinforcement) or presentation of a favorable stimulus (i.e., positive reinforcement). Combined, these dimensions categorize four motivations for NSSI. These categories are automatic negative reinforcement (e.g., to stop feeling bad about oneself), automatic positive reinforcement (e.g., to feel something even if it is pain), social negative reinforcement (e.g., to avoid doing something unpleasant with others), and social positive reinforcement (e.g., to communicate with others).

Although studies support the validity of all four functions, automatic negative reinforcement has received the greatest amount of empirical support. This is likely due to the fact that it is the most commonly endorsed function among both adolescents (Nixon, Cloutier, & Aggarwal, 2002; Nock & Prinstein, 2004) and adults (Brown, Comtois, & Linehan, 2002). Self-injuring adolescents reporting automatic negative reinforcement exhibit more internal distress, such as greater hopelessness, emotion reactivity, and physiological response to stressors (Nock & Mendes, 2008; Nock & Prinstein, 2005). Such evidence points toward a particularly aver-

sive automatic experience from which one may be motivated to escape. As expected, adolescents endorsing automatic positive reinforcement report greater anhedonia, inactivity, and PTSD symptoms such as psychic numbness (Nock & Prinstein, 2005; Weierich & Nock, 2008). In support of the social functions, adolescents who endorse social negative or positive reinforcement report greater history of peer victimization and socially oriented perfectionism, as well as an improvement in relationships with their fathers following NSSI episodes (Hilt et al., 2008; Hilt, Nock, Lloyd-Richardson, & Prinstein, 2008; Nock & Prinstein, 2005). These social functions are more often endorsed by adolescents than by adults (Lloyd-Richardson, Nock, & Prinstein, 2009). And unlike adults, adolescents who self-injure are just as likely to endorse social functions as automatic functions (Lloyd-Richardson et al., 2007). The reason for heightened youth-endorsed social functions remains unclear. One possibility is that during this developmental period, adolescents' sense of identity is strongly determined by their perception of social norms (see Heilbron & Prinstein, 2008).

Several other functions for NSSI have been proposed (see Klonsky, 2007; Suyemoto, 1998). For example, alternative functions include boundary definition (i.e., marking skin as a means of separating oneself from the environment), sensation seeking, sexually oriented gratification or punishment, or reduction of suicidal urges (i.e., an antisuicide function). There is less clarity surrounding these functions, and subsequently less evidence in support of them. This may in part be due to overextension of the term "function" to mean "general purpose or reason" for NSSI (Lloyd-Richardson et al., 2009). In the current chapter, this term strictly refers to antecedents and consequences of NSSI behavior.

Theories on Suicidal Behavior

Theories point toward a wide range of influences on suicide attempt and death. Some, for example, focus on societal impact. The broadest theoretical framework is Durkheim's (1897/1951) sociological theory on suicide, which classifies suicide death according to the relationship between society and an individual. According to Durkheim's theory, there are four classes of suicide. *Egoistic* suicide occurs when an individual fails to integrate him- or herself with society (e.g., an orphan, a social outcast). *Altruistic* suicide occurs when an individual kills him- or herself for the perceived greater good of society (e.g., a suicide bomber). *Fatalistic* suicide occurs when society overregulates an individual (e.g., a criminal on probation). Finally, *anomic* suicide occurs when there is a sudden change in relationship between an individual and society (e.g., a person who experiences a drastic decrease in income/class).

Other theoretical explanations for suicide attempt and death focus on the individual, and point toward core psychological characteristics. Beck's (1967) *cognitive theory* emphasizes how negative thoughts pertaining to oneself, the world, and the future contribute to depression and potentially suicidal ideation. Beck has also proposed that an activated suicide schema affects information-processing biases (e.g., memory, interpretation, attentional biases) and increases hopeless and suicidal thinking. The role of hopelessness has received a substantial amount of support, as it is a powerful psychological risk factor for suicidal thoughts and behaviors (e.g., Beck, Steer, Kovacs, & Garrison, 1985; Smith, Alloy, & Abramson, 2006). More recently, Wenzel and Beck (2008) have explained how hopelessness may contribute to not only suicidal thoughts, but also behaviors. Specifically, hopelessness may interact with attentional fixation (i.e., narrowing of focus on suicide as a viable option to circumstances) to exacerbate suicidal thoughts and the likelihood of attempting suicide.

Other psychological theories focus on the comparable but distinct construct of entrapment. For example, Baumeister's (1990) *escape theory* similarly proposes that the intolerability of negative automatic thoughts and the resultant need for escape lead to suicidal thoughts and behaviors. Williams's (1997) *cry of pain* model further clarifies that individuals who attempt suicide do not wish to die, but instead wish to escape from feeling an overwhelming sense of defeat.

Other theories integrate both the sociological and psychological perspectives. The most strongly supported integrative theory is Joiner's (2005) *interpersonal-psychological theory* of suicidal behavior, which argues that there are three key elements contributing to suicide attempt and death. First, individuals must believe that they impose a burden on significant figures in their lives (i.e., perceived burdensomeness). Studies have indeed demonstrated that perceived burdensomeness is associated with suicidal ideation, intent, and lethality of suicide attempt method (Joiner et al., 2002, 2009), and that such risk factors have an even stronger effect than hopelessness (Van Orden, Lynam, Hollar, & Joiner, 2006). The second element of this model is that individuals must experience a lack of belongingness and connectivity to those around them (i.e., thwarted

belongingness). Similar to perceived burdensomeness, thwarted belongingness is associated with suicidal ideation (Joiner et al., 2009). Finally, such individuals must also have the capacity and courage to attempt suicide (i.e., capability for suicide). This last element also provides a theoretical explanation for why those who engage in NSSI are at greater risk of suicide attempts and death: Repeated self-injurious behaviors habituate an individual and reduce fear toward suicidal behaviors. To further support this final piece, studies have demonstrated that those who experience or engage in habituating behaviors (e.g., substance abuse, body modifications, surgery, violence, early life trauma) are more likely to attempt suicide (Joiner, 2005).

ETIOLOGICAL FINDINGS

While the aforementioned theories drive some research on SITB etiology, much of this field has identified risk factors for SITB outside any theoretical context. In order to integrate these distinct findings, below we organize risk factors according to three domains: biological, environmental, and psychological risk factors. We review each domain and highlight risk factors specific to a particular type of SITB when possible.

Biological Factors

Several decades of research suggest that suicidal behavior is associated with dysregulation of the neurobiological stress response system, specifically the hypothalamic–pituitary–adrenocortical (HPA) axis (Braquehais, Picouto, Casas, & Sher, 2012). Several studies have demonstrated this in the suicidal youth population by examining elevated plasma cortisol, a byproduct of the HPA axis, using multiple methods such as dexamethasone suppression tests (Pfeffer, Stokes, & Shindledecker, 1991) and examination of a continuous 24-hour cortisol secretory period (Dahl et al., 1991). Cortisol levels are associated not only with whether a patient is suicidal, but also with the severity of suicide-related outcomes (Pfeffer et al., 1991). Importantly, not all studies demonstrate hypercortisolism. Some have found *lower* levels of cortisol among individuals at risk of suicide (e.g., first-degree relatives of individuals who died by suicide; McGirr et al., 2010). Similarly, HPA axis dysfunction among youth engaging in NSSI has been shown to yield both hyper- and hypocortisolism (Barrocas et al., 2011; Kaess et al., 2012).

Closely linked to the activation of the HPA axis is the endogenous opioid system, which features abnormalities linked especially with NSSI behaviors. Individuals who engage in NSSI demonstrate lowered levels of beta-endorphins and met-enkephalins, which are endogenous opioid peptides associated with stress-induced analgesia and pain perception (e.g., Stanley et al., 2010). This is consistent with the fact that persons who self-injure demonstrate increased tolerance and lowered sensitivity to physical pain (Bohus et al., 2000; Claes, Vandereycken, & Vertommen, 2006). Some researchers propose that opioids facilitate perception not only of physical pain, but also of social pain in both animals and human beings (MacDonald & Leary, 2005). This is consistent with the notion that NSSI behavior can serve both intra- and interpersonal functions (Nock & Prinstein, 2004). Animal studies offer evidence suggesting that self-injurious behaviors (e.g., self-directed biting) serve a potentially regulatory function and increase beta-endorphin levels (Tiefenbacher et al., 2003).

Deficient serotonergic neurotransmission also has been associated with NSSI and suicidal behaviors. Individuals engaging in either form of self-injurious behavior typically exhibit serotonergic hypofunction (e.g., Herpertz, Sass, & Favazza, 1997; Mann, Oquendo, Underwood, & Arango, 1999). Among adolescents, decreased levels of platelet serotonin (5-HT) are related to greater severity of suicidal behaviors (Tyano et al., 2006). Other serotonergic abnormalities among suicidal youth include increased number of 5-HT2A receptors, protein, and messenger RNA expression throughout specific brain regions such as the prefrontal cortex and hippocampus (Pandey et al., 2002). Findings are mixed, as other studies report *reduced* 5-HT2A binding in the frontal cortex of patients who recently attempted suicide (see Desmyter, van Heeringen, & Audenaert, 2011).

Although most research has focused on serotonergic activity, some work suggests that the dopaminergic system may also contribute to suicidal and nonsuicidal self-injurious behaviors. Low levels of dopamine have been linked with self-injury in developmental disorders and Lesch–Nyhan disease (see Sher & Stanley, 2009). Although some studies demonstrate hypofunction of the dopaminergic system among suicidal individuals, it remains unclear whether this is driven by associated depressive symptoms (Mann, 2003).

Some brain structure abnormalities have been linked to SITBs. White matter hyperintensity, for example, is

one of the few structural abnormalities rigorously examined among suicidal youth. The connection between white matter hyperintensities and suicidal thoughts and behaviors depends on the subtype: periventricular hyperintensities (PVHs) versus deep white matter hyperintensities (DWMHs). PVHs exhibit an especially strong link to suicidal thoughts and behaviors, even when researchers control for depression (Ehrlich et al., 2004). DWMHs are also associated with these outcomes when examined in the parietal lobe, but not the frontal lobe (Ehrlich et al., 2003).

At least among adults, another structural marker that may distinguish suicidal from nonsuicidal people is gray matter volume. Research thus far suggests reduced gray matter volume in the frontal lobe of suicidal adults (see Desmyter et al., 2011), even after controlling for depression (Wagner et al., 2011). This needs to be tested among younger populations. Thus far, studies examining depressed adolescents similarly reveal reduced gray matter volume in the frontal lobe (Shad, Muddasani, & Rao, 2012).

Family studies point toward the possibility that there may be some genetic risk factors for SITBs, specifically suicide attempts. One adolescent twin study found that shared genes may account for nearly 50% of the variance in suicide attempts (Glowinski et al., 2001). The pattern of family clustering has been replicated more recently and in larger-scale studies, emphasizing the primary role that genetic factors play in explaining suicide-related outcomes (Tidemalm et al., 2011). This is likely not due to any shared risk of general psychopathology. Studies have shown that when researchers control for family history of psychopathology, adolescent suicide victims have more first-degree relatives who have also attempted suicide than demographically similar nonsuicidal adolescents have (Brent, Bridge, Johnson, & Connolly, 1996). Family clustering of suicidal ideation and attempts has also been found, although these outcomes may also be attributed to shared risk of psychopathology (Brent et al., 1996; Bridge, Brent, Johnson, & Connolly, 1997).

Research on specific genetic risk factors, thus far, has focused on candidate genes implicated in serotonergic and dopaminergic functioning. For example, the short allele of the serotonin transporter promoter gene (5-HTTLPR) is associated with suicidal behaviors and may also be associated with NSSI through its link to emotion dysregulation (Barrocas et al., 2011; Mann et al., 2000). Another potential example is the catechol-*O*-methyltransferase (COMT) gene, which contributes to metabolic functioning of dopamine (Barrocas et al., 2011). This is an area that requires a significant amount of research.

Psychological Factors

Nonsuicidal and suicidal SITBs share several psychological risk factors. Generally, a negative internal experience precedes engagement in SITBs. Negative automatic (i.e., self-oriented) and self-critical thoughts specifically characterize SITBs among children and adolescents (Nock & Kazdin, 2002; Wedig & Nock, 2007). These thoughts may be specifically related to hopelessness (Nock & Kazdin, 2002; Wilkinson et al., 2011), low self-esteem (Lundh, Karim, & Quilisch, 2007; Wedig & Nock, 2007), or body dissatisfaction (e.g., Muehlenkamp & Brausch, 2012). Perfectionism, especially socially prescribed perfectionism (i.e., perception of others' unrealistically high expectations of one's own behavior), may contribute to such negative or self-critical thoughts. This form of perfectionism is more characteristic of self-injurious youth than is self-oriented perfectionism (i.e., self-imposed expectations for oneself that are unrealistically high) (Boergers, Spirito, & Donaldson, 1998; O'Connor, Rasmussen, & Hawton, 2009).

Self-injurious youth are characterized not only by negative emotions, but also by distinctive ways they modulate such emotions. Research studies on NSSI and distress tolerance have used physiological measures to demonstrate that self-injuring youth exhibit greater skin conductance under stress than non-self-injuring youth do (Nock & Mendes, 2008). This is complemented by the fact that self-injuring individuals who even imagine engaging in NSSI experience a reduction of physiological arousal, indicating that tension reduction potentially reinforces NSSI behavior (Haines, Williams, Brain, & Wilson, 1995). Self-reported emotion regulation and reactivity (i.e., sensitivity) are also associated with NSSI behavior (Gratz, 2006; Nock, Wedig, Holmberg, & Hooley, 2008). Importantly, emotion regulation and reactivity can result in either exceptionally strong or weak emotional experiences. Some self-injurious youth report anhedonia and dissociation to be the driving motivations for NSSI (Gratz, Conrad, & Roemer, 2002; Zlotnick et al., 1996), although these are less common than other motives.

Several cognitive mechanisms may exacerbate these aforementioned psychological risk factors. For example, trying to suppress unwanted thoughts and emotions

can result in a strong rebound effect of such thoughts and emotions. Najmi, Wegner, and Nock (2007) found that this propensity for thought suppression mediated the links between emotion reactivity and NSSI and suicidal ideation among youth. The opposite approach of rumination can also be harmful, since distressed youth with ruminative thinking styles are more likely to engage in NSSI maintained via automatic negative reinforcement than are nonruminative youth (Hilt et al., 2008).

Importantly, a cognitive mechanism that is not in and of itself a risk factor can *still* contribute to SITB risk by interacting with the aforementioned psychological risk factors. An example of this is the fact that poor executive functioning (i.e., problem solving) is unrelated to suicide attempt when examined independently, but can increase the likelihood of an attempt when combined with poor emotion reactivity (Dour, Cha, & Nock, 2011). More distal cognitive mechanisms that increase risk of SITBs are dysfunctional attitudes, negative attributional biases, and overgeneralized autobiographical memory (Arie, Apter, Orbach, Yefet, & Zalzman, 2008; Hankin & Abela, 2011).

The well-known association between impulsiveness and SITBs is tempered by mixed findings of exactly what measure and type of impulsiveness such associations involve. For example, the degree to which adolescents consider themselves to be impulsive (i.e., self-report measure) is more predictive of NSSI than whether or not their actions reflect such impulsiveness (i.e., behavioral measure). Self-reported impulsiveness has been shown to consistently characterize adolescents who engage in NSSI (Janis & Nock, 2008) and potentially suicidal behaviors (O'Connor, Rasmussen, & Hawton, 2012). Within the same sample of adolescents (Janis & Nock, 2008), performance-based measures of behavioral disinhibition and risky decision making were not significantly related to NSSI behavior. One possible reason for this inconsistency is that impulsiveness is related differently to NSSI compared to other SITBs. Behavioral measures of reward-directed impulsiveness have been shown to be associated with other SITBs such as suicide attempts (Horesh, 2001; Mathias et al., 2011). Similar behavioral measures have been used to differentiate adolescents who engage in NSSI who have, versus have not, also attempted suicide (Dougherty et al., 2009). Another likely possibility is that only specific aspects of impulsiveness are related to SITBs. Finally, the behavioral measures used thus far may not accurately capture the type of impulsiveness that influences SITBs in natural settings. As researchers have highlighted in related fields of psychopathology (e.g., attention-deficit/hyperactivity disorder; Barkley, 1991), behavioral or laboratory-based measures of executive functioning have poor ecological validity. This may also be the case in the study of SITBs. In short, this particular area of SITB research requires a more systematic approach of examining the multifaceted risk factor of impulsiveness in relation to NSSI and suicide attempts.

One type of psychological risk factor more specific to NSSI behavior relates to interpersonal functioning. Adolescents who engage in NSSI demonstrate particular impairments in social problem-solving skills, such as selecting an optimal solution to interpersonal conflict (Nock & Mendes, 2008). Self-injuring youth also exhibit poor communication skills; they not only struggle with expressing their own emotions (Gratz, 2006), but also perceive poor communication with their peers (Hilt et al., 2008). Although social problem-solving skills and poor communication have also been demonstrated among suicidal youth (Howard-Pitney, LaFromboise, Basil, September, & Johnson, 1992; Riesch, Jacobson, Sawdey, Anderson, & Henriques, 2008), these risk factors are considered less relevant and are often accounted for by co-occurring depressive symptoms and hopelessness (Boergers et al., 1998; Speckens & Hawton, 2005).

Environmental Factors

The most widely researched long-term environmental risk factor for SITBs is childhood maltreatment, especially childhood sexual abuse. Victims of childhood sexual abuse are more likely to engage in NSSI, suicidal ideation, and suicide attempts during adolescence (Brown, Cohen, Johnson, & Smailes, 1999; Glassman, Weierich, Hooley, Deliberto, & Nock, 2007). It is especially alarming that 29–50% of adolescents who are sexually abused try to kill themselves, and that this association persists even after investigators control for psychological factors such as hopelessness (Martin, Bergen, Richardson, Roeger, & Allison, 2004). It remains unclear whether the effect of sexual abuse is stronger for male versus female victims; some argue that this effect raises suicide risk especially among boys (see Rhodes et al., 2011), and others argue that it raises risk among girls (Bergen, Martin, Richardson, Allison, & Roeger, 2003). One thing that is consistent across all victims is the fact that greater numbers and types

of perpetrators (e.g., family and nonfamily members) increase risk of suicide attempts (Eisenberg, Ackard, & Resnick, 2007). Other forms of childhood maltreatment, such as physical and emotional abuse, can also have a deleterious effect on adolescent SITBs (Beautrais, Joyce, & Mulder, 1996; Brown et al., 1999; Glassman et al., 2007). Some of the aforementioned research demonstrates the impact of neglect as well, although it may have a less direct impact on adolescent outcomes.

Other important risk factors for adolescent SITBs can be found in the immediate environment, such as family and school functioning. "Family functioning" can refer to the quality of relationships either among the family members themselves or with the self-injuring youth directly. For example, family conflict, poor parental care, and poor parental relationships (e.g., parental separation) all increase risk of suicide attempts during adolescence (Brent, Melhem, Donohoe, & Walker, 2009; Wilkinson et al., 2011), which is not otherwise accounted for by parental psychopathology (Beautrais et al., 1996). What has an especially strong impact on NSSI behavior is the quality of relationships between family members and the self-injuring youth, such that family loneliness (i.e., an adolescent's feeling alone when he or she is with the family) rather than general family dysfunction is associated with NSSI (Giletta et al., 2012; Wilkinson et al., 2011). Adolescents' feeling of connectedness with their family members can in fact protect against the otherwise harmful impact of other well-known risk factors, such as childhood sexual abuse (Eisenberg et al., 2007).

The importance of connectedness extends to the school setting, as the degree of integration with peers affects rates of SITBs among youth. Studies have found that adolescents who experience low engagement with the school setting (e.g., having religious convictions that deviate from a Catholic school culture) are more likely to engage in NSSI and attempt suicide (Young, Sweeting, & Ellaway, 2011). Beyond simply being different from others, the lack of peer tolerance in particular increases SITB risk. For example, Borges and colleagues (2011) report that experiencing discrimination in school because of one's heritage predicts which adolescents will engage in NSSI or experience suicidal ideation, whereas basic immigrant status (e.g., U.S.-born vs. non-U.S.-born) does not.

Other risk factors are general peer victimization and bullying among youth. Adolescents who experience peer victimization that is either overt (e.g., physical altercations) or relational (e.g., spreading rumors) are more likely to experience suicidal ideation, attempt, and NSSI behaviors (Giletta et al., 2012; Hilt et al., 2008; Pranjić & Bajraktarević, 2010). Adolescents who are bullied in multiple ways (e.g., sexual jokes, attacks on race/religion, judgments about physical appearance) and through multiple media (e.g., in person, online) are at greater risk of suicide-related outcomes (Hay & Meldrum, 2010; Klomek, Marrocco, Kleinman, Schonfeld, & Gould, 2008). In fact, those who are victims of both in-person bullying and cyberbullying are approximately five times more likely to engage in SITBs than are nonvictims (Schneider, O'Donnell, Stueve, & Coulter, 2012). Interestingly, any involvement in bullying—even as a perpetrator—increases the likelihood of SITBs, especially among girls (Hinduja & Patchin, 2010; Kim, Leventhal, Koh, & Boyce, 2009; Klomek et al., 2008). Peer victimization has not only an immediate but also a long-term impact on SITBs. Both men and women who recall incidents of childhood bullying, even decades after the bullying incidents, are at increased risk of attempting suicide (Klomek et al., 2009; Meltzer, Vostanis, Ford, Bebbington, & Dennis, 2011).

Peer influence serves not only as a source of stress but also as a reward, with the latter being a powerful motivator for SITBs. For example, an adolescent who perceives many friends or close friends to be engaging in NSSI is more likely to engage in this behavior themselves (Prinstein et al., 2010), and nearly 40% of adolescents who self-injure first learn about this behavior from their peers (Deliberto & Nock, 2008). Experimental paradigms have also demonstrated that people use social information to inform their own behavior, even when it is self-injurious or aggressive in nature (Berman & Walley, 2003). This is likely facilitated by the desire for conformity and self-identity that is particularly characteristic of this developmental period (Heilbron & Prinstein, 2008), and it helps explain the "contagion effects" that have been observed in adolescent inpatient units (Rosen & Walsh, 1989). Similar concerns are prompted by the increasing use of the mass media and specifically the Internet as a source of community and validation for self-injuring youth (Whitlock, Lader, & Conterio, 2007). Related work involving suicide deaths also demonstrate a "Werther effect," in which exposure to nonfictional (vs. fictional) portrayals of suicide in the media results in a subsequent increase in suicidal behaviors in the population (Pirkis & Blood, 2001).

Another potential explanation for suicide clusters is "assortative relating." Joiner (2003) suggests that per-

haps "suicide clusters" are preset, as people possessing similar characteristics are already more likely to form relationships with one another. In support of this explanation, Joiner reports that the concurrence of suicide risk is greater in self-selecting roommates than in randomly assigned roommates.

One environmental risk factor particularly notable and specific to suicide is household firearm ownership. This is a risk factor for suicide death across all age groups, and the strongest magnitude of association can be found among youth (5–19 years; Miller, Lippmann, Azrael, & Hemenway, 2007). This relationship is not accounted for by psychopathology or other suicide risk factors among either youth or adults (Miller et al., 2007; Miller, Barber, Azrael, Hemenway, & Molnar, 2009).

FUTURE DIRECTIONS

Although impressive progress has been made in the understanding of suicidal and nonsuicidal SITBs in recent years, there is a great deal of important work to be done in the years to come. Several recent papers have outlined key unanswered questions in the study of suicide and self-injury among youth (Brent, 2011; Nock, 2009a), the most important of which are highlighted below.

What Is Self-Harm?

As described in this chapter, researchers and clinicians have achieved increasing precision and consistency in the classification systems and definitions used in this area in recent years. However, further improvements are needed. For instance, the field lacks a method for clearly distinguishing between suicide ideation and suicide planning. That is, if a person thinks about killing him- or herself and imagines jumping off a bridge, does that constitute having a plan? If the person thinks of a method, but has not thought of a time and place to commit suicide, does the person have a plan? We know that having a plan increases the risk of suicide attempt, but it would be valuable to know what feature of planning conveys this increased risk. Similarly, our current assessments of suicidal intent do not neatly distinguish between suicidal and nonsuicidal self-injury. Most people who are suicidal report being ambivalent about wanting to die. However, the current standard is to consider those with zero intent as nonsuicidal, and those with all other levels of intent as suicidal. The development of methods that will more carefully quantify intent to die may improve our ability to predict and prevent suicidal behavior.

Our methods of assessing SITB presence, frequency, and characteristics also are quite crude. For example, the current state of the art in suicide assessment is retrospective self-report. Most researchers and clinicians currently do not have the ability to observe SITBs as they unfold in real time. Advances in technology, such as the development of electronic diaries and ambulatory physiological monitoring equipment, now make it possible to do so (e.g., Nock, Prinstein, & Sterba, 2009). Future efforts to use such tools to study SITBs should lead to major advances in our understanding of what these phenomena look like, and what factors trigger their occurrence.

Who Harms Themselves?

We now have comprehensive cross-national data on the epidemiology of suicidal thoughts and behaviors, as summarized above. However, complementary data are lacking for NSSI. The reason for this is that the large-scale, nationally representative surveys used to collect data on suicidal behavior have not included questions about NSSI. As the field moves forward, it will be important to include such assessments, so that we can obtain a better understanding of the actual scope of NSSI and monitor changes in the prevalence of this behavior over time. Also needed are data on how the prevalence and characteristics of NSSI may vary among those of different ages, sexes, and races/ethnicities.

Why Do People Harm Themselves?

Research over the past several decades has identified myriad risk factors for suicidal and nonsuicidal self-injury. However, much less is known about *how* or *why* these factors are associated with these outcomes. For example, we know that mental disorders increase the risk of SITBs, but we don't know why. What are the mechanisms through which this occurs? Relatedly, every theoretical model of SITBs suggests that they do not result from a single causal factor, but from the interaction of many different factors. Yet virtually all empirical studies of SITBs have examined bivariate, linear associations between putative risk factors and self-injurious outcomes. Future studies must begin to

help us understand how risk and protective factors work together to lead people to SITBs, and through what mechanisms or pathways this occurs.

How Do We Best Predict and Prevent These Behaviors?

Finally, and perhaps most importantly, we need more evidence-based methods of accurately predicting and/or preventing SITBs. Advances in our understanding of these behaviors have not yet been translated in to clinically useful tools for helping those at risk. To be sure, clinicians are assessing, monitoring, and treating people with SITBs. In fact, people in the United States are significantly more likely to receive treatment for SITBs than they were 10 years earlier (Kessler et al., 2005). But despite this increase in treatment, the rates of SITBs in the United States have remained unchanged. Building on the valuable work of many researchers, clinicians, and families, there is still a great deal of work to be done in order to decrease the enormous amount of personal suffering and broad societal costs associated with suicidal and nonsuicidal self-injury.

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PART IV

ANXIETY, OBSESSIVE–COMPULSIVE, AND STRESS DISORDERS

CHAPTER 8

Anxiety Disorders

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Fear and anxiety are common emotions that are a necessary part of the normal development of all children.[1] For some children, however, the levels of fear or anxiety are disproportionally high in relation to the cues or context (e.g., anxiety about grades for a student who is already receiving straight A's) or in relation to their developmental level (e.g., a fear of the dark for a 12-year-old). In such cases, when those emotions and their associated behaviors also lead to impairment in functioning—such as inability to attend school, make friends, perform academic tasks, or meet other developmental goals—their expression may be considered an anxiety disorder. Perhaps given the ubiquity of the emotions of fear and anxiety in everyday development, anxiety disorders collectively represent the most common type of psychiatric disorders among children (Anderson, Williams, McGee, & Silva, 1987; Costello & Angold, 1995; Kashani & Orvaschel, 1988; Kessler, Avenevoli, Costello, et al., 2012; Merikangas et al., 2010). Estimates from community samples show that one-third of adolescents will meet criteria for an anxiety disorder by the age of 18 (Merikangas et al., 2010), and studies of clinically referred samples show rates of anxiety disorders approaching 50% (Hammerness et al., 2008).

Anxiety disorders in childhood are more than just common. They are, by definition, associated with impairment in functioning, which in some cases can be extreme. For example, a considerable body of research shows that anxiety disorders in childhood are associated with later anxiety disorders, depression, substance use, and other negative mental health outcomes (Berg et al., 1989; Feehan, McGee, & Williams, 1993; Ferdinand & Verhulst, 1995; Flament et al., 1990; Keller et al., 1992; Langley, Bergman, McCracken, & Piacentini, 2004; Neal & Edelmann, 2003; Pine, Cohen, Gurley, Brook, & Ma, 1998; Woodward & Fergusson, 2001), and recent data from the National Comorbidity Study Replication—Adolescent Supplement suggests that having specific phobia, agoraphobia, social phobia (now known as social anxiety disorder), or panic disorder is the strongest predictor of most other subsequent disorders (Kessler, Avenevoli, McLaughlin, et al., 2012). Studies of community samples show that the presence of an anxiety disorder more than doubles the odds of impairment in family, educational, or peer functioning (e.g., Ezpeleta, Kessler, Erkanli, Costello, & Angold, 2001). Although this impairment can be more subtle than that caused by other disorders of childhood, such as externalizing disorders, the social costs of anxiety disorders are high. For example, a recent study estimated costs to families with clinically anxious children (e.g., health care costs, child care, missed

work or school days, lost leisure time) to be over 20 times higher than costs to families without such children (Bodden, Dirksen, & Bogels, 2008). Furthermore, when these disorders persist into adulthood, they continue to represent a high cost to society—accounting for an estimated 31.5% of 1990 adult mental health expenditures in the United States (DuPont et al., 1996). Although it is unclear whether this trend remains today, a recent systematic review found that across studies, anxiety disorders are responsible for both direct costs (e.g., treatment visits, drugs, emergency room visits), and indirect costs (e.g., reduced productivity, absence from work, early retirement), and that among the anxiety disorders, panic disorder and generalized anxiety disorder tend to shower higher direct costs than social phobia or specific phobia (Konnopka, Leichsenring, Leibing, & König, 2009).

Perhaps even more troubling than the current costs to society of this ongoing need for services is the number of children who are *not* receiving services. Data from the National Comorbidity Survey—Adolescent Supplement show that across adolescents with any of the more common disorders, the only other ones less likely to receive services than children with anxiety disorders (17.8%) are adolescents with substance use disorders (15.4%; Merikangas et al., 2011). When these numbers are compared with service utilization by adolescents with mood (37.7%), behavior (45.4%), and attentional disorders (59.8%), it is clear that adolescents with anxiety disorders significantly underutilize mental health services. To state this another way, the 2010 census reported that there are 74.18 million children under the age of 18 in the United States. Thus approximately 23.66 million children will suffer from an anxiety disorder sometime before the age of 18, and only 4.2 million of these will ever receive treatment for their illness, leaving 19.46 million children with untreated anxiety disorders to suffer in silence.

Not surprisingly, research on anxiety disorders in children has increased dramatically over the past 20 years in an effort to clarify the nature of the disorders, their impact, their etiology, and ultimately their treatment. What has emerged is a complex model detailing the interplay of genetics, temperament, early development, peers, family, and other factors in the course and expression of anxiety in children. Although far from complete, there is now a solid framework for understanding where anxiety disorders come from, how they change over time, and how they are related to each other and to other psychiatric disorders.

BRIEF HISTORICAL CONTEXT

Although a refined understanding of childhood anxiety disorders and their development is historically somewhat recent (e.g., Chorpita & Barlow, 1998; Rapee, Schniering, & Hudson, 2009; Vasey & Dadds, 2001), children's anxieties and fears have been described in the literature for over 100 years (Barrios & Hartmann, 1997). Some of the earliest research focused on case studies of childhood fears in the context of both psychoanalytic and behavioral theory. For example, in the classic case study of "Little Hans," Freud (1909/1955) defined and described several key unconscious processes operating in the development of phobia, such as the ego defense mechanisms of repression and displacement. Although the study of Little Hans has since been reconsidered (e.g., A. Freud, 1965), its value and place in psychoanalytic theory remain firmly ingrained. In a similar manner, the conditioned fear of a white laboratory rat in "Little Albert" provided early support for classical conditioning theories of the development of fears (Watson & Rayner, 1920). In this study, repeated pairings of a neutral stimulus (a white laboratory rat) and an aversive stimulus (a loud noise) resulted in the development of a conditioned fear response to the rat in 11-month-old Albert. In addition, Albert's fear generalized to a range of other stimuli, including a rabbit, a dog, a Santa Claus mask made with cotton balls, and a fur coat. Building on this work in yet another case study of a child, Mary Cover Jones (1924) described the treatment of 3-year-old Peter's fear of rabbits with a variety of behavioral techniques, including pairing the rabbit with a positive stimulus (food).

Although these and similar case studies of children served to further the interest and support for specific theoretical models and related therapeutic interventions, the study of anxiety disorders in children was essentially ignored until the latter part of the 20th century. This is both surprising and humbling, given the wealth of information and research over the last 80 years focused on the developmental progression of children's fears (e.g., see Barrios & Hartmann, 1997; Barrios & O'Dell, 1998; King, Hamilton, & Ollendick, 1988; Ollendick & King, 1991). In fact, prior to 1980, fear and anxiety reactions in children were largely ignored in psychiatric nosological systems; rather, they were studied as part of research investigating normative developmental reactions and were classified according to etiology (Hebb, 1946) or empirically based factor groupings (Miller, Barrett, Hampe, & Noble, 1972;

Ollendick, 1983; Scherer & Nakamura, 1968). That early research demonstrated that fears are common in children (e.g., Miller, 1983; Ollendick, 1983), that the number of fears reported by children declines with age (MacFarlane, Allen, & Honzik, 1954), and that the focus of the fear changes over time (e.g., Bauer, 1976). In addition, across studies, girls consistently endorse a greater number of fears than boys (Abe & Masui, 1981; Lapouse & Monk, 1958, 1959).

Formal psychiatric classification systems began to acknowledge the presence of pathological phobic reactions around the early 1950s. The first edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM; American Psychiatric Association [APA], 1952) identified phobias as psychoneurotic reactions, and in DSM-II (APA, 1968), the diagnostic category was changed to phobic neuroses. DSM-II introduced overanxious reaction as a distinct diagnostic category for children. These early DSM classification systems were heavily tied to psychoanalytic theory, purporting an unconscious process or conflict as the etiological mechanism for the phobic or overanxious reaction (Barlow, 2002). Although such theories have not stood the test of time, the inclusion of overanxious reaction in the psychiatric nosology marked a turning point for psychiatric classification, in that it began to give attention to anxiety disorders in children. Research on childhood anxiety disorders was relatively uncommon until the 1980s, and this lag may have been due in part to long-standing disagreements within the field as to what differentiates a clinical anxiety state from transient developmental fears and anxieties (Barrios & Hartmann, 1997; Strauss & Last, 1993). DSM-III (APA, 1980) and DSM-III-R (APA, 1987) represented the first attempts to delineate developmentally appropriate diagnostic criteria for phobic and other anxiety disorders in children. For example, separation anxiety disorder, avoidant disorder of childhood and adolescence, and overanxious disorder were posited as three anxiety disorders unique to childhood. At that time, children could be diagnosed with these three anxiety disorders in addition to any of the adult anxiety disorders, such as phobic disorder, obsessive–compulsive disorder, and posttraumatic stress disorder. Thus DSM-III and its revision precipitated a collection of studies examining the epidemiology and clinical characteristics of anxiety disorders in childhood (e.g., Francis, Last, & Strauss, 1987; Last, Francis, Hersen, Kazdin, & Strauss, 1987; Last, Hersen, Kazdin, Finkelstein, & Strauss, 1987; Last & Strauss, 1989). Those studies, in turn, led to changes and revisions in criteria for diagnosing anxiety disorders that were introduced in DSM-IV (APA, 1994).

This evolving classification system and the assessment instruments that followed (e.g., Silverman & Albano, 1996) enabled rigorous investigation into the prevalence, comorbidity, and severity of anxiety disorders in children. One highly consistent finding was that anxiety disorders are highly comorbid within themselves (homotypic comorbidity); that is, many children with an anxiety disorder have often had more than one—whether concurrently or across development (e.g., Benjamin, Costello, & Warren, 1990; Brady & Kendall, 1992; Kendall et al., 2010). Furthermore, a similar pattern has been shown with respect to depression and anxiety: Children with depression show elevated rates of anxiety disorders and vice versa, and anxiety disorders and depression are highly comorbid, especially across time (e.g., Costello, Mustillo, Erkanli, Keeler, & Angold, 2003, Hammerness et al., 2008).

Attempts to understand why anxiety disorders cooccur so often among themselves and with depression over the span of development led to some controversy regarding whether DSM-IV accurately represented distinct disorders, or whether it was artificially splitting subdimensions of broader pathological syndromes that truly occurred in nature (Brown, 1998; Caron & Rutter, 1991; Lilienfeld, Waldman, & Israel, 1994). Somewhat paradoxically, research has simultaneously demonstrated support for the validity of the DSM anxiety disorder syndromes (e.g., Comer & Kendall, 2004; Langer, Wood, Bergman, & Piacentini, 2010), as well as support for a single, overarching dimension underlying anxiety disorders that could perhaps better explain the high comorbidity observed among anxiety and depressive disorders (e.g., Chorpita, Albano, & Barlow, 1998; Lonigan, Carey, & Finch, 1994). Most recently, there have been attempts to unify these positions, and the emerging findings support the notion that both perspectives are likely to be valid. In other words, there is both a single underlying factor that contributes to the expression of anxiety disorders (and depression), and there are valid narrow-band syndromes of anxiety that are empirically distinct from one another. Collectively, this research paints a picture of a hierarchical model, which outlines multiple anxiety syndromes (e.g., separation anxiety, generalized anxiety, panic, social anxiety) associated with a higher-order factor common to most if not all anxiety disorders as well as depression. This hierarchical system enables us to understand the

relations among disorders (Chorpita, 2002; Clark & Watson, 1991; Craske, Rauch, et al., 2009; Joiner, Catanzaro, & Laurent, 1996; Lonigan et al., 1994). Given that such a conceptualization is relatively recent, research is only now beginning to investigate how this model behaves across the developmental span of childhood, and whether and which influences operate at the general level versus the syndrome-specific level. Before exploring these issues in more detail, this chapter first describes and examines the pathological syndromes of anxiety at the syndrome or disorder level.

DSM-5 ANXIETY DISORDERS

Although anxiety and fear are normal emotions, when they occur in the absence of typical cues and cause distress or impairment, they are referred to as anxiety disorders and phobias, respectively (Barlow, 1988). In DSM-5 (APA, 2013), children can be diagnosed with any of seven anxiety disorders: specific phobia, separation anxiety disorder, social anxiety disorder (formerly social phobia), selective mutism, panic disorder, agoraphobia, and generalized anxiety disorder. These disorders share anxious emotion as the predominant feature, expressed through specific and discrete cognitive, physiological, and behavioral reactions. Much of what distinguishes one anxiety disorder from the next is the focus of the child's anxiety. In this section, we define the core and related symptoms of specific DSM-5 anxiety disorders affecting children. A listing of DSM-5 criteria is provided in tabular form for each disorder. Whereas obsessive–compulsive disorder, posttraumatic stress disorder, and acute stress disorder were categorized with the anxiety disorders in DSM-IV, they are now categorized in DSM-5 with the obsessive–compulsive and related disorders and the trauma- and stressor-related disorders, respectively. (The reader interested in these disorders is referred to Piacentini, Chang, Snorrason, & Woods, Chapter 9, and Nader & Fletcher, Chapter 10, this volume, for a comprehensive review.)

Specific Phobia

Core Symptoms

Specific phobia (known as simple phobia prior to DSM-IV) refers to a pronounced fear of a specific situation or object (e.g., animals, heights, receiving an injection) that is disproportional to the actual danger posed and to the sociocultural context (see Table 8.1 for DSM-5 criteria). Exposure to the situation or object provokes fear, and in children, this fear may be expressed behaviorally as crying, throwing tantrums, freezing, or clinging to caregivers. The feared object or situation is actively avoided or is endured with great distress, and the fear and avoidance associated with the object causes major distress or impairment in functioning. Although DSM-IV required duration of symptoms for at least 6 months for children under the age of 18, in DSM-5 this criterion is extended to all ages, to minimize diagnosis of transient fears. Miller, Barrett, and Hampe (1974) differentiate specific phobia from normal developmental fears (e.g., a toddler's fear of strangers), in that the phobic reaction is excessive and out of proportion to the demands of the situation, cannot be reasoned away, leads to avoidance, persists over time, and interferes with activities or relationships. Although a great deal of research has examined specific phobia in children since Miller and colleagues' seminal description, the core features of the condition remain relatively unchanged.

Common fears and phobias of childhood include heights, darkness, loud noises (including thunder), injections, insects, dogs, and other small animals (Essau, Conradt, & Peterman, 2000; Silverman & Rabian, 1993; Strauss & Last, 1993). School phobia is also common in children, but the principal motivating condition for the observable avoidance behavior must be delineated for accurate differential diagnosis and prescriptive treatment planning (Kearney, 2001). A child may be diagnosed with a specific phobia of school if the fear is circumscribed to a particular school-related situation (e.g., fire drills) as opposed to fear of social or evaluative situations in the school setting, in which case social anxiety disorder might be a more appropriate diagnosis.

In the cognitive-behavioral models that have become increasingly well established over the past 40 years (Beck, Emery, & Greenberg, 2005; Kendall & MacDonald, 1993; Lang, 1968), the responses of children with phobias are often described in terms of three components of anxiety: behavioral, physiological, and cognitive. Behaviorally, avoidance is the predominant response of children with phobias. Avoidance may take the form of screaming, crying, throwing tantrums, or hiding in anticipation of confronting the feared stimulus. When contact with the phobic stimulus is unavoidable, clinging and begging caregivers for help to escape

TABLE 8.1. DSM-5 Diagnostic Criteria for Specific Phobia

A. Marked fear or anxiety about a specific object or situation (e.g., flying, heights, animals, receiving an injection, seeing blood).

Note: In children, the fear or anxiety may be expressed by crying, tantrums, freezing, or clinging.

B. The phobic object or situation almost always provokes immediate fear or anxiety.
C. The phobic object or situation is actively avoided or endured with intense fear or anxiety.
D. The fear or anxiety is out of proportion to the actual danger posed by the specific object or situation and to the sociocultural context.
E. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.
F. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
G. The disturbance is not better explained by the symptoms of another mental disorder, including fear, anxiety, and avoidance of situations associated with panic-like symptoms or other incapacitating symptoms (as in agoraphobia); objects or situations related to obsessions (as in obsessive–compulsive disorder); reminders of traumatic events (as in posttraumatic stress disorder); separation from home or attachment figures (as in separation anxiety disorder); or social situations (as in social anxiety disorder).

Specify if:

Code based on the phobic stimulus:

300.29 (F40.218) Animal (e.g., spiders, insects, dogs).
300.29 (F40.228) Natural environment (e.g., heights, storms, water).
300.29 (F40.23x) Blood-injection-injury (e.g., needles, invasive medical procedures).

Coding note: Select specific ICD-10-CM code as follows: **F40.230** fear of blood; **F40.231** fear of injections and transfusions; **F40.232** fear of other medical care; or **F40.233** fear of injury.

300.29 (F40.248) Situational (e.g., airplanes, elevators, enclosed places).
300.29 (F40.298) Other (e.g., situations that may lead to choking or vomiting; in children, e.g., loud sounds or costumed characters).

Coding note: When more than one phobic stimulus is present, code all ICD-10-CM codes that apply (e.g., for fear of snakes and flying, F40.218 specific phobia, animal, and F40.248 specific phobia, situational).

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the confrontation are common. Moreover, children with a specific phobia are apprehensive and hypervigilant regarding the feared stimulus. For example, children fearful of thunderstorms may scan the news or watch the sky prior to leaving home. Children with a specific phobia of dogs may go to great lengths to avoid walking down a street even when a dog is penned behind a fence. Children with specific phobia report physiological symptoms consistent with panic sensations, including rapid heart rate, sweating, hyperventilation, shakiness, and stomach upset. Cognitions of children with phobias are often characterized by catastrophic predictions or overestimation of the chance that a threatening event will occur upon exposure to the feared stimulus. Children with specific phobia also report anticipatory anxiety in the form of "What if" statements (Silverman & Rabian, 1993). For example, a child who has a phobia of thunderstorms may lament, "What if it storms on my way to school, and I get struck by lightning?"

Specifiers

According to DSM-5, there are five different kinds of specific phobia, which are identified by specifiers. The animal specifier includes fear of animals such as dogs, insects (e.g., bees, spiders, centipedes), and snakes. The natural environment specifier includes fear of events or situations occurring in the environment such as weather (e.g., storms, thunder), water, and heights. The situational specifier includes different kinds of situations such as driving, flying, crossing bridges, going through tunnels, riding elevators, or being in other enclosed spaces. The blood–injection–injury (BII) specifier includes fear of needles, invasive medical procedures,

and dental work. The last specifier, given simply as "other," is a category used when the feared object does not fall into one of the first four categories. Phobias in this category include fears of choking or vomiting, loud sounds (e.g., firecrackers, sirens), or costumed characters. In a community study of 1,035 German adolescents, of those with a diagnosis of specific phobia (3.5%), most fell into the animal or natural environment categories, and the "other" category was the least common (Essau et al., 2000). Across studies, fears of animals and heights are the most common types of specific phobia (Curtis, Magee, Eaton, Wittchen, & Kessler, 1998; Depla, ten Have, van Balkom, & de Graaf, 2008; Stinson et al., 2007).

Although there has been some speculation as to whether these categories represent clinically meaningful and valid subcategories (e.g., Antony, Brown, & Barlow, 1997), the research to date suggests that although there are some similarities, there is enough independence to warrant their continued separation. For example, using confirmatory factor analysis, Muris, Schmidt, and Merckelbach (1999) found that specific phobia symptoms in children ages 7–19 clustered into three types (animal phobia, BII, and environment/situation), and these appeared to be invariant across age and gender. In a recent review across the child, adolescent, and adult literatures in preparation for DSM-5 recommendations, both similarities and differences were found across the types (LeBeau et al., 2010). LeBeau and colleagues (2010) found similarities in age of onset, gender ratio, and treatment response, but differences in focus of fear, physiological fear response, impairment, and comorbidity. According to their review, natural environment and animal phobias share the most in common with other types, whereas the BII type shares the least with other types. As such, they recommended retaining these subcategories for the DSM-5.

Several studies have directly examined the similarities and differences across children with different types of specific phobia. In a large study of Korean children, different subtypes reportedly had different comorbidities and associated problems, suggesting distinctive profiles (Kim et al., 2010). For example, phobias of the animal subtype were associated with the presence of another anxiety disorder and oppositional defiant disorder (ODD), whereas natural environment phobias were associated with another anxiety disorder only, and BII phobias showed a significant association with attention-deficit/hyperactivity disorder (ADHD). Furthermore, although animal phobias were reported most frequently in their sample (49% of all individuals with specific phobia), children with natural environment and/or BII phobias demonstrated significantly higher scores on subscales of the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001) than children with animal phobias and children without a specific phobia diagnosis. Specifically, phobias of the natural environment type were related to higher scores on the Anxious/Depressed and Attention Problems CBCL subscales, and BII phobias were related to higher scores on the Attention Problems, Aggressive Behavior, and Externalizing Problems scales. These findings are consistent with a study by Ollendick, Öst, Reuterskiöld, and Costa (2010), who found that although there were no sociodemographic differences (age, sex, race, family structure, family income) between children with animal phobias and children with natural environment phobias, children with the natural environment type demonstrated significantly more internalizing problems, comorbid diagnoses, and lower life satisfaction than children with animal phobias; these findings suggest that the natural environment subtype is associated with greater clinical severity.

Associated Characteristics

In addition to experiencing fear and distress in the presence or anticipation of the phobic object or situation, children with a specific phobia may also demonstrate oppositional behaviors, presumably as a result of trying to avoid feared objects/situations. Adolescents with a specific phobia are likely to report somatic symptoms as well as depression (Essau et al., 2000; see section below for more details on comorbidities).

A vasovagal syncope or fainting response occurs in approximately 70–80% of adults with BII phobias (APA, 1994; Öst, Sterner, & Lindahl, 1984). Estimates specific to children are lacking at present. Decades of research and volumes on anxiety explain that this physiological response is diphasic: It is characterized by an initial brief acceleration of heart rate, followed by an immediate deceleration of heart rate and drop in blood pressure, which can lead to fainting (e.g., Barlow, 2002; Engel, 1978; Graham, Kabler, & Lunsford, 1961; Kozak & Montgomery, 1981). This response is unique to the BII type of specific phobia and is in contrast to the usual sustained acceleration of heart rate found in other specific phobia types. However, Ritz, Meuret, and Ayala (2010) recently critiqued the literature on the syncope response in the BII type. They argue that the

research to date is flawed by poor definitions of syncope; inconsistent findings on the initial acceleration of heart rate upon exposure to the feared stimulus; lack of clarity regarding which physiological parameters are important (i.e., heart rate, blood pressure, hyperventilation, adrenaline, vasopressin, etc.); lack of support for the diphasic response; and lack of emphasis on the role that cognitive variables, such as disgust and perceived loss of control, play in the fainting response. Thus, although it is clear that individuals with BII phobias show a unique pattern of physiological responses, the exact mechanisms of these physiological responses are not clearly understood.

Regardless of the mechanisms of syncope in BII phobias, it does appear that individuals with this type of specific phobia may be predisposed to this vasovagal response. For instance, according to some research, individuals with BII have an autonomic substrate that predisposes them to vasovagal syncope, and fainting during the blood phobic response is a manifestation of this underlying circulatory dysfunction (Accurso et al., 2001). It appears as though different parts of the brain are activated when individuals with BII, compared with individuals with spider phobia, are exposed to fear stimuli. When exposed to spider-related images, individuals with spider phobia showed increased activation in the dorsal anterior cingulate and anterior insula, whereas individuals with BII phobia showed increased activation in the thalamus and visual/attention areas (occipito-temporo-parietal cortex) when exposed to images related to blood, injections, and injuries (Caseras et al., 2010). However, it is unclear how or whether this functional neuroanatomical difference is related to vasovagal syncope, and whether this difference exists in children with BII.

Common Comorbidities

Several common comorbidities are found in children with specific phobia. In a community study of German adolescents, Essau and colleagues (2000) reported that 47.2% of children with specific phobia had another comorbid anxiety disorder, 36.1% had comorbid depressive disorders, 33.3% had comorbid somatoform disorders, and 8.3% had comorbid substance use disorders. Within the anxiety disorders, specific phobia co-occurred most commonly with posttraumatic stress disorder (13.9%), obsessive–compulsive disorder (11.1%), and anxiety disorder not otherwise specified (11.1%). In a community sample of adolescents, specific phobia was comorbid with separation anxiety disorder (odds ratio = 4.7) and social phobia (odds ratio = 7.2) (Lewinsohn, Zinbarg, Seeley, Lewinsohn, & Sack, 1997). In a community sample of Korean children ages 6–17, Kim and colleagues (2010) reported that 28.1% of children with specific phobia had at least one comorbid psychiatric diagnosis: 5.9% another anxiety disorder, 13% ADHD, and 13% ODD. Furthermore, in a study specifically examining the relation between depression and specific phobia by using data from the National Comorbidity Study, Choy, Fyer, and Goodwin (2007) found that individuals ages 15–54 with specific phobia experienced a significant increase in the likelihood of lifetime depression compared with those without specific phobia even after adjustments for lifetime comorbid anxiety disorders, and that the more fears an individual reported, the higher the risk for depression.

With regard to clinically referred children, Last, Perrin, Hersen, and Kazdin (1992) reported that 75% of referred children with specific phobia had a lifetime history of additional anxiety disorders, 32.5% had a lifetime history of any depressive disorder, and 22.5% had a lifetime history of any behavior disorder. The most common additional specific anxiety diagnosis was separation anxiety disorder (38.8%). In another clinic-referred sample, the most common concurrent comorbid diagnoses of specific phobia were generalized anxiety disorder, social anxiety disorder, and separation anxiety disorder (18.2%, 12.1%, and 9.1%, respectively) (Leyfer, Gallo, Cooper-Vince, & Pincus, 2013).

Epidemiology

The 12-month and lifetime prevalences for specific phobia in the National Comorbidity Study Replication—Adolescent Supplement, a large representative community sample of adolescents ages 13–18, were estimated at 15.8% and 19.3%, respectively—the highest rates of all DSM-IV psychological disorders (Kessler, Avenevoli, Costello, et al., 2012; Merikangas et al., 2010). In international community samples, 1-year prevalence of specific phobia was estimated at 7.9% in Korean children ages 6 to 17 (Kim et al., 2010), and lifetime prevalence at 3.5% in German adolescents ages 12–17 (Essau et al., 2000). In a primary care sample of children ages 8–17, the 1-year prevalence of specific phobia was 10% (Chavira, Stein, Bailey, & Stein, 2004). Among children referred to a specialty anxiety clinic, specific phobia was the third most common anxiety

disorder (27.6%) and the third most common comorbid diagnosis (10.4%) (Leyfer, Gallo, Cooper-Vince, & Pincus, 2013).

Developmental Course and Prognosis

Phobias of animals, darkness, insects, blood, and injury usually begin before age 7 (Marks & Gelder, 1966) and parallel the onset of normative fears in children, although the phobic diagnosis suggests that the fears have greater intensity and stability over time. Our understanding of the patterns of onset for childhood phobias is largely based on the retrospective report of adult phobic patients. For example, in the National Epidemiological Survey on Alcohol and Related Conditions, the mean age of onset across all types of specific phobia was 9.7 years (Stinson et al., 2007). Specifically, adult phobic patients place the onset of animal phobia between 6 and 7 years, environmental phobia at 6–12 years, blood phobia at 7–9 years, and doctors/dental/injection phobia at 9–15 years (Becker et al., 2007; Liddell & Lyons, 1978; Öst, 1987). Situational phobias tend to have a later onset, often in adolescence or young adulthood (Becker et al., 2007; Öst, 1987).

In contrast to the wealth of literature documenting the natural course of fears in children and retrospective reports from adults on the course of phobias, little empirical research has been conducted prospectively on the course of phobic disorders in childhood. In a classic and widely cited study, Agras, Chapin, and Oliveau (1972) followed a community sample of phobic individuals consisting of 10 children under the age of 20 years, and 20 adults. Participants were followed over a 5-year period, during which none received treatment for his or her phobia. Results from this study indicated that many phobic conditions resolve without active intervention. However, other researchers (e.g., Ollendick, 1979) have argued that although children improved in this study, they were not completely asymptomatic over the course of the follow-up assessment. It does appear that remission rates are higher in child and adolescent samples (Agras et al., 1972; Milne et al., 1995) than in adult samples (Stinson et al., 2007; Trumpf, Becker, Vriends, Meyer, & Margraf, 2009), and that remission rates may be associated with protective factors such as positive mental health and life satisfaction (Trumpf et al., 2009). Despite the finding that specific phobia is associated with significant psychosocial impairment (Essau et al., 2000), very few affected individuals (13.9% in adolescence and 8% in adulthood) actually seek treatment for the disorder, with mean age at first treatment in adults estimated at 31.3 years (Essau et al., 2000; Stinson et al., 2007).

Separation Anxiety Disorder

Core Symptoms

Separation anxiety disorder (hereafter abbreviated as SAD) is characterized by excessive anxiety and fear concerning separation from home or from caregivers to whom the individual is attached. DSM-5 outlines eight core symptoms, of which any three are required to meet criterion A (see Table 8.2). Three of those eight symptoms are related to distress and worry about separation from or harm to attachment figures. For example, children with SAD may worry about being kidnapped, getting lost, or having their parents involved in an accident. Three more symptoms are related to avoidance of work, school, being alone, or sleeping alone, and the last two symptoms of the first criterion involve nightmares and somatic complaints. Some research suggests that of these eight symptoms, the most common are recurrent excessive distress upon separation, reported by 87.4% of parents of children with SAD; reluctance to sleep separated from caregiver, reported by 85.7% of those parents; and reluctance to be alone, reported by 81.0% of those parents (Allen, Lavallee, Herren, Ruhe, & Schneider, 2010). Alternatively, nightmares about separation were reported by only 7.2% of parents of children with SAD (Allen et al., 2010), and have been found to be the least common symptom of SAD, dating back to DSM-III (e.g., Francis et al., 1987). Based on extensive clinical observations of children with separation anxiety, Eisen and Schaefer (2005) outlined four key symptom dimensions associated with SAD: fear of being alone, fear of abandonment, fear of physical illness, and worry about calamitous events. These dimensions correspond roughly to the DSM-5 criteria, but emphasize dimensions posited to be more relevant to treatment considerations.

As outlined in criterion A, SAD symptoms must be inappropriate for the child's age and expected developmental level, given that fears of separation are part of normative development from approximately age 7 months to 6 years (e.g., Bernstein & Borchardt, 1991). The changes from DSM-IV to DSM-5 are relatively minor, with the main emphasis involving a rewording to make the diagnosis more appropriate for adults as well as children, and removal of the criterion that the disorder onset must be prior to age 18 (the disorder has now been moved from a section on disorders diagnosed

TABLE 8.2. DSM-5 Diagnostic Criteria for Separation Anxiety Disorder

A. Developmentally inappropriate and excessive fear or anxiety concerning separation from those to whom the individual is attached, as evidenced by at least three of the following:
   1. Recurrent excessive distress when anticipating or experiencing separation from home or from major attachment figures.
   2. Persistent and excessive worry about losing major attachment figures or about possible harm to them, such as illness, injury, disasters, or death.
   3. Persistent and excessive worry about experiencing an untoward event (e.g., getting lost, being kidnapped, having an accident, becoming ill) that causes separation from a major attachment figure.
   4. Persistent reluctance or refusal to go out, away from home, to school, to work, or elsewhere because of fear of separation.
   5. Persistent and excessive fear of or reluctance about being alone or without major attachment figures at home or in other settings.
   6. Persistent reluctance or refusal to sleep away from home or to go to sleep without being near a major attachment figure.
   7. Repeated nightmares involving the theme of separation.
   8. Repeated complaints of physical symptoms (e.g., headaches, stomachaches, nausea, vomiting) when separation from major attachment figures occurs or is anticipated.

B. The fear, anxiety, or avoidance is persistent, lasting at least 4 weeks in children and adolescents and typically 6 months or more in adults.

C. The disturbance causes clinically significant distress or impairment in social, academic, occupational, or other important areas of functioning.

D. The disturbance is not better explained by another mental disorder, such as refusing to leave home because of excessive resistance to change in autism spectrum disorder; delusions or hallucinations concerning separation in psychotic disorders; refusal to go outside without a trusted companion in agoraphobia; worries about ill health or other harm befalling significant others in generalized anxiety disorder; or concerns about having an illness in illness anxiety disorder.

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in childhood to the anxiety disorders section). For example, symptom 4 of criterion A now includes avoiding going to work as an example of separation-relevant avoidance (see Table 8.2). Likewise, symptom 5 has been reworded to emphasize separation from "attachment figures" as opposed to "significant adults," giving a bit more flexibility for the application of this diagnosis across the lifespan (e.g., for adults, anxiety could be triggered by separation from their offspring; Hock, McBride, & Gnezda, 1989). In addition, the duration criterion was extended from 4 weeks to 6 months for adults (minimum duration for children and adolescents is still 4 weeks), to minimize diagnosis of transient fears of separation anxiety. Finally, unchanged from DSM-IV is the requirement that the disturbance should cause marked impairment and should not be better accounted for by another diagnosis.

Associated Characteristics

Although distress about separation is one of the defining characteristics of SAD, one of the most common and interfering symptoms involves school refusal behavior. In its most extreme form, school refusal behavior involves complete avoidance of school; milder forms can include pleas to stay home, leaving school early, visits to the school nurse, or phone calls to the caregiver (Kearney, 2001). Although many anxiety disorders can co-occur with school refusal, SAD is the most common, with estimates from about 38% (Last & Strauss, 1990) to 50% (Borchardt, Giesler, Bernstein, & Crosby, 1994) among children with school refusal referred to outpatient clinics, and estimates as high as 57% among children with school refusal in inpatient settings (Borchardt et al., 1994). The association is even stronger in the other direction; for example, Last, Francis, and colleagues (1987) reported school refusal behavior in 73% of children with SAD, whereas school refusal behavior occurs only at a rate of 1% in the general population (Last & Strauss, 1990).

Another symptom that is often quite pronounced among children with separation anxiety is complaints of aches, pains, or other symptoms of physical illness. For example, Last (1991) found that somatic complaints were evidenced by 78% of children with SAD, which was the second highest rate for all anxiety disorders and

significantly higher than the rate of such complaints among all other anxiety disorders combined (53%). Furthermore, although somatic complaints commonly co-occur with other anxiety disorders and even among typical children (e.g., Alfvén, 1993), with SAD such complaints usually occur in anticipation of separation, such as at bedtime or before school. Common somatic complaints include headaches, stomachaches, or nausea (e.g., Egger, Costello, Erkanli, & Angold, 1999). Interestingly, when somatic complaints co-occur with SAD, the rates of school refusal are noted to be significantly higher (58% vs. 39%; Last, 1991).

Common Comorbidities

In a clinic-referred sample, SAD was associated with a number of concurrent comorbid anxiety diagnoses, with generalized anxiety disorder, specific phobia, and social anxiety disorder being the most common (23.7%, 21.1% and 17.1%) (Leyfer et al., 2013). In a retrospective study of SAD, 86.1% of adults who met criteria for childhood SAD also met criteria for another psychiatric disorder (Shear, Jin, Ruscio, Walters, & Kessler, 2006). Other anxiety disorders were the most common comorbid diagnoses (65.3%), with over one-third of adults with childhood SAD reporting symptoms of specific phobia and social phobia. Mood disorders (53.1%), impulse control disorders (48.3%), and substance use disorders (28.8%) were also common (Shear et al., 2006). Although panic disorder was only comorbid among 15.9% in adults with childhood SAD in Shear and colleagues' (2006) sample, considerable research has tested the idea that childhood-onset separation anxiety has a unique association with panic disorder in adulthood; both supportive results (e.g., Hayward, Wilson, Lagle, Killen, & Taylor, 2004; Silove et al., 1995) and unsupportive findings (Aschenbrand, Kendall, Webb, Safford, & Flannery-Schroeder, 2003) have been obtained. This controversial issue is discussed further in the section below on panic disorder.

Epidemiology

Twelve-month and lifetime prevalence estimates of childhood SAD range from 1 to 7.6% (Costello et al., 2003; Kessler, Avenevoli, Costello, et al., 2012; Merikangas et al., 2010; Shear et al., 2006). Among clinic-referred samples of anxious children, rates of SAD have ranged from 10 to 33%, perhaps as a function of child age and clinic type (Chavira, Garland, Yeh, McCabe, & Hough, 2009; Last, Francis, et al., 1987; Leyfer et al., 2013). Whereas many of the anxiety disorders discussed in this chapter increase in prevalence over the course of development, given the nature of the condition, SAD decreases in prevalence from childhood through adolescence (Costello et al., 2003).

Developmental Course and Prognosis

SAD is most often diagnosed in prepubertal children (Bowen, Offord, & Boyle, 1990; Kashani & Orvaschel, 1988), with an average age of onset reported at just around age 7 (Lewinsohn, Holm-Denoma, Small, Seeley, & Joiner, 2008), although separation anxiety can occur at any age (Bell-Dolan & Brazeal, 1993; Nielsen et al., 2000). In one study examining the developmental differences in the expression of separation anxiety symptoms, Francis and colleagues (1987) found age differences but not gender differences with regard to which DSM-III criteria were most frequently endorsed. Young prepubertal children (ages 5–8) were most likely to report fears of harm befalling attachment figures, nightmares, or school refusal; children ages 9–12 endorsed excessive distress at the time of separation; and adolescents (ages 13–16) most often endorsed somatic complaints and school refusal. Moreover, younger children endorsed a greater number of symptoms overall relative to adolescents.

In terms of course, research suggests that about 80% of cases of SAD remit within 18 months (Foley, Pickles, Maes, Silberg & Eaves, 2004). Similar results regarding high rates of symptom remission have been found in younger samples as well. For example, Kearney, Sims, Pursell, and Tillotson (2003) found that separation anxiety symptoms present in 3-year-olds were no longer present in about half of the children when they were assessed again 3.5 years later. Although this seems encouraging in terms of prognosis, Foley and colleagues (2004) found that 41% of separation anxiety cases still had some psychiatric disorder 18 months later, which suggests that for two out of five children with separation anxiety, the disorder may simply be replaced by something else rather than by full remission of all disorders.

Three factors were noted in children for whom an SAD diagnosis persisted over time: (1) significantly higher prevalence of ODD; (2) significantly more impairment associated with symptoms of ADHD; and (3) mothers who were less satisfied with their marriages (Foley et al., 2004). This same research has shown that children with persistent SAD are at a significantly increased risk of major depression, relative to those with

transient SAD. Other research has shown that persistent SAD is associated with poor mental health outcomes, with 73.5% of adults who had SAD as adolescents showing some psychiatric diagnosis in young adulthood, most commonly depression (e.g., Lewinsohn et al., 2008). Some cases of separation anxiety persist into adulthood, and these are associated with a high degree of impairment, neuroticism, depression, and poor response to treatment (Silove, Marnane, Wagner, Manicavasagar, & Rees, 2010).

Social Anxiety Disorder (Formerly Social Phobia)

Core Symptoms

The essential feature of social anxiety disorder (hereafter abbreviated as SOC; formerly social phobia in DSM-IV) is a marked and persistent fear of one or more social situations—including social interactions (e.g., having a conversation with another person), being observed by others (e.g., being seen while eating in a cafeteria), and performing before others (e.g., speaking in front of the class)—where the child fears that he or she will behave in a way or show anxiety symptoms that will be negatively evaluated or will offend others (see Table 8.3 for DSM-5 criteria). In children, these fears must exist in peer situations and not just in situations with adults. Exposure to the feared social or performance situation provokes fear or anxiety. In children this fear response may present as crying, having tantrums, clinging, freezing, shrinking, or refusal to speak. Children with SOC may either actively avoid these situations or endure them with marked fear or anxiety. In DSM-IV, individuals with SOC had to recognize that the fear was excessive or unreasonable, but this was not necessary for children due to cognitive-developmental reasons. However, in DSM-5 individuals of all ages do not need to recognize that the fear is excessive or unreasonable; nevertheless, the fear or anxiety must be considered out of proportion to the actual danger posed by the situation and to the sociocultural context, and if another medical condition is present (e.g., disfigurement, obesity), the fear, anxiety, or avoidance is unrelated or is excessive. Symptoms are persistent, last for 6 or more months and cause significant interference in functioning or marked distress.

TABLE 8.3. DSM-5 Diagnostic Criteria for Social Anxiety Disorder (Social Phobia)

A. Marked fear or anxiety about one or more social situations in which the individual is exposed to possible scrutiny by others. Examples include social interactions (e.g., having a conversation, meeting unfamiliar people), being observed (e.g., eating or drinking), and performing in front of others (e.g., giving a speech).

   Note: In children, the anxiety must occur in peer settings and not just during interactions with adults.

B. The individual fears that he or she will act in a way or show anxiety symptoms that will be negatively evaluated (i.e., will be humiliating or embarrassing; will lead to rejection or offend others).

C. The social situations almost always provoke fear or anxiety.

   Note: In children, the fear or anxiety may be expressed by crying, tantrums, freezing, clinging, shrinking, or failing to speak in social situations.

D. The social situations are avoided or endured with intense fear or anxiety.

E. The fear or anxiety is out of proportion to the actual threat posed by the social situation and to the sociocultural context.

F. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.

G. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

H. The fear, anxiety, or avoidance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

I. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder, such as panic disorder, body dysmorphic disorder, or autism spectrum disorder.

J. If another medical condition (e.g., Parkinson's disease, obesity, disfigurement from burns or injury) is present, the fear, anxiety, or avoidance is clearly unrelated or is excessive.

Specify if:

Performance only: If the fear is restricted to speaking or performing in public.

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Children and adolescents with SOC often fear a number of different situations. In a study of children with SOC, the top most feared social situations identified on the Anxiety Disorders Interview Schedule—Child and Parent Version (ADIS-C/P) included (1) speaking to new or unfamiliar people (64%%), (2) answering questions in class (49%), (3) speaking to adults (47%), (4) oral reports or reading aloud (44%), and (5) musical or athletic performances (44%) (Bernstein, Bernat, Davis & Layne, 2008). In a similar study of adolescents with SOC, the top most feared social situations identified on the ADIS-C/P included (1) oral reports or reading aloud (90.5%), (2) attending dances (90.5%), (3) parties or activity nights (87.3%), (4) asking the teacher a question or asking for help (87.3%), and (5) musical or athletic performances (87.3%) (Beidel et al., 2007). Children with SOC often have fewer friends than children without SOC, have trouble making friends, are reluctant to join group activities, and endorse feelings of loneliness on self-report measures (Beidel, Turner, & Morris, 1999; Beidel et al., 2007; Bernstein et al., 2008; La Greca, 2001).

In feared situations, a child with SOC will experience excessive concerns about embarrassment, negative evaluation, and rejection. Observations and responses of children with SOC reveal their thoughts to be characterized by negative self-focus (Alfano, Beidel, & Turner, 2006; Higa & Daleiden, 2008) and accompanied by a range of autonomic symptoms and sensations (Albano, 1995; Albano, Marten, Holt, Heimberg, & Barlow, 1995). Complaints of stomachaches and illness are common, especially among younger children. Older children and adolescents become overly concerned with the physical manifestations of anxiety, much like adults with SOC. Fears of blushing or shaking during an oral report, unsteady voice while speaking to peers, or sweating that others may notice serve to magnify a child's SOC. Research has demonstrated that the aforementioned physical responses of children with SOC are consistent with those of their adult counterparts (see Beidel & Morris, 1993, 1995). Behaviorally, younger children may manifest excessive clinging and crying, whereas older children are likely to shrink from social contact and avoid being the focus of attention.

Specifiers

DSM-IV included a generalized subtype of social phobia, which was used to indicate whether the social fear included most social situations. Data suggest that the generalized subtype is the most common form of SOC in children and adolescents (Beidel & Morris, 1993; Hofmann et al., 1999), and that individuals with generalized SOC may be distinguished from those with the nongeneralized subtype by way of earlier age of onset, greater impairment in functioning, higher risk for comorbid conditions, a greater likelihood of earlier inhibited temperament, and stronger familial transmission (Beidel & Turner, 2007; Hofmann & Barlow, 2002; Mannuzza et al., 1995). However, in a recent review of the literature, Bögels and colleagues (2010) did not find support for a unique generalized subtype. Instead, they found greater support for a dimensional view of SOC in which severity of the condition is a function of the number of feared situations, and they argued that the use of the generalized specifier is therefore not useful. For instance, in a sample of adolescents with SOC, 92% met criteria for the generalized subtype (Beidel et al., 2007). Bögels and colleagues argue that in fact, more findings support the use of a performance-only subtype than the generalized subtype; hence DSM-5 does not include a generalized subtype, but does include a performance-only specifier to indicate fears that are restricted to speaking or performing in public.

Associated Characteristics

Although some suggest that having a shy temperament may be associated with SOC, recent data from the National Comorbidity Survey Replication—Adolescent Supplement suggest that only 12% of adolescents who self-identify as shy also meet criteria for SOC (Burstein, Ameli-Grillon, & Merikangas, 2011). On the other hand, about 70% of adolescents who meet lifetime criteria for SOC self-identify as shy. Furthermore, those with SOC are more likely to meet criteria for other psychiatric disorders and to demonstrate more impairment than those who are characterized as shy. Thus shyness may be a characteristic on which individuals fall along a continuum, with adolescents meeting criteria for SOC falling at the extreme end of that continuum.

Difficulties with peers constitute a common associated problem for children and adolescents with SOC. Children with SOC receive fewer positive outcomes from their interactions with peers at school, compared with nonanxious matched controls (Spence, Donovan, & Brechman-Toussaint, 1999); are more likely to be nominated by their peers as seeking anxious solitude (Gazelle, Workman, & Allan, 2010); and are less likely to be accepted by their peers and more likely to ex-

perience peer victimization (Erath, Flanagan, & Bierman, 2007; McCabe, Antony, Summerfeldt, Liss, & Swinson, 2003). However, it is unclear whether problems with peers contribute to the development of SOC or whether symptoms of SOC precede peer problems. Some research supports the former; for instance, in the Waterloo longitudinal study, Rubin (1993) found that peer isolation in second grade was correlated with social incompetence, shyness, and unpopularity in fifth grade. More recently, in a 5-year longitudinal study, peer neglect status in the first grade was correlated with social anxiety in the fifth grade (Morris, 2004). On the other hand, in another 5-year longitudinal study, a bidirectional relation between SOC and peer rejection emerged, in which anxious withdrawal contributed to peer rejection and peer rejection contributed to anxious withdrawal (Gazelle & Ladd, 2003).

Either as a result of lack of healthy peer relationships or perhaps as a cause of negative peer relations, or both, children with SOC exhibit poor social skills (Alfano et al., 2006; Beidel et al., 1999, 2007; Ginsburg, La Greca, & Silverman, 1998; Inderbitzen-Nolan, Anderson, & Johnson, 2007; Spence et al., 1999). For example, children with SOC exhibit reduced nonverbal communication (e.g., reduced facial activity; Melfsen, Osterlow, & Florin, 2000), as well as demonstrate impaired perception of social cues (e.g., interpretation of facial expressions) relative to nonanxious controls (Melfsen & Florin, 2002; Simonian, Beidel, Turner, Berkes, & Long, 2001).

Another associated feature of SOC is the experience of self-focused attention (SFA). Cognitive models of SOC in adults propose that the experience of a socially threatening situation elicits or heightens anxious apprehension and induces a shift in focus from external stimuli to detailed monitoring of the self (Clark & Wells, 1995; Hofmann & Barlow, 2002; Rapee & Heimberg, 1997). This self-focus produces increased awareness of feared anxiety responses and interferes with processing the situation and other people's behavior. Several studies have examined SFA, which is defined as "an awareness of self-referent, internally generated information that stands in contrast to an awareness of externally generated information derived through sensory receptors" (Ingram, 1990, p. 156), and negative self-imagery (NSI), which is defined as inaccurate visual impressions of the self (Alfano, Beidel, & Turner, 2008; Clark & Wells, 1995) in younger populations. For instance, Alfano and colleagues (2008) experimentally manipulated NSI in socially anxious and nonanxious adolescents. Socially anxious adolescents reported significantly more anxiety, rated their own performance as poor, and were observed to demonstrate more anxiety and poorer performance than nonanxious adolescents with induced NSI and a control group. Furthermore, in a community sample of children and adolescents, Higa and Daleiden (2008) found that children with elevated social anxiety reported heightened SFA. In a study of physiological arousal, Anderson and Hope (2009) found that although there was no difference between adolescents with SOC and nonanxious adolescents on objective physiological arousal, adolescents with SOC perceived elevated physiological arousal during two anxiety-provoking situations. These authors suggested that socially anxious adolescents had heightened SFA, which led them to be more aware of small increases in physiological arousal compared with nonanxious adolescents, who also demonstrated slight physiological arousal but did not perceive the arousal.

Research also suggests that negative cognitions persist even after a social event has occurred. According to Clark and Wells (1995), individuals with SOC engage in ruminative processes following a social event, in which they review the distressing event and reexperience negative feelings and cognitions. In a recent study of such postevent processing, children ages 8–12 with SOC demonstrated more negative and less positive postevent processing than healthy controls (Schmitz, Kramer, Blechert, & Tuschen-Caffier, 2010). Treatment specifically designed to target such negative cognitive processing appears to effectively increase positive appraisals and decrease state anxiety in socially anxious adolescents (Parr & Cartwright-Hatton, 2009). Thus emerging research suggests that adult cognitive models of SOC may extend to younger populations.

Common Comorbidities

Across studies of clinical samples of children and adolescents with SOC, the most common comorbid diagnosis is generalized anxiety disorder; other common comorbid anxiety disorders are SAD and specific phobia (Beidel et al., 2007; Bernstein et al., 2008; Leyfer et al., 2013). Children with SOC also demonstrate significantly higher levels of depressed mood than normal children (Beidel et al., 1999, 2007; Francis, Last, & Strauss, 1992; La Greca & Lopez, 1998; Leyfer et al., 2013). In fact, SOC in childhood appears to be a risk factor for the development of depression in adolescence and adulthood. In a retrospective study of adults with

comorbid major depressive disorder and SOC, adults reported SOC onset prior to major depression onset; the mean age of onset of SOC was 11.7 years, and that of major depression was 22 years (Dalrymple & Zimmerman, 2011). Furthermore, in prospective and retrospective studies, adults with childhood and adolescent onset of SOC have greater severity and treatment-resistant forms of major depression, compared with those who have adult-onset SOC (Beesdo et al., 2007; Dalrymple & Zimmerman, 2011).

SOC in childhood and adolescence also appears to be a risk factor for the development of substance use disorders. In the Oregon longitudinal study of depression, having a diagnosis of SOC at baseline was associated with greater odds of developing alcohol and cannabis dependence, even after the researchers controlled for gender, depression, and conduct disorder (Buckner et al., 2008). In fact, the relation between SOC and alcohol and cannabis dependence remained even after other anxiety disorders were controlled for, suggesting that SOC serves as a unique risk factor for substance dependence.

Epidemiology

After specific phobia, SOC is the next most common anxiety disorder in community prevalence studies, occurring in 8.2% of adolescents and in 9.1% across the lifespan (Kessler, Avenevoli, Costello, et al., 2012; Merikangas et al., 2010). These findings are similar to findings in samples from other countries. For instance, in a study of Dutch adolescents, the 6-month prevalence rate for SOC was 6.3% (Verhulst, van der Ende, Ferdinand, & Kasius, 1997). Furthermore, rates of SOC (6%) are also similar among children receiving public mental health services (Chavira et al., 2009). Among clinic-referred samples, SOC is the second most common anxiety disorder as well, occurring in 34% of children and adolescents (Leyfer et al., 2013).

Developmental Course and Prognosis

Although the average age of onset for SOC is between 10 and 13 years (e.g., Essau et al., 2000; Strauss & Last, 1993; Wittchen, Stein, & Kessler, 1999), it is not usually diagnosed until late adolescence or early adulthood. Perhaps owing to the nature of this disorder, individuals with SOC take significantly longer to seek help after symptom onset than individuals with other anxiety disorders do (Wagner, Silove, Marnane, & Rouen, 2006), and those with the most social fears tend to be the least likely to seek treatment (Ruscio et al., 2008).

Children and adolescents with SOC are at high risk for developing major depression (Last et al., 1992), with the likelihood increasing over time. Epidemiological studies indicate that SOC in early adolescence is a direct pathway to the development of substance use disorders by middle to late adolescence (Kessler et al., 1994). It is possible that adolescents stumble into the vicious cycle of drinking to ease their social anxiety, allowing them to enter challenging situations, and then form a dependence on use of alcohol to continue their social behavior. SOC (in addition to other anxiety disorders) is also associated with significant impairment in role functioning, delayed or unstable marriage, and an overall poor quality of life (Forthofer, Kessler, Story, & Gotlib, 1996; Kessler, Foster, Saunders, & Stang, 1995; Kessler & Frank, 1997). As compared with their peers without the disorder, girls with SOC are more likely to fail to complete high school and enter college, and both young men and young women with SOC who enter college are more likely to fail to graduate (Kessler et al., 1995). Such truncated educational attainment is associated with a number of adverse life course and societal consequences (see Kessler et al., 1995), including longer dependence on the family of origin, less training for and entering into the work force, and greater demands on health care systems.

Selective Mutism

Core Symptoms

A new development for the DSM-5 is the inclusion of selective mutism (hereafter abbreviated as SM) as an anxiety disorder. In the DSM-IV, SM was classified among the disorders usually first diagnosed in infancy, childhood, or adolescence. SM is characterized by lack of speech in situations where speaking is socially expected (e.g., school, social situations) in children who have little or no trouble speaking in other situations (e.g., with family) (see Table 8.4 for DSM-5 criteria). SM symptoms must be present for at least 1 month and should not be restricted to the first month of school. Furthermore, the inability to speak is not due to a lack of knowledge of the primary language required in the social situation, and it cannot be accounted for by a communication disorder or another developmental disorder; although these can be present, they are not the main reason for the failure to speak.

TABLE 8.4. DSM-5 Diagnostic Criteria for Selective Mutism

A. Consistent failure to speak in specific social situations in which there is an expectation for speaking (e.g., at school) despite speaking in other situations.
B. The disturbance interferes with educational or occupational achievement or with social communication.
C. The duration of the disturbance is at least 1 month (not limited to the first month of school).
D. The failure to speak is not attributable to a lack of knowledge of, or comfort with, the spoken language required in the social situation.
E. The disturbance is not better explained by a communication disorder (e.g., childhood-onset fluency disorder) and does not occur exclusively during the course of autism spectrum disorder, schizophrenia, or another psychotic disorder.

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Associated Characteristics

Similar to children with SOC, children with SM demonstrate lower social competence than their peers. For instance, teachers and parents rate children with SM as lower on verbal and nonverbal social skills than children without SM (Cunningham, McHolm, & Boyle, 2006), and as lower on verbal social skills than children with other anxiety disorders (Carbone et al., 2010). Furthermore, teachers rate children with SM as lower than nonanxious controls on social assertion, self-control, and total social skills, and parents rate children with SM as lower on social responsibility and total social skills than nonanxious controls (Carbone et al., 2010).

Despite the suggestion that SM is a variant of or related to ODD, given the staunch refusal by children with SM to speak even when encouraged by adults, the research does not support this claim. Although some children with SM do exhibit some mild oppositional symptoms (Kristensen, 2001), these behaviors are similar to those exhibited by children with other anxiety disorders when confronted with feared stimuli, and their oppositional behaviors appear to be confined to settings in which they are required to speak (Cunningham, McHolm, Boyle, & Patel, 2004; Cunningham et al., 2006).

Common Comorbidities

Given the high degree of comorbidity between SM and SOC (around 65%; Black & Uhde, 1995; Kristensen, 2000), some researchers propose that SM is a developmentally specific variant of SOC in young children or a developmental precursor to SOC (Bergman, Piacentini, & McCracken, 2002). This is further supported by family history research (Black & Uhde, 1995; Chavira, Shipon-Blum, Hitchcock, Cohan, & Stein, 2007; Cohan, Price, & Stein, 2006; Kristensen & Torgersen, 2002) and by treatment outcome research, which suggests that similar treatments work for both SM and SOC (Cohan, Chavira, & Stein, 2006; Standart & Le Couteur, 2003). In addition to SOC, other common comorbid diagnoses among children with SM include communication and elimination disorders (Cohan et al., 2008; Dummit et al., 1997; Kristensen, 2000; Steinhausen & Juzi, 1996) and ODD (Yeganeh, Beidel, & Turner, 2006).

Epidemiology

SMis a rare condition, with estimates of prevalence ranging between 0.03 and 0.2% in community samples (Bergman et al., 2002; Elizur & Perednik, 2003; Kolvin & Fundudis, 1981; Kopp & Gillberg, 1997; Kumpulainen, Räsänen, Raaska, & Somppi, 1998). Given how rare SM is, few clinic-referred epidemiological studies include SM as a diagnosis in their research, and thus the prevalence among referred populations is unknown. Whereas some research suggests that there may be a higher prevalence of SM in girls than in boys (e.g., Cunningham et al., 2004; Dummit et al., 1997; Kristensen, 2000), other work suggests that it occurs equally in both sexes (e.g., Bergman et al., 2002; Elizur & Perednik, 2003).

Developmental Course and Prognosis

SM is typically first noticed upon school entry (i.e., at about the age of 5), when pressures to speak in social

situations increase (Cunningham et al., 2004; Garcia, Freeman, Francis, Miller, & Leonard, 2004; Giddan, Ross, Sechler, & Becker, 1997), although reports of onset around age 3 exist (e.g., Remschmidt, Poller, Herpertz-Dahlmann, Hennighausen, & Gutenbrunner, 2001). However, despite being first noticed at entry to school, children are typically not referred for assessment and treatment until they are older (between 6 and 9 years of age) (Ford, Sladeczek, Carlson, & Kratochwill, 1998; Kumpulainen et al., 1998; Remschmidt et al., 2001; Standart & Le Couteur, 2003). Research on the course of SM is limited; however, in a study of 24 children seeking treatment for SM, 46% showed moderate to marked improvement, whereas 54% continued to show little to no improvement in the 5–10 years after treatment (Kolvin & Fundudis, 1981). In another study of follow-up data 12 years after referral, Remschmidt and colleagues (2001) reported that 81% of individuals with SM experienced gradual amelioration of symptoms, whereas 19% experienced abrupt relief of symptoms and 19% experienced periods of relapse. Notably, among those children who show improvement in SM symptoms, the majority do so by age 10, suggesting that those who fail to show improvements by middle childhood experience a more persistent form of the disorder (Kolvin & Fundudis, 1981). Moreover, even though children may experience reductions or complete absence of SM symptoms, research suggests that they still continue to experience difficulty in social situations (Kolvin & Fundudis, 1981; Remschmidt et al., 2001).

Panic Disorder and Agoraphobia

Core Symptoms

In DSM-IV, panic disorder and agoraphobia were linked together: A diagnosis of panic disorder was made with or without agoraphobia, and agoraphobia alone had to be noted as such (agoraphobia without history of panic disorder). Notably, in DSM-5 panic disorder and agoraphobia are now unlinked, each with separate diagnostic criteria. This change was made because research suggests that a number of adolescents and adults experience agoraphobia without panic symptoms (Wittchen et al., 2008). Despite this finding, however, the available research with children and adolescents to date has primarily examined the two conditions together, and hence we discuss them together in this section.

The core defining symptom of panic disorder is the presence of panic attacks. A panic attack is a discrete period of intense fear, physical discomfort, or both that culminates within a matter of minutes and is associated with at least 4 of a list of 13 potential symptoms, including such things as pounding heart, sweating, trembling, and shortness of breath. A panic attack is not a formal DSM diagnosis and can be experienced by individuals who do not meet diagnostic criteria for panic disorder. A diagnosis of panic disorder is defined by the occurrence of recurrent unexpected panic attacks in which at least one attack was followed by a month of either of the following: persisting worry or concern about experiencing future attacks or their consequences, or a marked maladaptive change in behavior related to the attacks (see Table 8.5). In addition, the panic attacks cannot result from the direct physical effects of a substance, such as medications or caffeine, or from another medical condition (e.g., hyperthyroidism). Throughout this section, the term "panic attack" is used to refer to discrete and intense periods of fear or discomfort that might or might not occur within the context of panic disorder, whereas the term "panic disorder" is used to refer the presence of the full constellation of symptoms as outlined in Table 8.5.

Symptoms associated with panic attacks most commonly reported by children and adolescents in both clinical and community samples include palpitations, trembling or shaking, dizziness, shortness of breath, faintness, sweating, and chest pain (Diler et al., 2004; Doerfler, Connor, Volungis, & Toscano, 2007; King, Ollendick, Mattis, Yang, & Tonge, 1996; Last & Strauss, 1989; Warren & Zgourides, 1988). Although somatic symptoms are more frequently reported than cognitive symptoms, a considerable proportion of children endorse symptoms such as fears of dying or "going crazy" (Doerfler et al., 2007; King et al., 1996). Moreover, there appears to be continuity between the presentation of panic symptoms in childhood and adulthood, without evidence to suggest that different diagnostic criteria are warranted for these age groups (Biederman et al., 1997; Craske et al., 2010). Those differences that have been observed in the experience of panic symptoms among adolescents and adults have suggested that adolescents worry less than adults do about subsequent attacks and their implications, report a lower likelihood of changing their behavior in response to the attacks, and are more reticent about feelings associated with the panic attacks (Craske et al., 2010; Wittchen, Reed, & Kessler, 1998).

TABLE 8.5. DSM-5 Diagnostic Criteria for Panic Disorder

A. Recurrent unexpected panic attacks. A panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur:
Note: The abrupt surge can occur from a calm state or an anxious state.

1. Palpitations, pounding heart, or accelerated heart rate.
2. Sweating.
3. Trembling or shaking.
4. Sensations of shortness of breath or smothering.
5. Feelings of choking.
6. Chest pain or discomfort.
7. Nausea or abdominal distress.
8. Feeling dizzy, unsteady, light-headed, or faint.
9. Chills or heat sensations.
10. Paresthesias (numbness or tingling sensations).
11. Derealization (feelings of unreality) or depersonalization (being detached from oneself).
12. Fear of losing control or "going crazy."
13. Fear of dying.

Note: Culture-specific symptoms (e.g., tinnitus, neck soreness, headache, uncontrollable screaming or crying) may be seen. Such symptoms should not count as one of the four required symptoms.

B. At least one of the attacks has been followed by 1 month (or more) of one or both of the following:

1. Persistent concern or worry about additional panic attacks or their consequences (e.g., losing control, having a heart attack, "going crazy").
2. A significant maladaptive change in behavior related to the attacks (e.g., behaviors designed to avoid having panic attacks, such as avoidance of exercise or unfamiliar situations).

C. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism, cardiopulmonary disorders).

D. The disturbance is not better explained by another mental disorder (e.g., the panic attacks do not occur only in response to feared social situations, as in social anxiety disorder; in response to circumscribed phobic objects or situations, as in specific phobia; in response to obsessions, as in obsessive–compulsive disorder; in response to reminders of traumatic events, as in posttraumatic stress disorder; or in response to separation from attachment figures, as in separation anxiety disorder).

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Related Symptoms

In addition to experiencing panic symptoms, children and adolescents with panic disorder may display concomitant agoraphobia, defined as the fear of being in situations from which escape may be difficult or embarrassing, or in which help is not readily available in the event of a panic attack (Kearney, Albano, Eisen, Allan, & Barlow, 1997; Masi, Favilla, Mucci, & Millepiedi, 2000). In one study (Kearney et al., 1997), situations reported as most often avoided by adolescents with panic disorder included restaurants/school cafeterias, crowds, small rooms, auditoriums, elevators, parks, grocery stores, shopping malls, being home alone, and movie theaters. Two of the most commonly endorsed symptoms of adolescents diagnosed with agoraphobia, both independently and in the presence of panic disorder, are enduring situations with intense anxiety when avoidance is not possible and needing a companion when away from home (Biederman et al., 1997; Doerfler et al., 2007). A child with panic disorder may also avoid school situations such as riding the bus or attending gym class, or may present with an outright refusal to attend school. In some cases, a parent or close friend becomes the child's "safety person," and activities are endured in the presence of this person. To ensure attendance, a parent may attempt to accompany the child during the school day. Although this behavior resembles SAD, the differential diagnosis

must be made according to the focus of the child's fear. In panic disorder, the fear is of the panic attack itself or the physical sensations accompanying the attack, and is not triggered by the fear of becoming lost or separated from a caregiver or loved one.

In a large normative sample (N = 3,021) ages 14–24 at the baseline assessment and followed longitudinally for 10 years, Wittchen and colleagues (2008) observed that agoraphobia, although often considered a related feature of panic, is a discrete disorder that can be conceptualized independently of both panic attacks and panic disorder. Specifically, in this sample, agoraphobia evidenced sex and age differences with respect to incidence and onset that were distinct from those observed with panic attacks and panic disorder. The progression and stability of agoraphobia was also different from that of panic disorder, and panic attacks were not reliably identified as a precursor to the onset of agoraphobia. These findings are consistent with the recent changes in DSM-5, suggesting that rather than an outcome of panic disorder, agoraphobia is an anxiety disorder in its own right; this builds on previous findings of agoraphobia in the absence of panic disorder in adolescents (e.g., Biederman et al., 1997; see Table 8.6 for DSM-5 criteria for agoraphobia). Although rates of agoraphobia as high as 15% have been cited in clinical samples (Biederman et al., 1997), Wittchen and colleagues (2008) reported an incidence of 0.6% for agoraphobia with no history of panic in their normative sample when employing strict DSM-IV hierarchical rules for diagnosis, and an estimated incidence of 5.3% when attending only to the endorsement of marked fear in one or more situations and disregarding whether or not there was a concurrent presence of "panic-like" symptoms. Most recently, as reported in the National Comorbidity Survey Replication—Adolescent Supple-

TABLE 8.6. DSM-5 Diagnostic Criteria for Agoraphobia

A. Marked fear or anxiety about two (or more) of the following five situations:
   1. Using public transportation (e.g., automobiles, buses, trains, ships, planes).
   2. Being in open spaces (e.g., parking lots, marketplaces, bridges).
   3. Being in enclosed places (e.g., shops, theaters, cinemas).
   4. Standing in line or being in a crowd.
   5. Being outside of the home alone.

B. The individual fears of avoids these situations because of thoughts that escape might be difficult or help might not be available in the event of developing panic-like symptoms or other incapacitating or embarrassing symptoms (e.g., fear of falling in the elderly; fear of incontinence).

C. The agoraphobic situations almost always provoke fear or anxiety.

D. The agoraphobic situations are actively avoided, require the presence of a companion, or are endured with intense fear or anxiety.

E. The fear or anxiety is out of proportion to the actual danger posed by the agoraphobic situations and to the sociocultural context.

F. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.

G. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

H. If another medical condition (e.g., inflammatory bowel disease, Parkinson's disease) is present, the fear, anxiety, or avoidance is clearly excessive.

I. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder—for example, the symptoms are not confined to specific phobia, situational type; do not involve only social situations (as in social anxiety disorder); and are not related exclusively to obsessions (as in obsessive–compulsive disorder), perceived defects or flaws in physical appearance (as in body dysmorphic disorder), reminders of traumatic events (as in posttraumatic stress disorder), or fear of separation (as in separation anxiety disorder).

Note: Agoraphobia is diagnosed irrespective of the presence of panic disorder. If an individual's presentation meets criteria for panic disorder and agoraphobia, both diagnoses should be assigned.

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ment, the 12-month prevalence rate for agoraphobia among a community sample of adolescents ages 13–17 years was 1.8% (Kessler, Avenevoli, Costello, et al., 2012); the lifetime prevalence of agoraphobia in this same sample was 2.4% (Merikangas et al., 2010). One possible reason for the disparity in terms of prevalence estimates and the general lack of current data pertaining to agoraphobia in the absence of panic disorder is that those with agoraphobia only have been found to be least likely to seek clinical attention for their symptoms (Wittchen et al., 2008). Evidence has also suggested that agoraphobia in the absence of panic disorder does not tend to aggregate in families, but might potentially contribute to the familial transmission of panic disorder (Nocon et al., 2008).

Associated Characteristics

Both panic attacks and panic disorder have been associated with increased risk of suicidal ideation and suicide attempts (Goodwin & Roy-Byrne, 2006). However, it has been suggested that major depression, commonly comorbid with panic disorder, might interact with panic symptoms and suicide attempts in multiple ways. For example, the co-occurrence of panic disorder and depression could result in subsequent suicide attempts; conversely, the co-occurrence of panic disorder and suicide attempts could indicate an especially severe case of depression; finally, depression might result from panic disorder, with suicide attempts indicating particularly severe cases of comorbid anxiety and depression (Goodwin & Roy-Byrne, 2006). Given the higher prevalence of suicide attempts observed in cases of comorbid panic and depression (25%) than in cases of depression (16%) or panic disorder (5.2%) alone, it seems that the association between panic and suicide attempts is best explained by the co-occurrence of depression with panic disorder (Roy-Byrne et al., 2000). More recent findings are consistent with the general hypothesis that depression may be a mediator between anxiety disorders and suicidal ideation (Greene, Chorpita, & Austin, 2009).

Respiratory illnesses also appear to be commonly associated with panic disorder. In a longitudinal study conducted with a community sample, being female, having respiratory illnesses at age 15, or having parents who had experiences with respiratory illnesses at age 18 were factors associated with increased risk of developing subsequent panic disorder with agoraphobia (Craske, Poulton, Tsao, & Plotkin, 2001). For boys, high levels of emotional reactivity, a personal history of asthma, or a greater incidence of colds and ear infections by age 3 were associated with an increased risk of later panic disorder with agoraphobia. Findings from this study suggested that experiences with respiratory illness during childhood positively differentiated individuals with and without panic disorder with agoraphobia by ages 18 and 21 from nondisordered controls (Craske et al., 2001).

Common Comorbidities

Panic disorder is frequently comorbid with other anxiety disorders (Biederman et al., 1997), as well as with depressive disorders (Bittner et al., 2004). In a longitudinal community-based study, the presence of panic disorder was associated with a greater likelihood of having at least one other DSM diagnosis (89.4% vs. 52.8%), any anxiety disorder (54.6% vs. 25.0%), any mood disorder (42.7% vs. 15.5%), and any substance disorder (60.4% vs. 27.5%) (Goodwin et al., 2004). Indeed, even the presence of panic attacks alone has been found to function as a nonspecific "risk marker" for psychopathology and comorbidity (Goodwin et al., 2004; Reed & Wittchen, 1998). Among clinical samples, significant rates of comorbid major depression (50%; Diler et al., 2004), separation anxiety (89%), and generalized anxiety (86%) have been reported (Doerfler et al., 2007). In addition to anxiety and depression, panic disorder has also been found to be comorbid with mania/hypomania, ADHD, and ODD (Doerfler et al., 2007).

The relation between SAD and panic disorder has been perhaps more closely studied than the comorbidity of panic with other diagnoses because researchers have sought to address whether separation experiences during childhood might contribute to the later development of panic (e.g., Gittelman & Klein, 1985; Mattis & Ollendick, 1997) or whether SAD might be a childhood expression of adult panic disorder. In a longitudinal study of children of parents both with and without major depression and panic disorder, Biederman and colleagues (2007) reported that SAD at baseline was the best predictor of panic disorder 5 years later. Moreover, childhood SAD has also been found to be the best predictor of childhood-onset panic disorder as reported retrospectively by adults (Biederman et al., 2005). However, although a range of studies provide support for a link between childhood SAD and the subsequent development of panic disorder, separation anxiety also

predicts other subsequent psychopathology, suggesting that it may be a nonspecific marker of later anxiety and depression rather than a specific risk factor for panic (Biederman et al., 2007; Craske et al., 2010). Children diagnosed with both disorders exhibit significantly greater levels of impairment, evidence more severe psychopathology, and have a higher rate of comorbidity than those diagnosed with SAD alone (Doerfler, Toscano, & Connor, 2008).

Epidemiology

The prevalence of panic disorder is lower among children and adolescents than other anxiety disorders (Hayward & Sanborn, 2002) with prevalence rates typically increasing during adolescence, particularly in girls (Wittchen et al., 2008). In clinical samples, prevalence rates for panic disorder have ranged from 2% (Diler et al., 2004) to 13% (Doerfler et al., 2007), whereas rates ranging from 1.6% (Reed & Wittchen, 1998) to 8.7% (Hayward et al., 2004) have been reported in community samples. Most recently, as reported in the National Comorbidity Survey Replication—Adolescent Supplement, the 12-month prevalence rate for panic disorder (with or without agoraphobia) among a community sample of adolescents ages 13–17 years was 1.9% (Kessler, Avenevoli, Costello, et al., 2012); the lifetime prevalence of panic disorder in this same sample was 2.3% (Merikangas et al., 2010). Conversely, much higher rates of panic attacks have been reported among nonreferred adolescents (e.g., Hayward et al., 2004; Wittchen et al., 2008), suggesting that as many as 16% of adolescents may have experienced a panic attack as defined by DSM (King et al., 1997).

Consistent with the pattern for adults with panic disorder, rates appear to be twice as high among adolescent girls as boys (King et al., 1997; Last & Strauss, 1989; Ollendick, Mattis, & King, 1994; Reed & Wittchen, 1998). In a longitudinal community-based study, Wittchen and colleagues (2008) noted an absence of gender differences prior to the age of 15 with respect to the rates of panic attacks observed; concerning panic disorder, although small gender differences are evident prior to age 14, differential rates of the disorder between boys and girls increased markedly between the ages of 14 and 25. Moreover, between the ages of 13 and 26 an increase in the incidence of new cases of panic disorder in girls was observed, whereas the increase of new cases among boys was less pronounced (Wittchen et al., 2008).

Developmental Course and Prognosis

At one time, panic disorder was considered an anxiety disorder of adulthood that did not occur in children and only rarely occurred in adolescents (see Kearney & Silverman, 1992; Moreau & Weissman, 1992; Nelles & Barlow, 1988). Children were thought to be incapable of forming catastrophic misinterpretations of bodily sensations—cognitions that are central to the disorder. However, over time findings have emerged supporting the existence of panic attacks and panic disorder in children and adolescents (e.g., Abelson & Alessi, 1992; Black & Robbins, 1990; Biederman et al., 1997; Doerfler et al., 2007; Hayward, Killen, Kraemer, & Taylor, 2000; Kearney, Albano, Eisen, Allan, & Barlow, 1997; Last & Strauss, 1989; Moreau & Follett, 1993; Moreau & Weissman, 1992; Ollendick, 1995; Ollendick et al., 1994). Historically, although studies have indicated the presence of panic disorder in children under the age of 13 (e.g., Biederman et al., 1997; Kearney et al., 1997), adolescents constituted the majority of these samples (e.g., Last & Strauss, 1989).

In their review of the literature specific to panic attacks and panic disorder in children, Moreau and Follett (1993) cited studies in which the onset of panic attacks occurred in children as young as between the ages of 1 and 5, but they noted that the highest rate of the onset of panic disorder appeared to be between the ages of 15 and 19. These authors also cited six case reports of panic disorder in a combined sample of 22 children, 12 of whom were under the age of 10 when symptoms of panic were first reported, as well as three studies of clinically referred children and adolescents in which 7 children and 27 adolescents were diagnosed with panic disorder (Moreau & Follett, 1993). Ollendick and colleagues (1994) similarly suggested that whereas panic attacks are common among adolescents, with 40–60% of adolescents surveyed reporting having experienced a panic attack, they are present but less frequently observed in children. Interestingly, Hayward and colleagues (1992) reported that among 754 children ages 10.3–15.6 years, the increased occurrence of panic attacks observed was associated with pubertal progression as assessed through the Tanner self-staging method, which is a means of determining an individual's level of pubertal development. Specifically, participants in this study were presented with standardized written and pictorial descriptions of five stages of physical development during puberty, and were asked to indicate which stage best depicted their pubertal

development. Overall, panic attacks were more commonly reported by girls evidencing advanced pubertal development, regardless of age (Hayward et al., 1992).

More recent studies have also documented the presence of panic disorder in children, but with similarly small numbers. Diler and colleagues (2004) observed that among 42 children diagnosed with panic disorder, 88% were age 13 or over. Biederman and colleagues (2007) similarly reported that six children in their sample experienced panic disorder with an onset prior to age 13. Two additional studies reported mean ages of onset of panic disorder during childhood (5.1 years [Biederman et al., 2005] and 11.4 years [Doerfler et al., 2008]); however, the first study was of a sample whose family members were diagnosed with panic disorder or agoraphobia, and the second was of a clinic-referred sample whose referrals were typically under the age of 10. Together these findings converge to suggest that cases of childhood panic disorder are few in number, in the context of a diagnosis that has a very low prevalence rate relative to the other anxiety disorders in this age group (Diler et al., 2004; Hayward & Sanborn, 2002; Reed & Wittchen, 1998; Wittchen et al., 1998, 2008).

The course for childhood panic disorder is typically chronic, and continuity has been found between child and adult presentations of this disorder (Biederman et al., 1997). In a community-based study employing retrospective and longitudinal prospective data collected at two time points 19.7 months apart from adolescents who were ages 14–17 at baseline, panic disorder was found to be one of the most stable anxiety disorders, even when both threshold and subthreshold diagnoses at the baseline and follow-up assessments were taken into account (Wittchen, Lieb, Pfister, & Schuster, 2000). Moreover, panic disorder was associated with one of the lowest complete remission rates (50%) (Wittchen et al., 2000), suggesting a particularly chronic and unremitting course for this disorder in the absence of intervention. In data taken from the original National Comorbidity Survey, Goodwin and Hamilton (2002) observed that individuals who had panic disorder with an early onset (at or prior to age 20) accompanied by fear (defined as feeling afraid of subsequent attacks after the first panic attack) had significantly earlier onsets of a range of comorbid disorders, had families with higher rates of psychological disorders, and had an increased risk for and lethality of suicide attempts relative to those whose panic attacks did not fit these criteria. Similarly, examination of data from the Harvard–Brown Anxiety Research Project, a prospective 15-year longitudinal study of anxiety disorders, revealed that adults with an early age of onset (less than 20 years) of panic disorder were more likely to have comorbid major depressive disorder, generalized anxiety disorder, and social phobia at baseline; and that adults with early-onset panic disorder with agoraphobia were more likely than those with late onset of these disorders to experience recurrence of symptoms after a period of remission (Ramsawh, Weisberg, Dyck, Stout & Keller, 2011). Interestingly, none of the other anxiety disorders in this study evidenced differences between early and late onset, suggesting that early-onset panic disorder represents a particularly serious condition.

Generalized Anxiety Disorder

Core Symptoms

The hallmark feature of generalized anxiety disorder (hereafter abbreviated as GAD) is extreme, uncontrollable worry about several events and activities, occurring more days than not, for at least 6 months (see Table 8.7). Unrealistic and excessive worrying about future events was present in over 95% of a clinic sample of children with overanxious disorder of childhood and adolescence (OAD) (Strauss, Lease, Last, & Francis, 1988).[2] The uncontrollable worry characteristic of GAD may be focused on a number of general life concerns, including the future, past behavior, and competence in areas such as sports, academics, and peer relationships. The most frequently reported worries of a clinical sample of children with GAD included tests/grades, natural disasters, being physically attacked, future school performance, and being bullied or scapegoated by peers (Weems, Silverman, & La Greca, 2000). It is not uncommon for children with GAD to worry about a number of adult concerns as well, such as the family finances (Bell-Dolan & Brazeal, 1993). Children with GAD may experience worry concerning performance in school, athletics, social relationships, and so on, often to the point of being perfectionistic (Bell-Dolan & Brazeal, 1993; Strauss, 1990). Consequently, these children impose exceedingly high standards for achievement on themselves and are excessively self-critical if they fail to meet these standards.

Several studies have sought to discover what distinguishes normative from clinical worry in children and adolescents. For example, research has demonstrated that although nonreferred children also worry about

TABLE 8.7. DSM-5 Diagnostic Criteria for Generalized Anxiety Disorder

A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).
B. The individual finds it difficult to control the worry.
C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months):

   Note: Only one item is required in children.

   1. Restlessn or feeling keyed up or on edge.
   2. Being easily fatigued.
   3. Difficulty concentrating or mind going blank.
   4. Irritability.
   5. Muscle tension.
   6. Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep).

D. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism).
F. The disturbance is not better explained by another mental disorder (e.g., anxiety or worry about having panic attacks in panic disorder, negative evaluation in social anxiety disorder [social phobia], contamination or other obsessions in obsessive–compulsive disorder, separation from attachment figures in separation anxiety disorder, reminders of traumatic events in posttraumatic stress disorder, gaining weight in anorexia nervosa, physical complaints in somatic symptom disorder, perceived appearance flaws in body dysmorphic disorder, having a serious illness in illness anxiety disorder, or the content of delusional beliefs in schizophrenia or delusional disorder).

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low-frequency events (e.g., being robbed, stabbed, shot at) (Silverman, La Greca, & Wasserstein, 1995), children with GAD may not recognize that such events have a low probability of occurrence. Other research has found that the self-reported intensity of worry, as opposed to the number of worries, differentiated clinic-referred children from nonclinical controls (Muris, Meesters, Merckelbach, Sermon, & Zwakhalen, 1998; Perrin & Last, 1997; Weems et al., 2000). Furthermore, intensity of worry is most predictive of clinician ratings of impairment for children with GAD (Layne, Bernat, Victor, & Bernstein, 2009). In fact, these studies demonstrated that nonreferred children report just as many worries as clinical samples, suggesting that the intensity of worry may be the mechanism leading to a sense of uncontrollability over the worry process (Weems et al., 2000).

Early cognitive theories conceptualized worry as an avoidant coping strategy in response to perceived future threats (Borkovec, 1994; Borkovec, Alcaine, & Behar, 2004). According to these theories, worry is a cognitive approach to identifying ways to prepare for the worst or to stop bad things from happening. Furthermore, avoidance models of worry suggest that worry as a coping strategy is negatively reinforced by the reduction of somatic responses and emotional processing of negative events, and that this reduction maintains future worry. However, a growing body of research suggests that worry actually causes physiological activation (for a thorough review, see Newman & Llera, 2011), thus calling into question the avoidance theory of worry. Newman and Llera (2011) have proposed a revised "contrast avoidance" model of worry to account for these discrepant findings. They suggest that those with GAD employ worry as a strategy to avoid a negative contrast. In other words, individuals with GAD prefer to feel chronically distressed, instead of experiencing a shift from a positive state to a negative state or from a moderately negative state to an extremely negative state (e.g., "If I expect the worst, I won't be disappointed"; Borkovec & Roemer, 1995). Newman and Llera argue that worry in their model is not reinforced by reduction in somatic responses, but rather by relief when the negative event does not occur. Research is needed to examine whether these cognitive models of worry apply to children.

In addition to emphasizing excessive and uncontrollable worry, DSM-5 outlines six specific somatic symptoms, of which one is required to make the diagnosis in children and adolescents (i.e., restlessness, fatigue, trouble concentrating, irritability, tensed muscles, and/or disturbed sleep; see Table 8.7). Similar to adults with GAD, many children with GAD are referred for treatment by their pediatricians or by gastrointestinal specialists because of significant somatic complaints (Bell-Dolan & Brazeal, 1993). In one study of children with GAD, the most common symptoms associated with worry included restlessness, difficulty concentrating, and sleep disturbance (Layne et al., 2009); another study found that children with a primary diagnosis of GAD experienced greater sleep disturbances than children with other primary anxiety disorder diagnoses (Alfano, Pina, Zerr, & Villalta, 2010). Some research has suggested that other symptoms, such as headaches, stomachaches, muscle tension, sweating, and trembling, are commonly reported among children with GAD (Eisen & Engler, 1995); however, Tracey, Chorpita, Douban, and Barlow (1997) found the muscle tension symptom to be infrequently endorsed by both children and their parents in a clinical sample evaluated with DSM-IV criteria. Similarly, Comer, Pincus, and Hofmann (2012) found in a large sample of 650 anxious children that muscle tension showed the lowest sensitivity across DSM-IV associated symptoms and had the lowest prevalence among children with GAD. On the other hand, irritability and restlessness demonstrated favorable diagnostic value in this study. Furthermore, Comer and colleagues found that in their sample, fatigue, difficulty concentrating, and sleep disturbances (which some argue overlap with symptoms of depression) continued to be related to a diagnosis of GAD even after depression was controlled for.

To explore further the distinction between somatic and worry symptoms of GAD, Higa-McMillan, Smith, Chorpita, and Hayashi (2008) examined symptoms reported on the ADIS-C/P in a clinically referred sample of 289 children and adolescents. Confirmatory factor analysis supported a two-factor model of GAD, in which worry symptoms clustered together on a separate factor from somatic symptoms. Higa-McMillan and colleagues also found that the GAD somatic factor was almost as strongly related to social phobia and major depressive disorder factors as it was to the GAD worry factor; this finding complements work by Tracey and colleagues (1997), who found that the negative predictive power of the somatic criterion for a diagnosis of GAD was low because children with other anxiety disorders also endorsed somatic symptoms. Lending further support to the idea that somatic complaints are not especially good indicators of GAD, Kendall and Pimentel (2003) found that parents consistently reported more somatic symptoms in their offspring than the children reported in themselves, and Tracey and colleagues and Kendall and Pimentel also found that adolescents reported more somatic symptoms than children. Thus it appears that somatic symptoms may not play as significant a role as worry in the phenomenology of GAD in young children as they do in adolescents and adults; this may be due to developmental differences, since younger children are still learning to become aware of somatic experiences and to link these to feelings of anxiety and worry. Nevertheless, the disparity in findings between this work and that of Comer and colleagues (2012) described above suggests the need for further research.

Associated Characteristics

Children and adolescents with GAD experience a number of associated symptoms and characteristics. For instance, in a clinical sample of 157 referred children and adolescents with GAD, feelings of tension, apprehensive expectation, negative self-image, need for reassurance, and irritability were among the most common associated symptoms, occurring in more than 75% of the sample (Masi et al., 2004). Children and teens with GAD also lack perceived control over their environment, and this relation exists even after adjustment for general negative affect (Frala, Leen-Feldner, Blumenthal, & Barreto, 2010).

A growing body of research suggests that intolerance of uncertainty (abbreviated in this discussion as IU) is a cognitive vulnerability factor of worry and GAD in adults (e.g., Dugas, Buhr, & Ladouceur, 2004), and recent work suggests that IU may play a role in GAD among children (Comer et al., 2009; Fialko, Bolton, & Perrin, 2012). IU is described as the tendency to hold a negative set of beliefs about uncertain events and their consequences or the inability to tolerate ambiguity (Koerner & Dugas, 2008). IU is considered a cognitive disposition that may confer risk for GAD because it is a higher-order vulnerability factor that predisposes individuals toward other cognitive processes involved in the maintenance of worry in adults. These processes include thought suppression and distraction strategies (i.e., cognitive avoidance [CA]); viewing events as

threats that will be difficult to cope with (i.e., negative problem orientation); and beliefs that worrying can help to solve problems and prevent feared outcomes (i.e., positive beliefs about worry [PB]) (Borkovec, 1994; Dugas, Gagnon, Ladouceur, & Freeston, 1998). Fialko and colleagues (2012) recently tested Dugas and colleagues' (1998) model of IU, examining whether worry frequency mediated the hypothesized relation between cognitive processes (IU, PB, and CA) and anxiety in a sample of 515 children and adolescents. They found that among adolescents ages 13–19, Dugas and colleagues' model fit relatively well, with IU acting as a higher-order vulnerability factor for both CA and PB. They also found support for a direct path between IU and anxiety, as well as between CA and anxiety. They concluded that IU and CA are significant risk factors not only for worries but also for anxiety. Furthermore, in children ages 7–12, they found that IU had indirect paths to anxiety via CA and worry, as well as a direct path to anxiety similar to the adolescent sample. However, they did not find support for PB in the child sample, suggesting that PB may develop over time. Taken together, it appears that IU and CA play a significant role in worries and potentially GAD in children and adolescents, just as they do in adults. In fact, functional magnetic resonance imaging research has demonstrated that IU is positively correlated with activity in frontal and limbic regions during uncertainty tasks in adolescents, further implicating this trait in the development and maintenance of GAD (Krain et al., 2008).

Common Comorbidities

Among the anxiety disorders, GAD is one of the most frequently comorbid (e.g., Masi et al., 2004). For instance, in a clinic-referred sample at a specialty clinic for anxiety and related concerns, GAD was not only the most common diagnosis (37%), but also one of the most common comorbid diagnoses (15.6%; the rate for SOC was 15.8%) (Leyfer et al., 2013). In addition, children and adolescents with GAD are often comorbid for a number of other psychiatric disorders. In the Leyfer and colleagues (2013) study of clinic-referred children, 71% of children with GAD had a comorbid diagnosis; SOC was the most common comorbid diagnosis (33.1%), followed by specific phobia (16.9%), SAD (15.4%), and depression (12.3%). However, patterns of comorbidity seem to change somewhat by sample, perhaps reflecting referral patterns. For instance, in the Masi and colleagues (2004) sample of 157 clinically referred children and adolescents with GAD, depression was the most common comorbid psychiatric diagnosis, occurring in 56% of their sample. Other comorbid conditions included specific phobia (42%), SAD (31.8%), social phobia (28%), externalizing disorder (21%), obsessive–compulsive disorder (19.7%), panic disorder (16.6%), and bipolar disorder (11%). In this sample, children with GAD were more likely than adolescents to have a comorbid diagnosis of SAD, and boys with GAD were more likely than girls to have a comorbid externalizing disorder (Masi et al., 2004).

Masi and colleagues' (2004) finding that depression is the most common comorbid diagnosis among children and adolescents with GAD is consistent with other research, which suggests that GAD may have a stronger relation to unipolar depression than it does to the other anxiety disorders. For instance, in the Higa-McMillan and colleagues (2008) study, GAD evidenced a stronger relation to depression than it did to social phobia. This finding is consistent with a substantial body of evidence in adults (e.g., Brown, Chorpita, & Barlow, 1998; Moffitt et al., 2007) as well as a study by Lahey and colleagues (2008), which also demonstrated that GAD is structurally more closely linked to the depressive disorders than to other anxiety disorders. Furthermore, epidemiological research suggests that adolescent GAD predicts depression in young adulthood (Copeland, Shanahan, Costello, & Angold, 2009).

Epidemiology

Although GAD is not uncommon in children and adolescents, with rates in community samples ranging from 0.16 to 10.8% (Cartwright-Hatton, McNicol, & Doubleday, 2006), it was the least common anxiety disorder among teens ages 13–18 reported in the National Comorbidity Study Replication—Adolescent Supplement, with 12-month prevalence rates of 1.1% and lifetime rates of 2.2% (Kessler, Avenevoli, Costello, et al., 2012; Merikangas et al., 2010). When OAD was removed from DSM-IV and replaced with GAD, community prevalence rates dropped, suggesting that some children who would have received a diagnosis of OAD in the past remain undiagnosed with GAD criteria (Beesdo, Knappe, & Pine, 2009). Nevertheless, in a recent study, GAD was the most common anxiety disorder diagnosis (37.1%) among children referred to a specialty anxiety clinic (Leyfer et al., 2013).

Developmental Course and Prognosis

Given that OAD was a diagnosis specific to childhood in DSM-III and DSM-III-R, as well as the fact that it was removed as a diagnosis from DSM-IV, research on the developmental course and prognosis for OAD and GAD in childhood are somewhat conflicting, despite some research suggesting a high degree of overlap between the two conditions (e.g., Kendall & Warman, 1996; Tracey et al., 1997). For instance, studies examining DSM-III and DSM-III-R diagnoses suggested that OAD may begin as early as age 4 years (Beitchman, Wekerle, & Hood, 1987), with the reported mean age of onset ranging from 8.8 years (Last et al., 1992) to 13.4 years (Last, Hersen, et al., 1987). On the other hand, research on GAD suggests that onset is much later—in the late teens and early 20s (Wittchen, Zhao, Kessler, & Eaton, 1994). Moreover, whereas research on OAD has found that older children present with a higher total number of overanxious symptoms and self-report significantly higher levels of anxiety and depression than younger children (Strauss et al., 1988), research on GAD suggests that there are no differences in the number or type of symptoms reported by children and adolescents with GAD (Masi et al., 2004).

Research on symptoms of GAD in community samples has also produced mixed findings on the developmental course of GAD symptoms. For instance, in one study symptoms of other anxiety disorders decreased or stabilized over the course of development, while symptoms of GAD increased among girls with age (Hale, Raaijmakers, Muris, van Hoof, & Meeus, 2008). In contrast, in another study GAD symptoms decreased between late childhood and early adolescence, followed by a slight increase in middle adolescence onward (van Oort, Greaves-Lord, Verhulst, Ormel, & Huizink, 2009). van Oort and colleagues (2009) attributed these mixed findings to the different methodologies and measures used by the two studies, and argued for additional research to sort out these differences.

SITUATIONAL AND CONTEXTUAL FACTORS

Race and Ethnicity

There is some research examining whether there are racial and ethnic differences in the presentation of anxiety symptoms among children and adolescents. In the majority of studies, the groups most commonly contrasted are European Americans, African Americans, and Hispanics/Latinos (e.g., Creveling, Varela, Weems, & Corey, 2010; Hill & Bush, 2001; Latzman et al., 2011; Walton, Johnson, & Algina, 1999; Wren et al., 2007). These examinations have yielded somewhat equivocal findings, which are particularly challenging to reconcile because of between-study variations in methodology and participants. In addition, findings across these studies generally suggest that only a small proportion of the variance observed in child anxiety is attributable to race. For example, among a normal sample of kindergarten-age children and their mothers, Hill and Bush (2001) observed similar reports of child anxiety from African American and European American mothers, but higher levels of self-reported anxiety among European American children relative to African American children. Conversely, Walton and colleagues (1999) reported that African American mothers reported lower levels of anxiety than did European American mothers, whereas African American children reported higher levels of anxiety than did European American children. However, children in Walton and colleagues' study were older (ages 10–18), and half of the sample was chronically ill. Indeed, although Walton and colleagues reported an informant × race interaction, this interaction depended on the setting of the assessment, suggesting that differences between racial groups with respect to child and maternal reports were most pronounced in anxiety-producing situations (e.g., being in a medical or dental clinic). Moreover, the informant × race interaction was present for only those children with chronic health concerns. Interestingly, in this sample child sex was also associated with child reports of anxiety, but the observed effects were dependent on both the informant (child or mother) and the setting (stressful or nonstressful).

Similarly, Latzman and colleagues (2011) observed variations for race, age, and sex in self-reported anxiety on the Revised Children's Anxiety and Depression Scale (RCADS)—a measure of anxiety and depression symptom dimensions. Specifically, in a normal school-age sample (grades 2–12), African American girls endorsed more symptoms of obsessive–compulsive disorder in elementary and middle school, whereas European American girls endorsed greater numbers of social phobia symptoms in high school. For elementary school boys, more symptoms of obsessive–compulsive disorder were observed for African American boys than for European American boys. When the data

were examined categorically and clinical cutoff scores were used, significant differences were observed only for girls: African American elementary school girls more frequently endorsed clinical levels of obsessive–compulsive disorder symptoms, and European American high school girls more frequently endorsed clinical levels of panic symptoms. However, Latzman and colleagues specifically noted that these differences, although statistically significant, were small in magnitude.

Austin and Chorpita (2004) also observed ethnic group differences for specific symptoms of anxiety in a large school-based sample of children and adolescents (N = 1,126). Comparing European American, Chinese American, Filipino American, Native Hawaiian, and Japanese American school children, all ranging in age from 7 to 18, the authors did not observe any significant between-group differences on the temperamental variable of negative affectivity underlying anxiety and depression. However, significant between-group differences were noted for separation anxiety, panic, social phobia, and obsessive–compulsive symptoms as assessed by the RCADS. Specifically, Native Hawaiians scored significantly higher than Filipino Americans, Japanese Americans, and European Americans on the separation anxiety scale, and scored significantly higher than Japanese Americans and European Americans on the panic scale. Filipino Americans scored significantly higher than Japanese Americans and European Americans on the panic scale and significantly higher than European Americans on the social phobia scale. Chinese Americans scored significantly higher than Native Hawaiians and European Americans on the social phobia scale. Finally, Native Hawaiian and Filipino Americans reported significantly higher levels of obsessive–compulsive symptoms than Japanese Americans and European Americans. Ethnicity was also found to be related to clinically elevated levels of panic and separation anxiety, such that the Native Hawaiian and Filipino American groups had proportionally more cases of clinical elevations in these domains than did Chinese Americans, Japanese Americans, and European Americans.

Conversely, in a primary care sample of children ages 8–13, Wren and colleagues (2007) noted no effects of ethnicity on the reporting of anxiety across European American, Latino, African American, Asian/Pacific, and biracial groups. However, effects of child sex and age and parental education on reports of child anxiety were observed. Similarly, in a large school-based sample (N = 1,961) of children and adolescents ages 8–18 years, Okamura and colleagues (2014) did not observe ethnic differences with respect to child-reported anxiety. However, significant ethnic group differences were observed in comparison to European American children when child anxiety was assessed via parent report. Specifically, relative to European American children, Chinese American parents reported significantly more symptoms of obsessive–compulsive disorder and rated their children as significantly higher with respect to total anxiety. Filipino American parents also reported that their children experienced significantly more symptoms of separation anxiety, panic, and total anxiety than did parents of European American children. Finally, Japanese American parents endorsed significantly more symptoms of social phobia and total anxiety for their children compared with European American parents, and Native Hawaiian parents endorsed significantly higher levels of panic symptoms for their children when compared with European American parents.

In spite of somewhat inconsistent findings with respect to the influence of race on symptoms of child anxiety, some interesting variability with respect to the relation between parenting variables and child anxiety has been reported in the context of ethnic differences. Specifically, Creveling and colleagues (2010) found perceived maternal control (e.g., the extent to which mothers made decisions for or directed the activities of their children) to be significantly related to the children's feelings of autonomy, self-confidence, and anxiety for African American, Latino, and European American children. However, among the European American children only, the relation between maternal control and child anxiety was fully mediated by a child's feeling unloved or misunderstood. Lacking confidence in one's own abilities partially mediated this relation only among European American children. For Latino children, feeling unloved or misunderstood only partially mediated the effect of maternal control on child anxiety, but neither feeling unloved nor lacking confidence mediated this relation among African American children. Finally, although ethnicity did not moderate the relations between maternal control and anxiety or between maternal control and feelings of autonomy and self-confidence, it did interact significantly with maternal control to influence feeling unloved and misunderstood; specifically, maternal control was

more strongly associated with feeling unloved and misunderstood for European American children than for African American children (Creveling et al., 2010).

Similarly, Hill and Bush (2001) observed a differential effect between African American and European American families for the extent to which parental efficacy (e.g., feelings of confidence in the parenting role) was associated with child anxiety. Specifically, in this sample of normal kindergarten-age children and their mothers, Hill and Bush observed that feelings of confidence in parenting abilities were positively associated with positive parenting practices, such as communication, and negatively associated with negative parenting practices, such as inconsistent discipline; moreover, parents who reported higher levels of efficacy had children reporting lower levels of anxiety. However, this relationship was stronger for European American families than for African American families (although the two groups did not differ in terms of mean levels of parenting efficacy), leading the authors to suggest that parental efficacy might only indirectly affect child anxiety (through positive parenting practices), or that additional extrafamilial supports might be available to African American children that compensate for lower maternal efficacy. It is important to note that no differences between African American and European American parents were noted with respect to specific parenting behaviors, including negative communication, enforcement, hostile control, inconsistent discipline, love withdrawal, and parenting efficacy. Overall, these authors suggest that parenting practices and their influence on child anxiety are generally similar across the two ethnic groups studied (Hill & Bush, 2001).

Socioeconomic Status

Recent studies examining the relation between socioeconomic status (SES) and anxiety have noted an association, although in some instances the size of this effect is small and in other instances variables often correlated with family SES (e.g., prenatal drug exposure, household density) are more strongly related to child anxiety status than is SES per se. Several studies have yielded evidence suggesting an inverse relation between familial SES and child anxiety. In a normal school sample of 216 Filipino adolescents in Hawaii, anxiety was associated with various indicators of lower status, including the education and employment of the primary family earner (Guerrero, Hishinuma, Andrade, Nishimura, & Cunanan, 2006). Similarly, Vine and colleagues (2012), in a sample of 498 school children ages 11–13, observed higher levels of physical anxiety and separation/panic anxiety (as measured by the Multidimensional Anxiety Scale for Children, or MASC) among children from lower-income families. Indeed, even after controlling for numerous other familial risk factors (including parental divorce, parental unemployment, and exposure to stressful events), Melchior and colleagues (2010) found low family income to be a significant predictor of childhood depression and anxiety among a normal sample of 941 French children ages 4–18. Specifically, children whose families had experienced low income at any time during the 8-year follow-up period were nearly twice as likely to present with internalizing symptoms as those whose families had not. Moreover, children in families whose income had either declined during the study period or remained persistently low were more likely to present with internalizing symptoms than children in families whose income had been persistently high during this time frame.

In a longitudinal study of an individual's social position (defined by current or most recent occupation for one's parent or oneself during childhood and adulthood, respectively), lower social position during childhood was associated with greater risk for adult anxiety and depression; however, this relation became nonsignificant after adjustments for adult social position and childhood psychological disorder (Stansfeld, Clark, Rodgers, Caldwell, & Power, 2011). Conversely, adult social position was associated with greater risk of anxiety and depression, even after adjustments for childhood social position and childhood disorder. Stansfeld and colleagues (2011) suggest that these findings provide only limited support for an "accumulation of risk" model, in which childhood social position confers a risk of later adult psychological disorder. However, these authors indicated that their findings provide support for a "health selection" model, whereby anxiety and depression during childhood might influence later social position in part because of difficulties in obtaining upward mobility through education and later employment opportunities. Finally, when assessing child anxiety via parent report, Okamura and colleagues (2014) noted significant inverse relations between familial SES (as defined by parental education and occupation) and total anxiety, panic, and obsessive–compulsive scores as measured by a parent version of the RCADS, such

that higher SES was associated with fewer caregiver-reported symptoms.

Other research has challenged these associations noted between family SES and child anxiety. For example, although Dirks, Boyle, and Georgiades (2011) found that psychopathology more generally accounted for a statistically significant but small proportion of variability in adult SES (2.78%), in their study neither parent- nor teacher-rated child anxiety was associated with later adult SES. Similarly, Leech, Larkby, Day, and Day (2006) followed children from the prenatal period through age 10 and observed multiple significant predictors of anxiety over time, including lower IQ scores, attention problems, prenatal exposure to marijuana, household density during prenatal development, and injuries during childhood; however, neither race nor SES was a significant long-term predictor of anxiety. Casting further doubt on the findings mentioned above, Farrell, Sijbenga, and Barrett (2009) found that instead of low SES being a risk factor for anxiety, higher anxiety was associated with higher SES. Although this effect was small, children (ages 8–12) in this study who attended high-SES schools reported higher levels of anxiety on the Spence Children's Anxiety Scale (SCAS) than did their counterparts in low-SES schools. Whether this finding is truly contradictory to those reported above is unclear, however, given that the findings of Vine and colleagues (2012) indicated a negative association between household income and child anxiety, but a positive association between neighborhood income and child anxiety. To explain these findings, Vine and colleagues suggest "group density" theories in which individuals of similar disadvantaged circumstances living together, typically in the context of low levels of income inequality, demonstrate more positive mental health outcomes. As such, the positive associations between SES and anxiety noted by both Farrell and colleagues and Vine and colleagues reflect characteristics of the larger environment in which a child resides, rather than characteristics of the specific home setting. Vine and colleagues also suggest that future studies examine potential interactions between family and neighborhood SES and their influence on anxiety.

Gender

Historically, girls have presented with higher rates of internalizing symptoms than boys, and this has been the case for anxiety in general across development. Indeed, multiple recent studies have supported higher levels of self-reported anxiety among girls than among boys in samples drawn from the United States (Okamura et al., 2014; Wren et al., 2007), Canada (Auerbach, Richardt, Kertz, & Eberhart, 2012; Jacques & Mash, 2004), Australia (Farrell et al., 2009), and Norway (Derdikman-Eiron et al., 2011; Leikanger, Ingul, & Larsson, 2012). This gender difference has also been found in studies using various self-report measures of anxiety, including the Screen for Child Anxiety Related Emotional Disorders (SCARED) (Leikanger et al., 2012; Wren et al., 2007); the MASC (Auerbach et al., 2012); the State–Trait Anxiety Inventory for Children (STAIC) (Jacques & Mash, 2004); the Revised Children's Manifest Anxiety Scale (RCMAS) (Farrell et al., 2009); the SCAS (Farrell et al., 2009); and the RCADS (Chorpita, Yim, Moffitt, Umemoto, & Francis, 2000; Okamura et al., 2014). However, although gender differences were observed in self-reported anxiety among a sample of normal children ages 8–13, Wren and colleagues (2007) and Ebesutani, Okamura, Higa-McMillan, and Chorpita (2011) both observed that such differences were not present when children were assessed via parent report. Okamura and colleagues (2014) also failed to observe significant gender differences for total anxiety scores when children were assessed via parent report, but did observe significantly higher parent reports of girls' social phobia symptoms relative to boys'. In addition, two studies noted interactions between gender and age: 15-year-old girls reported a greater increase in symptoms of social phobia than did boys (Leikanger et al., 2012); and older girls (those in grades 10 and 11) reported higher levels of anxiety than both older boys and younger girls (those in grades 4 and 5) (Jacques & Mash, 2004).

Perhaps more informative to understanding the nature of gender differences in child anxiety, however, is a recent set of findings suggesting that gender role orientation (i.e., how closely children identify with masculine or feminine roles and behaviors), rather than biological sex, accounts for more variability in anxiety symptom presentation. Muris, Meesters, and Knoops (2005) observed a positive association between femininity as identified by scores on the Children's Sex Role Inventory (Boldizar, 1991) and preference for girls' toys and activities, as well as self-reported anxiety and fear, in a sample of 209 school children ages 10–13. Although a masculine gender role orientation was negatively associated with fear, there was no significant relation observed between masculinity and

anxiety. Indeed, although girls did report more symptoms of fear and anxiety than boys did in this study, the relation between biological sex and anxiety was not observable after gender role orientation was taken into account. Moreover, the relation between gender role orientation and fear and anxiety was stronger for girls than for boys, suggesting that gender role orientation might play a larger role in understanding the expression of fear and anxiety for girls than for boys (Muris et al., 2005).

Carter, Silverman, and Jaccard (2011), in a sample of 175 clinic-referred children ages 9–13, also observed significantly higher levels of anxiety endorsed by girls than by boys, but in addition reported that both pubertal development and gender role orientation were significant predictors of anxiety symptomatology. Specifically, both boys and girls who self-reported more advanced pubertal development also self-reported higher levels of femininity and anxiety, whereas both boys and girls who endorsed higher levels of masculinity self-reported lower levels of anxiety. Similar to the findings reported by Muris and colleagues (2005), Carter and colleagues also reported that pubertal development and gender role orientation explained more variability in anxiety than did biological sex, suggesting that early pubertal development may act as a risk factor for anxiety, whereas identification with a masculine gender role orientation may serve as a protective factor. Finally, Palapattu, Kingery, and Ginsburg (2006), in a normal sample of 114 African American adolescents ages 14–19, observed a negative relation between masculinity and anxiety and a positive relation between femininity and anxiety. As reported in other studies, Palapattu and colleagues also observed higher levels of anxiety reported by girls compared with boys; however, gender role orientation explained a significant proportion of additional variance in anxiety scores beyond that accounted for by biological sex, and was considered to be more important than biological sex in explaining observed anxiety symptomatology. These authors also noted that self-esteem acted as a protective factor with respect to anxiety in this sample, and that this relation was most marked among those endorsing high levels of femininity (Palapattu et al., 2006). Together, these findings suggest rather reliable differences between girls and boys with respect to their experience of symptoms of anxiety, but also indicate that the traits encompassing feminine and masculine gender role orientations might better explain individual differences in anxious symptomatology.

Age

Findings with respect to age differences in anxiety generally suggest stability over time, although the nature of the anxiety does change across development (Weems & Costa, 2005). Specifically, younger children generally report more fears than do older children (Broeren & Muris, 2009), whereas generalized anxiety (Broeren & Muris, 2009) and social anxieties (Ranta et al., 2007; Weems & Costa, 2005) tend to peak during adolescence, particularly among girls (Leikanger et al., 2012). Specifically, Weems and Costa (2005), in a cross-sectional study of 145 normal children in three age groups (6–9, 10–13, and 14–17), noted that concerns regarding separation were most common in the youngest age group; fears related to death and danger were most prevalent in the middle age group; and social and performance concerns were those most often reported by the oldest cohort of adolescents. Similarly, Broeren and Muris (2009), in a normal sample of 226 Dutch children, noted higher fear scores among younger children (ages 4–5) and higher generalized anxiety scores among older children (ages 6–9). With respect to fear, in a sample of 388 school children ages 4–13, an inverse relation between anxiety sensitivity (i.e., the belief that symptoms of anxiety can be harmful; Reiss, Peterson, Gursky, & McNally, 1986) and age was also observed, such that older children reported less fear associated with physical symptoms of anxiety (Muris, Mayer, Freher, Duncan, & van den Hout, 2010). The extent to which specific symptoms are associated with anxiety also changes with age (Boylan, Miller, Vaillancourt, & Szatmari, 2011). Specifically, in a sample of 1,329 children ages 4–7 who were studied prospectively for a period of 8 years, the factor structure of anxiety and depression remained stable across development, whereas the specific items related to each factor changed with age. These findings suggest that the presence of anxious symptomatology is relatively stable over time, and that only the specific expression of fears and worries tends to change with development (Weems & Costa, 2005). Along those lines, Broeren and Muris concluded that (with the exception of specific fears, which clearly exhibit an age-related effect) the overall contribution of developmental factors to the expression of anxiety symptoms is small, and that other factors play a more important role in explaining the development and maintenance of anxiety disorders.

More generally, diagnoses of anxiety have also been observed to be stable over time (Carballo et al., 2010)

with specific symptoms aggregating into disorder-specific clusters among children as young as ages 2–3 (Mian, Godoy, Briggs-Gowan, & Carter, 2012). Carballo and colleagues (2010) followed a sample of 1,869 children between the ages of 2 and 18 at first diagnosis prospectively for a period of 14 years. They noted high diagnostic stability across time for all of the *International Classification of Diseases*, 10th revision (ICD-10) anxiety disorders studied, including phobic disorders, social anxiety disorders, obsessive–compulsive disorder, stress-related disorders, and "other" anxiety disorders. Moreover, Turner and Barrett (2003) demonstrated that the differentiation between anxiety and depression was stable across age. Similarly, Mian and colleagues (2012), in a sample of 1,110 children ages 22.6–47.9 months, found that symptoms of anxiety in this age group consistently aggregated into symptom clusters matching current diagnostic categories of generalized anxiety, obsessive–compulsive symptoms, separation anxiety, and social phobia. Such findings suggest that even at this early stage of development, specific clinical presentations of anxiety can be observed. Finally, in a review of behavioral genetic studies of anxiety, Franić, Middeldorp, Dolan, Ligthart, and Boomsma (2010) noted that the heritability of anxiety increases over time, as the influence of shared environmental factors lessens throughout the maturation from childhood to adolescence. Moreover, these authors suggest that the temporal stability of anxiety may be stronger than has previously been reported in longitudinal studies of anxiety, given the use of different reporters across development: Parents are often queried to assess the symptomatology of younger children, whereas older children typically provide self-reports of their experience of anxiety (Franić et al., 2010). Taken together, findings with respect to age differences in the presentation of anxiety suggest relative stability over time in the context of changing specific presentations across age.

ETIOLOGY

Genetics

Symptoms of anxiety aggregate in families (e.g., Turner, Beidel, & Costello, 1987); that is, anxious children are more likely to have anxious parents (e.g., Rosenbaum et al., 1992), and anxious parents are more likely to have anxious children (e.g., Beidel & Turner, 1997). Given that parents and children typically share both genetic material and a familial environment, the challenge has been to determine the respective contributions of each of these factors to the development of anxiety. Twin studies are one of the most common means of obtaining estimates of the heritability of specific phenotypic presentations and allow for the variance in a given phenotype to be attributed to three sources: (1) additive genetic influences, (2) common or shared environmental factors, and (3) nonshared environmental experiences (Gregory & Eley, 2007). As defined by Gregory and Eley (2007) in their comprehensive review of the genetic literature specific to child anxiety, additive genetic effects represent the sum of the effects of specific alleles, whereas shared environmental factors consist of experiences that effectively increase similarity among family members. In contrast, nonshared environmental factors represent those experiences that result in family members differing from one another (in most models, these factors also include measurement error).

Interestingly, the relative contributions of genetic and shared environmental factors appear to be inversely related to one another over the course of development (Bartels et al., 2007). Measuring anxiety with broad-syndrome self-report, teacher report, and parent report scales, Bartels and colleagues (2007) observed in a sample of twins followed from birth to age 12 years that genetic influences tended to decrease over development, while shared environmental influences increased (see also Eley et al., 2003; Hallett, Ronald, Rijsdijk, & Eley, 2009). Although the relative contributions of these influences vary across development, genetic factors explained the largest proportion of variability in anxiety among young children (Bartels et al., 2007). In contrast, nonshared environmental contributions remained more constant across development, but tended to account for the least amount of variance in anxiety presentations (Bartels et al., 2007). These effects were reported for both boys and girls, with somewhat stronger genetic effects observed for boys than girls, but findings have not yet suggested that different genes are responsible for different expressions of anxiety between the sexes (Bartels et al., 2007; Franić et al., 2010; Kendler, Gardner, & Lichtenstein, 2008).

Genetic and Environmental Contributions to Anxiety

In two studies assessing the relative contributions of genetic and environmental factors to anxiety-related dimensions (e.g., negative cognitions, negative affect, fear, social anxiety, obsessive–compulsive behaviors)

(Eley et al., 2003; Hallett et al., 2009), genetic factors were found to account for the largest proportion of variability, consistent with findings reported by Bartels and colleagues (2007). Specifically, across three different developmental time points from ages 4 to 9, genetic influences accounted for 39–64% of the variance in phenotypic presentation (Eley et al., 2003; Hallett et al., 2009). In contrast, shared environmental factors accounted for the lowest proportion of variability (3–21% across these three age groups), but, consistent again with observations made by Bartels and colleagues, the influence of shared environmental factors was lowest among the 4-year-old sample (range = 3–17%) and highest among the 9-year-old sample (range = 11–23%); the converse was true of the genetic influences, which were highest among 4-year-olds (range = 39–64%) and lowest among 9-year-olds (range = 46–58%). Nonshared environmental effects consistently accounted for approximately one-third of the variance in presentation (range = 22–43%) (Eley et al., 2003; Hallett et al., 2009).

More specifically, for 4-year-olds, obsessive–compulsive behaviors and shyness/inhibition were the behaviors most influenced by genetic factors (with 54% and 64% of the variance attributed to genetic influences, respectively), whereas shared environmental influences were strongest for separation anxiety (with 35% of the variance being attributed to such influences) (Eley et al., 2003). Among older children, negative affect (i.e., general emotional distress common to both anxiety and depression, comprising feelings of fear, anger, and sadness; Joiner et al., 1996; Watson & Clark, 1984) was the factor least influenced by genetic factors (with heritability estimates of .50 at age 7 and .46 at age 9), whereas social anxiety at age 7 (.61) and fear at age 9 (.58) yielded the highest heritability estimates (Hallett et al., 2009).

In research examining the symptom syndromes of specific phobia, separation anxiety, and social phobia among a twin sample ages 6–6½ years, the heritability estimate was significant for specific phobia (46%), but not for separation anxiety (21%) or social phobia (14%) (Eley, Rijsdijk, Perrin, O'Connor, & Bolton, 2008). Although genetic, shared environmental, and nonshared environmental influences each significantly contributed to specific phobia, only nonshared environmental influences were significantly associated with separation anxiety (59%) and social phobia (76%) (Eley, Rijsdijk, et al., 2008). Similarly, in another study, separation anxiety symptoms were attributable largely to nonshared environmental factors (50%, in contrast to 22% genetic and 28% shared environmental factors), and specific phobia symptoms were most attributable to genetic factors (58%, in contrast to 19% shared and 23% nonshared environmental influences) (Bolton et al., 2006). Interestingly, however, when these symptom presentations met diagnostic criteria, the largest proportion of variability in both SAD and specific phobia was due to genetic factors (73% and 60%, respectively). For both disorder categories, shared environmental influences failed to contribute to the variance, whereas approximately one-third of variance was attributable to nonshared environmental influences (Bolton et al., 2006).

In contrast to the findings reported above, Ogliari and colleagues (2006, 2010) observed that the best-fitting multivariate models for their twin data were those in which contributions were made only by genetic and nonshared environmental factors to each of four diagnostic presentations of anxiety assessed by the SCARED (Birmaher et al., 1997). Specifically, for generalized anxiety, social phobia, panic, and separation anxiety, approximately half (49–60%) of the variability observed in these presentations was attributable to genetic factors, whereas 40–51% of variability was attributable to nonshared environmental factors. However, as noted by the authors, these discrepant findings might be due in part to methodological differences between the two sets of studies—namely, the use of child self-report questionnaires assessing DSM-IV symptom criteria with a considerably smaller sample (i.e., 378 twin pairs; Ogliari et al., 2006, 2010), in contrast to maternal reports of anxiety-related behaviors in relatively larger samples (i.e., samples ranging from 854 to 4,564 twin pairs; Eley et al., 2003; Eley, Rijsdijk, et al., 2008; Hallett et al., 2009). Yet, using parent and child reports obtained via the Achenbach CBCL and Youth Self-Report form, respectively, Kendler and colleagues (2008) also failed to find evidence of shared environmental influences on symptoms of anxiety and depression, instead reporting significant genetic contributions with heritability estimates ranging from 72 to 89%. Clearly, continued research is required to elucidate the role of shared environmental factors in the phenotypic expression of anxiety.

Genetic and Environmental Influences on Comorbidity

In addition to looking at the relative contributions of genetic, shared environmental, and nonshared environmental influences to specific anxiety-related dimen-

sions (i.e., general distress or negative mood, separation anxiety, fears, obsessive–compulsive behaviors, and shyness/inhibition), Eley and colleagues (2003) examined how these three factors influenced shared variance among these anxiety-related dimensions and thus might contribute to the comorbidity of anxiety disorders. Shared genetic contributions accounted for 12–62% of the covariance between factors, with general distress and shyness/inhibition sharing considerable overlap with the other scales. In contrast, obsessive–compulsive behaviors shared little genetic overlap with the other scales. Shared environmental factors accounted for 43% of the overlap between separation anxiety and fears and between fears and obsessive–compulsive behaviors, while accounting for 78% of the covariation between separation anxiety and obsessive–compulsive behaviors. Across scales, nonshared environmental influences tended to account for relatively low levels (10–36%) of overlap between the behaviors (Eley et al., 2003). Hallett and colleagues (2009) observed that the highest proportion of variability in symptom overlap was accounted for by shared environmental factors (22–57%) and genetic factors (24–57%), with less of the overlap between phenotypes being attributable to nonshared environmental influences (11–36%). Moreover, the results of Hallett and colleagues' study on the one hand suggest genetic specificity, such that rather than identifying a single underlying factor related to multiple lower-order factors, the data supported independent factors that did not share high levels of genetic overlap. On the other hand, relatively high correlations were observed between the negative cognitions subscale and subscales for each of the other anxiety-related behaviors, suggesting that 42–57% of the overlap of each scale with negative cognitions was attributable to genetic factors. Together, such findings are in contrast to the "generalist genes" theory, which suggests that genes confer only a general risk for anxiety, whereas environmental influences are responsible for specific presentations. Specifically, the findings of Hallett and colleagues suggest that genetic influences are active at both a general level (e.g., negative cognitions) and a specific level (e.g., social anxiety). Collectively, the findings reported by Eley and colleagues and Hallett and colleagues indicate that both genetic and shared environmental factors contribute to comorbidity between anxiety symptom presentations, with nonshared environmental influences playing a smaller role.

With respect to the "symptom syndrome" phenotypes of specific phobia, separation anxiety, and social phobia (defined by meeting the DSM-IV symptom criteria for a specific disorder except for the diagnostic criterion regarding level of impairment), shared environmental influences contributed significantly to the comorbidity of each of these syndromes with the other. Specifically, correlations among the syndrome pairs ranged from .98 to .99. The comorbidity between specific phobia and social phobia represented the only case in which nonshared environmental effects exerted a significant influence (r = .33) (Eley, Rijsdijk, et al., 2008). The relations between separation anxiety and either specific phobia or social phobia were not significantly accounted for by genetic factors (Eley, Rijsdijk, et al., 2008). Findings that shared environmental influences contribute to the comorbidity among these three syndromes suggest that specific aspects of the family environment (e.g., those that are shared and serve to make family members more similar to one another) may have a general influence on multiple anxiety presentations; conversely, the more modest contributions of genetic factors to the overlap of these syndromes suggest that different biological processes may underlie these varying phenotypic presentations (Eley, Rijsdijk, et al., 2008).

Similar to those findings reported above with respect to genetic and environmental influences on anxiety, Ogliari and colleagues (2006, 2010) found no evidence that shared environmental influences contribute to observed comorbidity in anxiety presentations. These authors report considerable genetic influences on comorbidity (ranging from 40% for the overlap of generalized anxiety and social phobia to 61% for the overlap between social phobia and panic), with only modest influences of nonshared environmental factors (ranging from 1% for social phobia and panic to 34% for generalized anxiety and panic) (Ogliari et al., 2006, 2010). Again, as indicated above, such differences across studies could be attributable to methodological variations across the studies. Accordingly, further study is required to ascertain not only the relative contributions of genetic and environmental influences to anxiety symptomatology and comorbidity, but also the specific role that shared environmental factors play in these phenotypes and their overlap.

Genetic Influences across Development

In the context of efforts to ascertain the relative contributions of genetic and environmental factors to anxiety, the changing role of genetic influences over the

course of development cannot be ignored. Kendler and colleagues (2008) report support for a dynamic model of genetic influences on anxiety, in which new genetic effects continue to emerge across development (innovation) while the overall impact of genetic factors declines with increasing age (attenuation).

Other studies have examined the nature of genetic influences across development in the context of heterotypic (i.e., an earlier disorder predicts a different subsequent disorder) and homotypic (i.e., an earlier disorder predicts the same disorder later in time) continuity. For example, findings from a recent study suggest heterotypic continuity between SAD during childhood and adult-onset panic attacks, such that these two phenotypes are linked in a way that has not been observed for OAD during childhood and later panic attacks (Roberson-Nay, Eaves, Hettema, Kendler, & Silberg, 2012). Furthermore, in an investigation of homotypic and heterotypic continuity and the extent to which genetic and environmental factors influence these relations during development, stability in anxiety-related symptoms over time (homotypic continuity) was largely attributable to genetic factors, whereas shared environmental factors exerted the greatest influence over heterotypic continuity (Trzaskowski, Zavos, Haworth, Plomin, & Eley, 2012). Specifically, in their sample of twin pairs (the same sample investigated by Hallett et al., 2009) assessed at ages 7 and 9, Trzaskowski and colleagues (2012) found within-trait correlations over time ranging from .45 for negative affect to .54 for social anxiety, with 57–67% of this continuity attributable to genetic factors. Conversely, only 8% (negative cognitions) to 28% (negative affect) of this continuity was attributable to shared environmental influences, and only 13% (fear) to 26% (negative cognitions) was attributable to nonshared environmental factors. In contrast, heterotypic continuity was most influenced by shared environmental factors, which accounted for 21% (negative cognitions at age 7, negative affect at age 9) to 62% (negative affect at age 7, fear at age 9) of the covariance between these traits over time. Genetic influences on heterotypic continuity were generally lower (28–66%; genetic factors did explain 66% of the covariance between negative cognitions at age 7 and negative affect at age 9), as were nonshared environmental influences (4–28%). With respect to the strong contribution of genetic factors to the relation between early negative cognitions and later negative affect, Trzaskowski and colleagues indicate that the scales assessing these traits contain several symptoms that are shared between anxiety and depression; accordingly, the heterotypic continuity observed between these traits may be indicative of the more general relation between anxiety and depression over time. Moreover, the substantial influence of shared environmental factors on the relation between early negative affect and later fear suggests that parents may play a significant role in the development of fear during childhood. Most importantly, perhaps, these findings illustrate that the relative contributions of genetic and environmental factors to the homotypic and heterotypic continuity of anxiety vary as a function of the specific traits assessed (Trzaskowski et al., 2012).

In an effort to identify individuals at risk for specific disorders, researchers have begun studying "endophenotypes," which are "intermediate phenotypes that are more proximal to the genes influencing a disorder than its signs and symptoms, and can be considered risk markers of a disorder" (Gregory & Eley, 2007, p. 208). One endophenotype specific to anxiety might be anxiety sensitivity, reported by Eley, Gregory, Clark, and Ehlers (2007) to be heritable among a sample of 8-year-old twins and to share considerable genetic overlap with symptoms of panic. As such, it might serve as a useful indicator of risk for the development of panic. Anxiety sensitivity has also been found to demonstrate a stability over time that is largely due to genetic factors (61%), whereas nonshared environmental influences (39%) are associated with specific variations at individual assessment points (Zavos, Gregory, & Eley, 2012). More specifically, in their investigation of 1,300 twin and sibling pairs across three time points (midadolescence, late adolescence, and early adulthood), Zavos and colleagues (2012) observed moderate estimates of heritability for anxiety sensitivity across development, suggesting genetic continuity, but also noted new genetic influences emerging in late adolescence, consistent with Kendler and colleagues' (2008) findings of genetic innovation. Across all time points, shared environmental contributions were nonsignificant (Zavos et al., 2012). These findings suggest support for both learning and trait hypotheses, such that the considerable contribution of nonshared environmental factors at each time point (41–54%) underscores the importance of learning in the development and expression of such symptoms, whereas the genetic stability of these symptoms indicates a trait-like variable (Zavos et al., 2012). However, these findings must be interpreted with caution, given the equivocal support that has been observed for the validity of the construct of anxiety sensitivity in children; specifically, no empirical support currently exists

to discriminate this sensitivity from fear or trait anxiety in children (e.g., Chorpita & Daleiden, 2000; Chorpita & Lilienfeld, 1999). Accordingly, rather than providing data with respect to an endophenotype of anxiety, these findings might instead refer to the general construct—or phenotype—of trait anxiety.

The Role of Specific Genes in Anxiety

As Gregory and Eley (2007) note in their review of the literature, research attempting to identify specific genes responsible for specific anxiety presentations has been limited by the fact that numerous genes are typically responsible for any given phenotypic expression. Gregory and Eley state that so-called "linkage studies," in which specific genes responsible for specific phenotypic expressions are sought, are of limited utility; in contrast, however, "association studies," based on comparing the frequencies of alleles in identified case and control participants, can be more informative with respect to specific genetic influences on anxiety presentations. Accordingly, a small group of recent studies have suggested that the serotonin transporter (5-HTT) allele might be implicated in the development of anxiety. As noted in their review of these studies among children and adolescents, Murray, Creswell, and Cooper (2009) indicate that the findings yielded to date in this area of inquiry are contradictory and inconsistent. Specifically, some studies have failed to find a significant relation between the 5-HTT gene and features of anxiety (Schmidt, Fox, Rubin, Hu, & Hamer, 2002). In other instances, relations between the 5-HTT allele and anxiety-related behaviors have been observed, but with different forms of the allele (e.g., Arbelle et al., 2003; Battaglia et al., 2005), suggesting that additional factors might moderate an existent relation between this gene and anxiety symptom presentations (Murray et al., 2009).

Indeed, a gene × environment interaction emerged between the 5-HTT gene and maternal reports of low social support, such that the short 5-HTT allele was associated with higher levels of behavioral inhibition during childhood, but only in the context of low social support (Fox et al., 2005). Similarly, a gene × environment interaction was observed by which the 5-HTT gene interacted with prenatal maternal anxiety symptoms to influence the risk for later emotional difficulties (Tiemeier et al., 2012). Finally, evidence of another significant gene × environment interaction was supported: Stressful life events presented a greater risk for anxiety and depression in the context of a specific 5-HTT genotype (i.e., one that is associated with lower serotonin transcriptional efficiency) (Petersen et al., 2012).

In addition, one genetic disorder—22q11.2 deletion syndrome, or 22qDS—may be linked to the anxiety disorders. Specifically, in a review study of children and adolescents (ages 4–19) diagnosed with 22qDS, across seven independent studies 39% of participants met diagnostic criteria for one or more anxiety disorder, whereas only 17% of controls did; indeed, of the psychiatric disorders reported in these studies, anxiety disorders were the most common (Jolin, Weller, & Weller, 2012). Six of these studies included data with respect to specific DSM-IV anxiety disorders, indicating that most common among children with 22qDS was specific phobia (31%), followed by GAD (13%), SAD (9%), and obsessive–compulsive disorder (8%). Collectively, such findings are far from conclusive with respect to identifying specific genes that are active in the expression of anxiety, but they do suggest potential avenues for future study.

Neurobiology

Although it is known from animal research and psychopharmacological treatment research that several neurotransmitters (e.g., gamma-aminobutyric acid, norepinephrine, serotonin, substance P) are implicated in the anxiety disorders, most research on the neuropsychopathology of child anxiety has focused on the neuroanatomy of the brain. This research on neuroanatomy of psychological disorders, known as "affective neuroscience" (Vasa & Pine, 2004), examines structural differences in the brains of individuals with and without anxiety (or inhibited temperament) with magnetic resonance imaging (MRI) and the way the brain functions in individuals with and without anxiety disorders with functional MRI (fMRI) and positron emission tomography (PET) scans. Structural MRI techniques focus primarily on the size of different brain matter, whereas the functional imaging techniques allow researchers to examine how the brain responds to certain stimuli or events. As is typical for this type of research, animal models are frequently used to develop hypotheses about neural circuits in humans (LeDoux, 1995, 1998).

Brain Structure and Function

In a recent large study (N = 265) of personality traits and brain structure in healthy adults, among the Big

Five personality traits (i.e., Extraversion, Agreeableness, Conscientiousness, Neuroticism, and Openness), Neuroticism was identified as the trait most clearly linked to brain structure (Bjornebekk et al., 2013). Neuroticism has been shown to be a risk factor for the development of psychopathology, especially anxiety and depression (e.g., Bienvenu, Hettema, Neale, Prescott, & Kendler, 2007; Cox, MacPherson, Enns, & McWilliams, 2004; Hettema, Neale, Myers, Prescott, & Kendler, 2006). In the Bjornebekk and colleagues (2013) study, higher anxiety, depression, and vulnerability to stress were associated with smaller total brain volume, decrease in white matter microstructure, and smaller cortical surface area in the frontotemporal regions.

AMYGDALA

With regard to specific brain regions among individuals with anxiety disorders, research has primarily implicated the amygdala, a part of the limbic system located in the temporal lobe responsible for processing emotional reactions and memories. The location of the amygdala allows it to integrate information from sensory inputs from the cortex, thalamus, and hippocampus, and to send out information through the hypothalamus, brainstem, and cortex. In addition to focusing on the amygdala, contemporary models of anxiety disorders highlight a network of brain regions, including the insular cortex, prefrontal cortex (PFC), hippocampus, orbitofrontal cortex (OFC), and anterior cingulate cortex (ACC) (Craske, Rauch, et al., 2009). Using MRI, Schienle, Ebner, and Schafer (2011) found that adults with GAD had larger volumes of the amygdala and the dorsomedial PFC than healthy adults had, and self-reports on symptom severity were positively correlated with volumes of the dorsomedial PFC and the ACC. Similarly, in an MRI study of children and adolescents with GAD, right and total amygdala volumes were larger than those of healthy controls, whereas intracranial, cerebral, cerebral gray and white matter, temporal lobe, hippocampal, and basal ganglia volumes and measures of the midsagittal area of the corpus callosum did not differ between groups (De Bellis et al., 2000). Another structural MRI study has implicated the superior temporal gyrus (STG), a ridge on the temporal cortex, in GAD in children. In this study, children and adolescents with GAD had larger total matter, white matter, and gray matter of the STG than healthy controls had (De Bellis et al., 2002). Furthermore, these investigators reported more pronounced asymmetry (i.e., right side larger than left) in total and STG white matter volumes in children and adolescents with GAD than in healthy controls, and there was a significant correlation between STG white matter asymmetry and child self-reported anxiety.

Not all findings are consistent, however. For example, in one study gray matter volume in the amygdala was significantly reduced in children and adolescents with anxiety disorders compared with healthy controls (Milham et al., 2005). It is unclear why these findings contradict most other findings on the amygdala in adult and child samples. The small sample size, mixed anxiety disorder sample, and/or disorder severity of the sample (children with anxiety disorders were classified as "treatment-resistant") may have led to the contradictory findings. Nevertheless, given how little research has been conducted to date in child samples, as well as the fact that most studies have relatively small sample sizes, additional research is needed to resolve the contradictory findings.

Adding to these findings on amygdala volume differences, functional imaging studies have consistently found that the amygdala and associated regions are activated during fear conditioning experiments in animals (LeDoux, 1998, 2000) and in healthy adults (Büchel & Dolan, 2000; LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998; Schneider et al., 1999). Furthermore, fMRI studies using face processing paradigms show preferential activation of the amygdala and related structures in response to fearful versus neutral or happy faces in normal adults (Breiter et al., 1996; Morris et al., 1996), and the amygdala and associated regions demonstrate more activity in individuals with anxiety disorders than in individuals without anxiety disorders upon exposure to feared stimuli (Nitschke et al., 2009). According to Craske, Rauch, and colleagues (2009), the amygdala plays an important role in the assessment of threat, as well as in the formation of associations regarding danger in the environment and mediation of responses to threat. They suggest that exaggerated sensitivity of the amygdala mediates abnormal threat assessment, abnormalities in learning about danger in the environment, and/or exaggerated fear responses. For instance, when viewing masked angry faces, children with GAD showed greater right amygdala activation than healthy controls did, and this activation was positively correlated with anxiety severity (Monk et al., 2008). Likewise, when viewing fearful expressions, adolescents with GAD showed increased right amygdala responses, par-

ticularly when they rated subjective degrees of internal fear (McClure et al., 2007). In another study of socially anxious adolescents, using anticipation of peer evaluation within a simulated Internet chat room, Guyer, Lau, and colleagues (2008) found that anxious adolescents showed greater amygdala activation than did healthy adolescents when viewing photographs of peers rated as less desirable relative to those deemed more desirable for an anticipated social interaction. Similarly, in a study of adolescents temperamentally at risk for anxiety, exaggerated amygdala response was detected among behaviorally inhibited adolescents when they were viewing emotional faces while providing subjective fear ratings (Pérez-Edgar et al., 2007). However, in this same study, compared with noninhibited adolescents, inhibited adolescents showed deactivation of the amygdala during passive viewing of emotional faces, suggesting that attention state may alter the underlying pattern of neural processing. On the other hand, in a study of healthy adolescents and adults, during passive viewing of fearful faces, adolescents demonstrated greater amygdala and fusiform activation than did adults (Guyer, Monk, et al., 2008).

Research has also found differences in amygdala functioning among children with anxiety disorders and depression. Thomas and colleagues (2001) found enhanced amygdala activation during viewing of emotional faces among children and adolescents with anxiety disorders, whereas children and adolescents with depression showed blunted amygdala response during viewing of emotional faces. Crossing attention to emotional faces with anxiety and depression, Beesdo, Lau, and colleagues (2009) found an even more complex interaction. Specifically, they found that when adolescents viewed fearful faces and focused their attention on internally experienced fear (vs. passive viewing), individuals with anxiety disorders and major depressive disorder showed greater amygdala activation than their healthy peers. However, when passively viewing fearful faces, the anxious adolescents demonstrated amygdala hyperactivation relative to their healthy peers, and the depressed adolescents demonstrated amygdala hypoactivation relative to their healthy peers. Thus it appears that disorder-specific biases emerge under unconstrained attention conditions.

BED NUCLEUS OF THE STRIA TERMINALIS

Complicating things further, whereas the amygdala appears to be consistently involved in short-term responses to threatening stimuli, the bed nucleus of the stria terminalis (BNST) has a slower response but continues to influence behavior long after the initiating stimulus has been terminated. The BNST is a region of the extended amygdala complex (Walker & Davis, 2008), and the pattern of connectivity in the BNST suggests that this region acts as a relay center coordinating the activity of autonomic, neuroendocrine, and somatic motor systems into fully organized physiological functions and behavior (Dumont, 2009). The BNST may be at least partially under the control of the medial PFC (Spencer, Buller, & Day, 2005), and it appears that it may receive emotional and learning associated information and may be involved in integrating these inputs with reward/motivational circuits (Jalabert, Aston-Jones, Herzog, Manzoni, & Georges, 2009). In a study of adults with GAD who engaged in a task with high uncertainty, adults with GAD demonstrated decreased activity in the amygdala and increased activity in the BNST (Yassa, Hazlett, Stark, & Hoehn-Saric, 2012). Thus whereas the amygdala may play a role in immediate threat-related situations, the BNST may take over in longer-term stress-related situations. This may in part explain some of the contradictory findings related to amygdala functioning described above. However, more research is needed, especially in child samples.

HIPPOCAMPUS AND PREFRONTAL CORTEX

Two other important structures that interact with the amygdala in fear-related processing are the hippocampus and the PFC. The hippocampus is adjacent to the amygdala in the limbic system and is associated with conversion of short-term into long-term memories, whereas the PFC is located on the anterior part of the frontal lobes and is associated with executive functioning. According to Craske, Rauch, and colleagues (2009), the ventromedial PFC and hippocampus supply top-down control over the amygdala. On extinction recall tasks, individuals first participate in fear conditioning (pairing a neutral stimulus with a fearful stimulus), and then they are subsequently tested during extinction (presentation of the neutral stimulus alone). During extinction recall, the ventromedial PFC controls the amygdala by inhibiting responses to learned threat cues. Furthermore, the hippocampus supplies information that is permissive of extinction recall by providing information regarding safe versus dangerous contexts. Thus, since the hippocampus and PFC share reciprocal projections with the amygdala, through which it

can modulate PFC neuronal activity and the PFC can modulate amygdala-mediated responses to emotionally salient stimuli (Garcia, Vouimba, Baudry, & Thompson, 1999; Quirk, Russo, Barron, & Lebron, 2000), these areas have been implicated in extinction learning. In contrast to fear acquisition, extinction learning involves modulation of lateral amygdala neuron activity through excitatory inputs from the ventromedial PFC onto inhibitory intra-amygdala interneurons (Quirk & Mueller, 2007). Interestingly, it appears that there may be greater connectivity between the amygdala and the hippocampus in adults than in adolescents. As described above, Guyer, Monk, and colleagues (2008) found greater amygdala activation and connectivity between the amygdala and hippocampus among healthy adolescents than adults during passive viewing of fearful faces. They interpreted this finding as evidence of maturation in learning or habituation to facial expressions in adults.

Regarding the PFC, research in adults has found that adults with GAD show increased amygdala connectivity with different PFC regions, such as the dorsomedial and ventromedial PFC, compared with healthy controls (Etkin, Prater, Schatzberg, Menon, & Greicius, 2009). In the Monk and colleagues (2008) studies described above, children with GAD showed strong right amygdala and right ventrolateral PFC coupling when viewing masked angry faces, suggesting that the PFC modulates the amygdala response to threat. Likewise, in the study of socially anxious adolescents described above, Guyer, Lau, and colleagues (2008) found coactivation in the amygdala and ventrolateral PFC circuitry when participants were viewing photographs of peers for an anticipated social interaction. The PFC has also been implicated in studies of healthy children and adolescents (Telzer et al., 2008) and in adolescents with GAD (McClure et al., 2007; Monk et al., 2006) during attentional bias tasks for angry faces.

The OFC is part of the PFC and is involved in decision making and guiding behavior; it seems to be particularly important in signaling the expected rewards or punishers of a planned action. According to Craske, Rauch, and colleagues (2009), the medial OFC mediates positive valuations (e.g., of reward and safety), whereas the lateral OFC mediates negative valuations (e.g., of punishment); thus medial OFC plays a role in suppression of fear, whereas lateral OFC appears to mediate negative cognitions such as obsessions and worry. Although increased activation within lateral OFC has not been consistent across anxiety disorders, it may be a hallmark function of conditions characterized by worry and obsessions (Milad & Rauch, 2007). Consistent with this finding in adults, adolescents with GAD, SOC, and SAD show significantly enhanced left OFC activation relative to healthy controls (Beesdo, Lau, et al., 2009).

INSULAR CORTEX AND ANTERIOR CINGULATE CORTEX

In addition to the PFC, two other regions of the cortex are implicated in the anxiety disorders; however, there is little research on these regions in children and adolescents. The ACC is located in the front of the cingulate cortex around the corpus callosum. The ACC has two components—the dorsal ACC and the ventral ACC. The dorsal ACC is sometimes referred to as the "cognitive component," as it is connected to the PFC and has been implicated in functions such as error detection, conflict monitoring, and attention; the ventral ACC is sometimes referred as the "affective component," because it is connected to the amygdala, nucleus accumbens, hypothalamus, and anterior insula and is involved in assessing the salience of motivation and emotion (Craske, Rauch, et al., 2009). The ACC appears to play a role in disorders characterized by pathological doubting, such as obsessive–compulsive disorder (formerly classified with the anxiety disorders) and GAD, because it plays a role in suppressing attention and response to cognitive (dorsal ACC) and affective (ventral ACC) stimuli. Although the research on pediatric samples is limited, the study by McClure and colleagues (2007) described above suggests that in addition to the amygdala and PFC, the ACC also plays a role in adolescent GAD.

The insular cortex (insula) is a portion of the cerebral cortex folded within the lateral sulcus (separating the temporal and parietal lobes). According to Craske, Rauch, and colleagues (2009), it mediates interoception and thus plays a role in awareness of and sensitivity to visceral activity. Given that stronger physiological responses to aversive stimuli elicit stronger classical conditioning, the insula is implicated in anxiety sensitivity, or fearfulness of the potentially harmful nature of the cognitive and behavioral correlates of anxiety (Reiss & McNally, 1985; Reiss et al., 1986). In a meta-analysis, Etkin and Wager (2007) found that adults with SOC, specific phobia, or posttraumatic stress disorder showed greater activity than comparison adults in the amygdala and insula, and a similar pattern was observed during fear conditioning in healthy participants. Interestingly,

hyperactivation in the amygdala and insula were more frequently observed with SOC and specific phobia than with posttraumatic stress disorder. To our awareness, no studies have examined the insula in child samples.

STRIATUM

The final set of neural circuitry that has been examined with regard to anxiety disorders is the striatum, which includes the nucleus accumbens, the putamen, and the caudate nucleus. These structures are located in the basal ganglia at the base of the forebrain and are involved in responding to reward-related cues. In studies of adolescents, those who had been classified as behaviorally inhibited in early childhood showed increased activation in the striatum, compared with adolescents classified as noninhibited in early childhood, while anticipating monetary gain or loss (Bar-Haim et al., 2009; Guyer et al., 2006). In a study of adolescents with anxiety disorders, while anticipating incentives of increasing magnitude, adolescents with SOC showed increasingly heightened caudate and putamen activation relative to that seen in the healthy comparison group and the group with GAD (Guyer et al., 2012). Thus it appears that, similar to findings in behaviorally inhibited adolescents, adolescents with SOC show similar neural responses in anticipation of incentives.

In summary, it appears that a number of neural circuits are involved in the anxiety disorders, including the amygdala, PFC, hippocampus, OFC, ACC, insular cortex, and striatum. The extent to which these regions are also affected in pediatric anxiety disorders has yet to be fully explored. Of the limited research to date that has been conducted on child and adolescent samples, most has focused almost exclusively on adolescents with GAD, and the sample sizes have been relatively small (N's < 20). Additional research in this area is needed and is likely to characterize the next decade of research on the psychopathology of the anxiety disorders in childhood.

Glucocorticoid Neurohormones (Cortisol)

In addition to examining brain structure and functioning, study of the neurobiology of stress and anxiety has focused on how the endocrine system functions in response to stress. The endocrine system uses hormones to send messages to the bodily organs, which are produced by several glands throughout the body. Cortisol, which is released by the hypothalamic–pituitary–adrenocortical (HPA) axis, is the most commonly studied stress hormone. The HPA axis is a complex chain of influences and feedback interactions between the hypothalamus (located in the midbrain), the pituitary gland (base of the brain), and the adrenal glands (on top of the kidneys). The hypothalamus releases corticotropin-releasing hormone (CRH) when the body is stressed. CRH then stimulates the pituitary gland to release adrenocorticotropic hormone (ACTH), which in turn stimulates the adrenal glands to release glucocorticoid hormones (or cortisol). Cortisol in turn acts on the hypothalamus and pituitary to suppress CRH and ACTH in a negative feedback loop. Although typically following a 24-hour circadian pattern, cortisol is secreted at increased levels during periods of heightened stress (Kirschbaum, Pirke, & Hellhammer, 1993).

Increases in cortisol have both immediate and delayed negative effects on various aspects of functioning. In the short term, cortisol can interfere with communication between different brain structures and can temporarily impair attentional and memory processes (Davis, Bruce, & Gunnar, 2002). Sustained increases in cortisol (e.g., in response to chronic stressors), however, have been associated with more detrimental outcomes, including anxiety disorders (e.g., Forbes et al., 2006; Granger, Weisz, & Kauneckis, 1994; Kallen et al., 2008). For instance, in a study of children with SAD (mean age = 8.45 years), these children showed higher cortisol secretion than did controls across the entire duration of the investigation, and their cortisol secretion increased when they anticipated being separated from a parent (Brand, Wilhelm, Kossowsky, Holsboer-Trachsler, & Schneider, 2011). Similarly, in a study of children with SOC (ages 6–12), these children showed elevated cortisol response compared with healthy controls during a public speaking task (van West, Claes, Sulon, & Deboutte, 2008). Furthermore, persistence of anxiety disorders is associated with changes in cortisol production. In a recent study of children with anxiety disorders receiving cognitive-behavioral treatment, persistence of anxiety disorders after treatment was related to increased daytime cortisol production; at a 1-year follow-up, daytime cortisol was lowest in the early remitters, higher in the late remitters, and highest in the nonremitters (Dierckx et al., 2012). In this study, remission status was also related to morning cortisol rise. Normal HPA axis functioning is associated with a rapid early morning rise in cortisol production; however, the nonremitters had the lowest cortisol morning

rise, compared with early remitters and late remitters (Dierckx et al., 2012). These findings suggest not only that anxiety disorders are associated with higher overall levels of cortisol, but that there appears to be a dysregulation of the HPA axis among those with persistent anxiety problems.

In fact, some research shows that although transient stressors result in increased cortisol secretion, chronic stress is associated with blunted cortisol secretion (Marin, Martin, Blackwell, Stetler, & Miller, 2007; Miller, Chen, & Zhou, 2007). In a meta-analysis of 107 studies, Miller and colleagues (2007) found that effects on the HPA axis depend on the features of the stress. In particular, it appears that both recent stress and ongoing stress are associated with increased HPA output, whereas distant traumas are associated with decreased HPA output to below normal levels, suggesting a down-regulation of the HPA axis. Miller and colleagues (2007) also found that stress that threatens physical integrity (e.g., combat, child abuse), as well as uncontrollable stress, elicits a slightly lower morning secretion with higher afternoon/evening and evening output. Consistent with this meta-analysis (which focused on studies with adults), a recent longitudinal study of 96 adolescents found that those with more internalizing problems in adolescence had higher morning cortisol; however, when the sample was examined longitudinally, those who had greater internalizing behaviors in childhood had lower morning cortisol levels as adolescents (Ruttle et al., 2011). Thus it appears that whereas the HPA axis is activated when children first display behaviors, long-term exposure may lead to dysregulation of the HPA axis over time.

Chronic or prolonged exposure to heightened levels of cortisol as a result of early stress or trauma also appears to have neurotoxic effects on the developing brain (Lupien, McEwen, Gunnar, & Heim, 2009; Sapolsky, Krey, & McEwen, 1986). Lupien and colleagues (2009) suggest that the specific effect of chronic stress on the developing brain is a result of the time at which the stress occurs during critical brain development periods. In other words, the effects of cortisol (as a result of prolonged or chronic stress) have the highest impact on the brain structures that are developing at the time of the stress. For example, it appears that stress and heightened glucocorticoids experienced during childhood may have a greater impact on the hippocampus, which is continuing to develop in childhood. On the other hand, the critical development period for the PFC is in adolescence, and thus chronic stress at this time appears to have a greater effect on the development and functioning of this structure (Lupien et al., 2009).

Temperament

An accumulation of findings over the last half century suggests that child temperament may be a general vulnerability factor for anxiety. *Temperament* generally refers to inherent basic dispositions, which underlie and modulate expressions of emotionality, activity, and sociability (Buss & Plomin, 1975, 1984; Thomas & Chess, 1985). Most research suggests that temperament is evident early in life, is strongly biologically based, and is generally stable throughout life (Buss & Plomin, 1984; Derryberry & Rothbart, 1984; Rothbart, 1989). Temperament is often considered an early form of personality, and accordingly, several studies have examined the relation among common temperamental factors and the Big Five model of personality (Angleitner & Ostendorf, 1994; Digman, 1994). For instance, in a sample of 624 children ages 6 to 7 in the People's Republic of China and the United States, Ahadi, Rothbart, and Ye (1993) found three temperamental factors that emerged on the Children's Behavior Questionnaire, a parent report measure of child temperament. The three basic temperament factors that emerged across the two cultures are consistent with three of the Big Five: Extraversion (Surgency), Neuroticism (Negative Affectivity/Emotional Stability), and Conscientiousness (Effortful Control).

The Tripartite Model of Emotion

Perhaps the greatest accumulation of recent research in this area builds on Clark and Watson's (1991) tripartite model of emotion and its relation to anxiety and depression in children (see also Mineka, Watson, & Clark, 1998). The tripartite model originally posited factors of Positive Affectivity (PA), Negative Affectivity (NA), and Physiological Hyperarousal (PH), to account for the relation of anxiety and depression (with PA and NA likened to Extraversion and Neuroticism, respectively; e.g., Ahadi et al., 1993; Lonigan & Phillips, 2001). Clark and Watson (1991) articulated a model in which NA represented a factor common to anxiety and depression, (low) PA represented a factor specific to depression, and PH represented a factor specific to anxiety. Considerable evidence has shown that both NA and PA appear to be temperamental constructs, acting as risk factors for anxiety and mood disorders (e.g., Lo-

nigan & Phillips, 2001; Mineka et al., 1998; Watson, Clark, & Harkness, 1994).

Given the implications of this model for understanding both the etiology and comorbidity of anxiety and depression, there have been ongoing efforts to investigate the validity of the tripartite model of emotion in child and adolescent samples (e.g., Chorpita, 2002; Chorpita, Albano, & Barlow, 1998; Joiner et al., 1996; Lonigan et al., 1994; Lonigan, Hooe, David, & Kistner, 1999; Lonigan, Phillips, & Hooe, 2003). The collective findings support a model in children and adolescents roughly consistent with the tripartite model in adults (e.g., Chorpita, Albano, & Barlow, 1998; Joiner et al., 1996). For example, Lonigan and colleagues (1994) found that measures related to low PA best discriminated children with depressive disorders from those with anxiety disorders. Lonigan and colleagues (1999) examined the relations of PA and NA measures with anxiety and depression measures in a school sample of 365 children and adolescents and found that NA and PA measures performed in a manner consistent with findings from adult samples, and that such findings were uniform across children and adolescents. Furthermore, Lonigan and colleagues (2003) found temporal stability of a two-factor orthogonal model of NA and PA in a longitudinal study of 4th- to 11th-grade children; this model predicted symptoms of anxiety and depression, providing additional support for the notion that NA and PA are temperamental factors.

Amidst a gathering of empirical support for the tripartite model, some revisions to the model in the late 1990s (Brown et al., 1998; Mineka et al., 1998) suggested that PH is not uniformly related to all anxiety disorders. For example, in a sample of 350 adults with anxiety disorders, Brown and colleagues (1998) found that PH was related positively only to measures of panic, but not to the other anxiety disorders measured. These results were first partially replicated in a sample of 100 children with anxiety and mood disorders (Chorpita, Plummer, & Moffitt, 2000). As had been done in previous studies in the child literature, tripartite scales were constructed by summing items from anxiety and depression measures that were selected to represent the constructs of NA, PA, and PH. Although consistencies with findings in the adult literature were enough to encourage continued research, the number of inconsistencies raised some questions about the utility of these early measurement strategies (Lonigan et al., 1999). The model outlined by Brown and colleagues in adults was therefore evaluated once more in a nonclinical sample of 1,578 children in grades 3 through 12, using a measure empirically designed to tap the tripartite factors in children (Chorpita, 2002). The results of that investigation were consistent with previous observations in adult samples; in particular, PH was positively related with panic only, and was not significantly positively correlated with other anxiety dimensions. The model also appeared robust across different grade levels and gender (Chorpita, 2002).

One particularly interesting feature in this line of investigation is that the relation between the general vulnerabilities in the model (i.e., NA) and generalized anxiety measures tend to be among the strongest links. In fact, early research in this area frequently used items taken from older measures of anxiety as indicators for NA, and a diversity of findings suggests that many of the early anxiety measures may actually have been better characterized as measures of a broad negative emotionality (Stark & Laurent, 2001). The similarity between NA and the general experience of anxious emotion has been raised elsewhere (Chorpita & Barlow, 1998); in the context of anxiety and depressive disorders, it suggests that anxiety itself may represent a risk factor for the development of anxiety disorders as well as depression. This notion is consistent with many of the patterns found in adult research, such as the tendency for the onset of anxiety disorders to precede depression but not the reverse, as well as observations of asymmetrical comorbidity (whereby anxiety disorders often co-occur with cases of depression, but depression co-occurs less frequently with cases of anxiety disorders). Findings in the child literature lend further support to this idea. In a prospective study of 330 children followed over a 3-year period, heightened anxiety symptoms predicted future high depression even after adjustments for past depression scores, but the reverse was not found (Cole, Peeke, Martin, Truglio, & Ceroczynski, 1998).

Despite growing empirical support for the applicability of the tripartite model to younger child samples, there is stronger support for its applicability in samples of older children and adolescents. For example, Jacques and Mash (2004) found that among a large community sample of elementary school children and high school adolescents ($N = 472$), the tripartite model was better supported in the older sample. Similarly, Lonigan and colleagues (1999) found that the tripartite model fit data from older children from a nonclinical sample ($N = 213$, ages 12–17) better than their younger counterparts ($N = 152$, ages 9–11). Moreover, in a recent multisample confirmatory factor-analytic study of 1,470 clinic-referred

and 757 school-based children (ages 7–18), Price and colleagues (2013) found support for separating anxiety and depression for all samples except for the nonclinical younger sample, suggesting that these constructs are more similar than different in subclinical children. Results from these studies support the notion that there is an underlying trait contributing to both anxiety and depression (i.e., NA), and that differentiation between anxiety and depression increases across development (De Bolle & De Fruyt, 2010).

Behavioral Inhibition

A classic model of temperament and its relation to anxiety involves the work of Kagan and colleagues regarding behavioral inhibition (BI; e.g., Biederman et al., 1990, 1993a, 1993b; Hirshfeld et al., 1992; Kagan, 1989, 1997; Rosenbaum et al., 1988, 1992; Rosenbaum, Biederman, Hirshfeld, Bolduc, & Chaloff, 1991). As defined by Kagan (1989, 1997), BI refers to a child's degree of sociability and degree of uncertainty toward novel objects, situations, and people, as displayed by observable behaviors manifested along the approach–withdrawal dimension. The criteria by which BI is measured include both behavior (speech latency and frequency to peers and adults, proximity to caregiver, physical inactivity, verbalization of distress) and physiology (heart rate, heart rate variability, blood pressure, pupil dilation, muscle tension, cortisol level, urinary norepinephrine levels, and vocal pitch) (Kagan, Reznick, Snidman, Gibbons, & Johnson, 1988). Children with consistent BI across time have been found to evidence greater autonomic reactivity, elevated morning cortisol levels, heightened startle responses, and more vigilant attention styles (Pérez-Edgar & Fox, 2005; Schmidt & Fox, 1998; Schmidt, Fox, Schulkin, & Gold, 1999). Functional imaging studies have also found those with BI to display heightened amygdala activation to novel neutral or threatening faces (Perez-Edgar et al., 2007; Schwartz, Wright, Shin, Kagan, & Rauch, 2003).

Approximately 15% of children are characterized as displaying BI across samples (Fox et al., 2005; Kagan, Reznick, Snidman, Gibbons, & Johnson, 1988). According to Kagan, Reznick, Snidman, Gibbons, and Johnson (1988), these children become shy and fearful as toddlers, and quiet, cautious, and introverted by the start of their primary school years. In standardized behavioral test situations, these children consistently refrain from spontaneous vocalizations when in the presence of a stranger, and cry and cling to their mothers rather than explore play settings and approach other children. At the other end of the scale, about 15% of the children studied demonstrated an opposing temperament of being sociable, bold, and gregarious. Moreover, as opposed to the inhibited cohort, these uninhibited children are untroubled by novel stimuli. Kagan and colleagues have followed two independent cohorts of children over an extended (7-year) period. Children were originally identified as inhibited or uninhibited at either 21 or 31 months of age during standardized behavioral tests when exposed to unfamiliar settings, people, and objects. These differences in behavior were largely maintained through repeated assessments at 4, 5, and 7 years of age, suggesting that such differences represent an enduring temperamental trait (see Kagan, Reznick, & Gibbons, 1989). Thus BI appears to be biologically based, is detectable early in life, is moderately stable across life, and appears to be under some genetic control (Kagan, Reznick, & Snidman, 1988; Robinson, Kagan, Reznick, & Corley, 1992; Smoller et al., 2003, 2005).

Kagan's original work on BI was designed to examine temperamental styles of infants, and thus no specific hypotheses regarding psychopathology were postulated. However, as attention turned toward the study of childhood anxiety disorders, the similarities between inhibited and anxious children became more apparent. In a recent review of the literature on BI and child anxiety, Degnan, Almas, and Fox (2010) reviewed more than 30 different studies that examined the relation between BI and child anxiety. In general, the research supports concurrent and longitudinal relations between BI and child anxiety. For instance, early childhood BI is significantly related to later diagnosis and symptoms of anxiety (e.g., Biederman et al., 1990; Hirshfield et al., 1992; Hirshfeld-Becker et al., 2007; van Brakel, Muris, Bögels, & Thomassen, 2006). Furthermore, Hudson and Dodd (2012) recently found that BI at age 4 was associated with increased risk for SOC, SAD, and GAD at age 9. Support for BI as a risk factor for SOC has been replicated in a number of different studies, suggesting that BI may share a uniquely strong relation with SOC above and beyond the other anxiety disorders (Biederman et al., 2001; Chronis-Tuscano et al., 2009; Essex, Klein, Slattery, Goldsmith, & Kalin, 2010; Muris, van Brakel, Arntz, & Schouten, 2011; Schwartz, Snidman, & Kagan, 1999).

Despite such apparent associations, however, at least a quarter of children identified as displaying BI do not

show any diagnosable anxiety disorder (e.g., Biederman et al., 2001; Gladstone, Parker, Mitchell, Wilhelm, & Malhi, 2005). Furthermore, at least one study has failed to show that children characterized as exhibiting extremely high BI at age 3 were at increased risk for anxiety disorders at age 21. Instead, these children were found to be at increased risk for depression at age 21 (Caspi et al., 2003). Thus, although BI is one of the most consistent individual risk factors for later anxiety (Fox et al., 2005; Mian, Wainwright, Briggs-Gowan, & Carter, 2011), the association between childhood BI and later anxiety still shows almost as much disassociation as it shows association across time (Degnan & Fox, 2007); this suggests that there are other risk factors that may interact with temperament across development (Hudson & Dodd, 2012; Muris et al., 2011).

The Behavioral Inhibition System

Whereas Kagan's work on BI has focused primarily on behavioral and physiological outputs of temperament, and specifically within a social context, other models of temperament and anxiety have focused more directly on the organization of biological systems that underlie motivation and emotion more generally (e.g., Gray & McNaughton, 1996). Gray (1982) detailed the operations of two functional brain systems that serve to motivate behavior—the behavioral inhibition system (BIS) and the behavioral activation system (BAS). Both systems function independently in typical individuals and are sensitive to different types of reinforcement. The BAS is sensitive to signals of reward and absence of punishment, and behavioral effects include appetitive approach behavior. On the other hand, the BIS is sensitive to signals of punishment, nonreward, and novelty. Behavioral effects of the BIS include inhibition of ongoing behavior, increased attention, and increased arousal. According to Gray, the primary, short-term outputs of the BIS involve narrowing of attention, inhibition of gross motor behavior, increased stimulus analysis (e.g., vigilance or scanning), increased central nervous system arousal (e.g., alertness), and priming of hypothalamic motor systems for possible rapid action that may be required (i.e., possible activation of the fight–flight system). Its phenomenology is characterized by increased caution, vigilance, and processing of threat-relevant information. In a study of 170 children ages 3–5, parent-reported withdrawal motivation (BIS) was associated with cortisol increase, whereas parent-reported approach motivation (BAS) was associated with cortisol decrease (Blair, Peters, & Granger, 2004).

Similar to research on the tripartite model, some work on Gray's model suggests that there may be a third system—the fight–flight–freeze system (FFFS; Gray & McNaughton, 2000), which is activated by aversive stimuli and motivates escape behavior. Overactivity in BIS is assumed to be an underlying factor across all anxiety disorders, whereas overactivity in FFFS is assumed to be related to panic disorder, SOC, and specific phobia (Gray & McNaughton, 2000; Zinbarg & Yoon, 2008). For instance, in a study of 175 clinically anxious and nonanxious children ages 8–18, Vervoort and colleagues (2010) found that BIS scores were highest among those with anxiety disorders; the BIS_Anxiety scale was significantly correlated with all subscales on a brief measure of anxiety disorder symptoms, whereas the BIS_FFFS scale was only significantly related to the panic and social anxiety subscales of this measure.

Effortful Control

Another temperamental trait that is garnering attention for its potential contribution to the development of anxiety is effortful control (EC), or the ability to engage executive functioning processes to inhibit reactive tendencies and substitute more adaptive responses (Derryberry & Rothbart, 1997; Lonigan & Phillips, 2001; Lonigan & Vasey, 2009; Posner & Rothbart, 2000). According to Lonigan and Phillips (2001), although high NA accounts for some of the variance observed in the development of anxiety disorders, there are potential moderators to consider, given that not everyone with high NA develops an anxiety disorder. Lonigan and Phillips suggest that the combined effects of high NA and low EC are required for the development of anxiety disorders, and some cross-sectional and longitudinal research has supported this theory. For instance, in two separate studies of children and adolescents, Muris and colleagues found that EC moderated the relation between NA and internalizing symptoms (Muris, 2006; Muris, Meesters, & Rompelberg, 2007), and in a study of 10-year-old children, EC and NA interacted to predict internalizing symptoms over a 3-year period (Oldehinkel, Hartman, Ferdinand, Verhulst, & Ormel, 2007). Thus, although temperament clearly plays a role in the development of anxiety disorders, the nature of this contribution appears to go beyond rudimentary main effects of common temperamental dimensions.

Cognitive and Learning Influences

In light of the review above, it is clear that any psychosocial influences might better be considered biopsychosocial in nature, given their important dynamic interaction with aspects of biology and temperament. In addition, more recent theorizing suggests that just as the general biological influences for anxiety overlap heavily with those for depression, so too do the general psychological influences for anxiety. Within this context, recent work has focused on detailing possible mechanisms or processes that may establish or intensify risk for negative emotions, especially regarding cognitive coping strategies (Kendall, 1992), information processing (McNally, 1996; Vasey, Daleiden, Williams, & Brown, 1995), social–familial transmission (Barrett, Rapee, Dadds, & Ryan, 1996; Chorpita, Brown, & Barlow, 1998), and complex forms of conditioning (Bouton, Mineka, & Barlow, 2001).

Information Processing

Early cognitive models of child anxiety were drawn largely from Beck's schema-based theory of adult anxiety (Beck, Emery, & Greenberg, 1985). Schemas are organized bodies of information stored in memory, which facilitate the processing of information that is consistent with the schemas and interfere with information that is inconsistent with them. In 1990, Kendall and Ronan proposed that childhood anxiety is a result of overactivity of threat-related schemas. Not long after, Daleiden and Vasey (1997) adapted Crick and Dodge's (1994) stage model of information processing in aggressive children to outline a more precise role of cognitions in child anxiety. There are six stages in the model: (1) *encoding*, in which information is selected for further processing; (2) *interpretation*, in which meaning is attached to ambiguous information and causal attributions, and outcome expectations are made; (3) *goal clarification or selection*, in which goals are revised and selected to meet the demands of the situation; (4) *response access or construction*, in which potential responses are retrieved or generated; (5) *response selection*, in which potential responses are evaluated; and (6) *enactment*, in which the best possible response is selected and enacted. Furthermore, memory is believed to influence every stage of the process, affecting both the content and the organization of information. Whereas the first two stages have garnered a wealth of support in the research over the last two decades, the third through sixth stages have not been as well studied; nor has memory processing been widely studied.

SELECTIVE ATTENTION

According to information-processing theories of anxiety (Beck et al., 1985; Daleiden & Vasey, 1997; Kendall & Ronan, 1990), children with heightened anxiety should selectively attend to threatening over nonthreatening information. In other words, they should demonstrate an attentional bias toward threat. In a meta-analysis, Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, and van IJzendoorn (2007) found a medium effect (d = 0.45) for threat-related attentional biases across all experimental paradigms, conditions, and populations, with studies of children (k = 11) also showing a medium effect (d = 0.50).

Two experimental paradigms have been widely studied in the child anxiety information-processing literature to date: a modified emotional Stroop task and a dot probe task. In the emotional Stroop task, participants are told to name the color of the ink a word or picture is printed in. Words or pictures are then varied, typically falling into threatening and nonthreatening/neutral categories. For instance, in studies assessing attentional bias among children with spider phobia, words such as "spider" or "crawling" would be considered threatening stimuli, whereas words such as "fence" or "grass" would be regarded as nonthreatening stimuli. Because threat-relevant words have captured the child's attention (bias toward threat), anxious children are expected to take longer to name the color of those words relative to the neutral words. Although findings using the modified Stroop task among children with heightened anxiety have not been completely consistent, the Bar-Haim and colleagues (2007) meta-analysis reported that across studies, anxious children were typically slower than controls to respond to threat words, and the differences between threat and nonthreat words were more pronounced in anxious children relative to controls.

On the other hand, Bar-Haim and colleagues (2007) found no difference between anxious and nonanxious control children in attentional bias on dot probe tasks. This is somewhat surprising, given earlier research suggesting that anxious children do evidence an attentional bias toward threat with this experimental paradigm (e.g., Vasey et al., 1995; Vasey, El-Hag, & Daleiden, 1996). In a dot probe task, children view two words or stimuli on a computer screen, one on top of

the other. Some trials pair a threatening and a nonthreatening stimulus at the same time on the screen, and in some trials the pairing is neutral–neutral. Immediately following the presentation of these stimuli, a small dot probe appears in the position previously occupied by one of the two words (randomly alternating across threatening and neutral positions). Children are instructed to respond when they see the dot probe appear (e.g., to press a button on a keyboard). The latency to detect this probe measures attention toward the word that just appeared within the probed screen location. Thus shorter latencies when the probe follows a threat word indicate attentional bias toward the threat word. One potential methodological explanation for Bar-Haim and colleagues' finding is that the Vasey and colleagues (1996) study was not included in that meta-analysis because it was a significant outlier.

INTERPRETATION BIAS

In addition to attending selectively to threatening over nonthreatening information, anxious children demonstrate clear interpretation biases. Research has generally demonstrated that across experimental paradigms, anxious children perceive more threat, perceive threat more quickly, make more threatening interpretations and predictions when presented with ambiguous situations, and select more threatening interpretations on homophone tasks (Barrett, Rapee, et al., 1996; Bell-Dolan, 1995; Cannon & Weems, 2010; Chorpita, Albano, & Barlow, 1996; Epkins, 1996; Hadwin, Frost, French, & Richards, 1997; Higa & Daleiden, 2008; Micco & Ehrenreich, 2008; Muris, Merckelbach, & Damsma, 2000; Taghavi, Moradi, Neshat-Doost, Yule, & Dalgleish, 2000; Weems, Berman, Silverman, & Saavedra, 2001; Weems, Costa, Watts, Taylor, & Cannon, 2007). Moreover, anxious children make more internal, stable, and global attributions for negative events than nonanxious controls do (Bell-Dolan & Last, 1990), and they tend to expect catastrophic outcomes, underestimate the future likelihood of positive outcomes, and have lower coping expectations (Chorpita et al., 1996; Micco & Ehrenreich, 2008; Leitenberg, Yost, & Carroll-Wilson, 1986; Spence et al., 1999). Nevertheless, not all studies have found support for interpretation biases (e.g., Bögels & Zigterman, 2000; In-Albon, Dubi, Rapee, & Schneider, 2009); the content specificity for interpretation biases has not been established (Bögels, Snieder, & Kindt, 2003; Dalgleish et al., 2003; Muris, Merckelbach, & Damsma, 2000); and at least one study has found that after adjustments for depressive symptoms, the relation between negative interpretations and anxiety symptoms was no longer significant (Eley, Gregory, et al., 2008). Thus, similar to research on selective attention, interpretation biases among anxious children appear to be less robust than those found among anxious adults or those the original theories would suggest. Therefore, some researchers have begun to question the downward extension of adult cognitive models to children.

DEVELOPMENT AND INFORMATION-PROCESSING BIASES IN CHILDREN

In a recent review, Field and Lester (2010) discuss two competing models that take development into account and compare these with the downward extension of cognitive theories in adults. In the first moderational model, Field and Lester suggest that information-processing biases may be present in all young children (anxious and nonanxious)—perhaps serving an evolutionary function—and that these biases diminish over time as a result of experiences with the environment for most children, but remain for those predisposed to anxiety. In other words, bias toward threatening information is a normal developmental process that decreases over time in typical individuals; however, those with a predisposition to anxiety do not learn to ignore or do not develop the ability to inhibit attention to threat, which makes them more vulnerable to biases in information processing (Kindt & van den Hout, 2001; Nightingale, Field, & Kindt, 2010). Research indicates that infants as young as 5 months of age and pre-school-age children show attentional biases to fear-relevant stimuli, including spiders, snakes, and angry faces (LoBue & DeLoache, 2008, 2010; Rakison & Derringer, 2008), and Creswell and colleagues (2008) found no differences between behaviorally inhibited and uninhibited infants' look times at angry, happy, and fearful faces. Furthermore, this model fits with attentional bias studies that have found no differences in anxious and nonanxious children under age 12 (e.g., Kindt, Bierman, & Brosschot, 1997; Kindt, van den Hout, de Jong, & Hoekzema, 2000; Waters, Lipp, & Spence, 2004).

In another attempt to explain some of the null findings in selective attention tasks, Lonigan and Vasey (2009) studied the moderating effects of EC on the relation between NA and attentional biases. They found that among children and adolescents, those who were high in NA and low in EC demonstrated significant

bias in favor of threat cues, whereas those high in NA and high in EC did not show this bias. Furthermore, although they did not find an age effect (which calls the moderational model into question), the youngest participants in their study were 10 years of age, which is the age above which some research has suggested that such biases tend to diminish among nonanxious children (Kindt et al., 2000). Taken together, these studies suggest the possibility that the capacity for effortful control develops around the same time that attentional biases diminish among nonanxious children (e.g., Posner & Rothbart, 2000), and thus both could be playing a role in the development of attentional biases among anxious children.

Field and Lester's (2010) second competing model appears to have more relevance for understanding interpretation biases. The acquisition model, which has also been described by other researchers (Alfano, Beidel, & Turner, 2002; Manassis & Bradley, 1994), suggests that the emergence of information-processing biases toward threat are linked to the development of cognitive, social, and emotional skills necessary to sustain them, which emerge during specific developmental stages in childhood. In other words, information-processing biases toward threat are not present in young children, but they emerge with developmental sophistication. Research examining cognitive development with theory-of-mind tasks and Piagetian conservation tasks has found that performance on these tasks predicted anxious interpretations and emotional reasoning scores (Muris, Mayer, Vermeulen, & Hiemstra, 2007). Thus current research seems to support an acquisition model of interpretation biases: As a child develops cognitively, his or her capacity for interpretation biases also develops. Field and Lester proposed two possible ways that trait anxiety interacts with development: (1) Anxious children develop information-processing biases as they develop the cognitive capacity for such biases, whereas nonanxious children do not; and (2) trait anxiety emerges as a result of acquiring an information-processing bias. According to Field and Lester, there is no evidence to support trait anxiety's moderating the developmental trajectory of interpretation biases, but there is research to support that anxiety is causally influenced by the acquisition of an interpretation bias (Mackintosh, Mathews, Yiend, Ridgeway, & Cook, 2006; MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002; Wilson, MacLeod, Mathews, & Rutherford, 2006). Clearly, more research is needed to specify these relations.

Conditioning Experiences

DIRECT CONDITIONING

Historical learning models of child anxiety date back to Pavlov's (1927/2003) classical conditioning and Watson and Rayner's (1920) demonstration of fear conditioning with Little Albert. That is, when an aversive stimulus (i.e., the unconditioned stimulus [US]; e.g., a loud noise), which elicits an unconditioned response (UR; e.g., crying), is repeatedly paired with a neutral stimulus (e.g., a white rat), over time the neutral stimulus (i.e., the conditioned stimulus [CS]) elicits a conditioned response (CR) in the absence of the US (i.e., crying upon presentation of the white rat without the loud noise). Because fear conditioning is acquired through an association between stimuli (i.e., the US and the CS), which mediates the CR, it is also referred to as "associative learning" (Davey, 1997; Field & Davey, 2001; for a thorough review, see Field, 2006). Although considerable retrospective research has found that anxious children and adults report traumatic conditioning experiences that they attribute to the onset of their symptoms (e.g., Gruner, Muris, & Merckelbach, 1999; Muris, Steerneman, Merckelbach, & Meesters, 1996; Ollendick & King, 1991; Öst & Hugdahl, 1981), less research has examined conditioning prospectively, in part due to ethical concerns about creating fears in humans. However, sophisticated research paradigms over the last two decades have allowed for the prospective examination of fear conditioning and have sought to eliminate long-term effects on participants.

Direct conditioning models that attempt to explain the development and maintenance of anxiety disorders have evolved to include individual differences in responding. Such individual differences include associative learning deficits (Grillon, 2002), greater stimulus generalization (Mineka & Zinbarg, 1996), and enhanced conditionability (Orr et al., 2000; Peri, Ben-Shakhar, Orr, & Shalev, 2000). In a meta-analysis of 20 studies of explicit threat cue learning among adults with and without anxiety disorders (N = 908), Lissek and colleagues (2005) found that relative to healthy controls, adults with anxiety acquired greater fear responses in simple conditioning paradigms in which the neutral cue (CS) was repeatedly paired with an anxiety-provoking stimulus (US), sometimes noted as CS+ and referred to as acquisition training or acquisition trials (d = 0.42). In addition, the effects of extinction training or extinction trials, in which the CS is presented without the US, was weaker among adults with anxiety

than among healthy controls ($d = 0.39$). Together, these findings suggest not only that adults with anxiety acquire fear more readily than those without anxiety, but that once this fear is conditioned, it is more difficult to extinguish in adults with anxiety disorders than adults without such disorders.

These differences between groups appear to be somewhat smaller in discrimination conditioning paradigms, in which a CS+ (e.g., tone) is repeatedly paired with a US (e.g., shock) and a CS+ (e.g., light) is never paired with the US (Lissek et al., 2005). In this paradigm, the CS– (i.e., the light) is sometimes viewed as a "safety stimulus," because it signals absence of the US, and discrimination learning is measured as the difference between the CRs to the CS+ and the CS–. Thus healthy controls should be able to suppress CRs during CS– trials and as a result should show superior discrimination learning, whereas those with anxiety disorders should demonstrate difficulty inhibiting fear even in the presence of safety cues and/or show overgeneralization from the CS+ to the CS– as a result of inability to discriminate features of the stimulus thus representing inferior discrimination learning. In the Lissek and colleagues (2005) meta-analysis, although the effect of discrimination learning was not significant during acquisition ($d = 0.08$), a nonsignificant trend emerged for discrimination learning during extinction ($d = 0.23$).

Although direct conditioning has not been as widely researched in child samples, several recent studies have examined effects of direct conditioning in youth samples and have yielded mixed findings. For instance, in a study of children ages 7–14 with and without anxiety disorders, Liberman, Lipp, Spence, and March (2006) exposed children to cartoon characters with (CS+) a very loud tone (105 dB, similar to a motorcycle or a jackhammer; US) and to different cartoon characters without (CS–) the loud tone. Children with anxiety disorders did not differentially rate the CS+ (cartoon character with the loud tone) or the CS– (cartoon character without the loud tone) as more or less fear-provoking after acquisition, but did rate the CS+ as more fear-provoking than the CS– after extinction. On the other hand, children without anxiety rated the CS+ as more fear-provoking than the CS– after acquisition but not after extinction. Furthermore, physiological measures did not evidence differential responding during acquisition trials for either anxious or nonanxious youth; however, during extinction, anxious children showed greater differential responding to the CS+ on extinction trials. Liberman and colleagues concluded that their results supported the notion that anxious children are resistant to extinction.

In another study of adolescents (mean age = 13.6 years) with and without anxiety disorders, Lau and colleagues (2008) presented adolescents with pictures of two females with neutral expressions. On some trials one of the faces was paired with a fearful face (CS+) and a loud, shrieking scream (US), while the other face remained neutral (CS–) and was not paired with the US. Lau and colleagues reported that regardless of CS type (i.e., CS+ or CS–), fear ratings were higher among anxious adolescents after acquisition trials than among nonanxious adolescents. However, across participants with and without anxiety, adolescents rated the CS+ as more fearful than the CS–, and all adolescents demonstrated greater resistance to extinction of fear ratings of the CS+ compared with the CS–.

Finally, in two additional studies, aversive conditioning among children ages 7–12 was examined using a discrimination task with two geometric figures, one paired with (CS+) and one paired without (CS–) an aversive tone (US). In the first study, Craske and colleagues (2008) found that, similar to Lau and colleagues' (2008) findings, fear responses to both CS+ and CS– were larger for anxious than for nonanxious children, but that anxious and nonanxious children showed similar levels of differential responding to the CS+ compared with the CS– during acquisition. Furthermore, similar to Liberman and colleagues' (2006) findings, anxious children in the Craske and colleagues study rated the CS+ as more unpleasant than the CS– compared with nonanxious children throughout acquisition, extinction, and a 2-week extinction retest. However, unlike Lau and colleagues and Liberman and colleagues, Craske and colleagues found that when CRs were collapsed across CS+ and CS–, anxious children demonstrated elevated CRs throughout extinction and the extinction retest. Similar to findings in the Craske and colleagues study, Waters, Henry, and Neumann (2009) found that anxious children showed larger skin conductance responses to both the CS+ and the CS– during acquisition, rated the CS+ as more arousing than the CS–, and showed greater resistance to extinction in skin conductance responses (but not arousal ratings) to the CS+ relative to the CS– compared with control children. Results from these studies provide additional support for the concept that anxious children and adolescents, similar to anxious adults, may have deficits in response inhibition to safety cues as well as delayed extinction, which may contribute to the development

of their condition. Nevertheless, given the mixed findings as well as the dearth of such research on pediatric populations, additional research in this area is needed.

CONTEXT CONDITIONING

Another type of learning involves conditioning to the situation within which the US is presented, and as such is referred to as "context conditioning." Thus, whereas explicit threat cue conditioning involves specific CSs that predict the US, in context conditioning the situation becomes predictive of the US and capable of eliciting a CR. For example, in animal studies of aversive conditioning, the animal not only becomes conditioned to the explicit CS or explicit cue (e.g., light) when it is repeatedly paired with the US (e.g., shock), but also becomes conditioned to the contextual CS or contextual cue (e.g., the cage where the shock was administered) (Blanchard & Blanchard, 1972). According to Craske, Rauch, and colleagues (2009), explicit threat cues elicit time-limited responses to imminent threat, whereas contextual cues elicit sustained anxiety responses to less certain threat. Furthermore, as noted above, some research has suggested that while the central nucleus of the amygdala may be involved in explicit threat conditioning, the BNST, the right anterior hippocampus, and the bilateral amygdala play a larger role in contextual conditioning (Alvarez, Biggs, Chen, Pine, & Grillon, 2008; Marschner, Kalisch, Vervliet, Vansteenwegen, & Büchel, 2008; Walker, Toufexis, & Davis, 2003; Yassa et al., 2012). Although context conditioning has not been as widely studied as explicit cue conditioning, the available research suggests that individuals with anxiety disorders evidence stronger conditioning to context than individuals without anxiety disorders do.

Although the research on contextual conditioning in youth with anxiety is limited, a growing body of research suggests that youth at risk for anxiety disorders may also be susceptible to contextual conditioning. For example, in a study of repeated trials of "safe–danger" sequences, adolescents high in Neuroticism demonstrated elevated startle reflex magnitude relative to individuals low in Neuroticism in conditions that were intermediately associated with threat of an aversive stimulus (i.e., biceps contraction) than in conditions that were close to the threat and in conditions that were far from the threat (Craske, Waters, et al., 2009). Craske, Waters, and colleagues (2009) interpreted these findings in light of the "strong situation" phenomenon, in which all participants (regardless of risk status) evidence enhanced startle in conditions with intense aversive stimuli, while anxious individuals evidence enhanced startle to less aversive stimuli. Similarly, all participants (regardless of risk status) evidence lower startle during baseline trials when they are reassured that no aversive stimulus will be presented, as was the case in this study. Thus this study demonstrates that adolescents high in Neuroticism are more likely to experience enhanced startle during contexts intermediary to threat than adolescents low in Neuroticism, providing initial support for the theory that adolescents with anxiety disorders, similar to adults with anxiety disorders, have a greater likelihood of conditioning to context than their nonanxious peers. Moreover, in a 4-year prospective longitudinal study of adolescents who participated in the Craske, Waters, and colleagues study, larger startle response magnitude during safe conditions predicted the first onset of anxiety disorders above and beyond the effects of comorbid depression, Neuroticism, and ratings of intensity of the aversive stimulus (Craske et al., 2012). Thus elevated startle in safe conditions or contextual conditionability may serve as a risk factor for the onset of anxiety disorders in youth.

VICARIOUS CONDITIONING AND INFORMATION TRANSFER

In addition to direct experiences with feared events or objects, indirect conditioning through observing another's fearful behavior (i.e., vicarious learning; Mineka & Cook, 1993) or through verbal communication (i.e., information transfer) is also believed to contribute to the development of fear and anxiety (Rachman, 1977). For example, toddlers show greater fear expressions and avoidance of fear-relevant and fear-irrelevant stimuli following negative reactions of their mothers (Dubi, Rapee, Emerton, & Schniering, 2008; Gerull & Rapee, 2002). Similarly, in a study of infants and their nonanxious mothers, infants were more likely to be fearful and avoidant of a stranger after watching their mothers behave in an anxious manner with the stranger than when their mothers interacted normally with the stranger (de Rosnay, Cooper, Tsigaras, & Murray, 2006). In addition to learning vicariously through parent behaviors, research has demonstrated that children can acquire fears by observing peers behaving fearfully. Broeren, Lester, Muris, and Field (2011) found that children (ages 8–10) who observed a film of a peer modeling fearful behavior toward a novel animal demonstrated increased fear beliefs about that animal (but not about a novel nonmodeled animal).

In a series of studies examining vicarious conditioning, Field, Muris, and colleagues (Askew & Field, 2007; Field & Lawson, 2003; Muris, Bodden, Merckelbach, Ollendick, & King, 2003; Muris et al., 2009) developed an innovative experimental paradigm in which children are exposed to pictures of novel animals. To test whether children can acquire a fear vicariously, Askew and Field (2007) exposed children ages 7–9 to pictures of three novel animals (Australian marsupials: the quoll, quokka, and cuscus, about which children in the United Kingdom would be unlikely to be knowledgeable) and paired these with pictures of scared facial expressions, happy facial expressions, or no faces and examined their fear cognitions and avoidance behavior. The investigators found that fearful attitudes toward the animals changed in a manner congruent with the facial expressions with which they were paired; that these beliefs persisted for up to 3 months; and that children demonstrated avoidance behavior when they believed a box contained an animal they had previously seen paired with fearful faces.

To examine whether children can acquire a fear through information transfer, Field and Lawson (2003) presented children with negative, positive, and no information about these same animals. They reported that verbal threat information significantly increased self-reported fear beliefs, emotional reaction time performance, and behavioral avoidance. These effects persisted when children were tested 6 months later (Field, Lawson, & Banerjee, 2008). Furthermore, although younger children (ages 6–8) formed stronger animal-threat and animal-safe associations as a result of information transfer than older children (ages 12–13) did, their self-reported fear and avoidance behaviors did not differ significantly from those of older children. Muris and colleagues have used a similar paradigm and have also found that providing children with negative information about novel animals results in increased self-reported fear beliefs (Muris et al., 2003) and fear-related reasoning biases (Muris et al., 2009).

Information transfer of fear has also been demonstrated with parents. Muris, van Zwol, Huijding, and Mayer (2010) gave parents of children ages 8–13 negative, positive, or ambiguous information about a novel animal. Then they gave parents open-ended vignettes describing confrontations with the animal and told parents to tell their children what would happen in these situations. Parents who received negative information about the animal described more threatening narratives of what would happen in the vignettes to their children, and these children demonstrated higher fear beliefs than children of parents who were given positive information about the animal. Furthermore, anxious parents who were given ambiguous information about the animal provided more threatening information about the animal; as a result, their children had higher fear beliefs than children of nonanxious parents who were also given ambiguous information.

Family Influences

The association between parent and child anxiety has been well established (e.g., Biederman et al., 2004; Bögels, van Oosten, Muris, & Smulders, 2001; Chavira et al., 2007; Manicavasagar, Silove, Rapee, Waters, & Momartin, 2001; Merikangas, Lieb, Wittchen, & Avenevoli, 2003; Schreier, Wittchen, Höfler, & Lieb, 2008), with recent findings suggesting that a child's risk of an anxiety disorder is 2.7 times greater when at least one parent has a lifetime history of anxiety and 4.7 times greater when at least one parent has a current anxiety disorder (van Gastel, Legerstee, & Ferdinand, 2009). However, the mechanisms underlying this relationship remain less well understood. During the past decade, a wealth of research has accumulated examining familial influences on child anxiety, prompting multiple reviews of this literature in an effort to synthesize the many (at times discrepant) findings in this area (e.g., Bögels & Brechman-Toussaint, 2006; Drake & Ginsburg, 2012; Ginsburg, Grover, & Ialongo, 2005; Rapee, 2012).

Collectively, this research has suggested numerous parenting and family variables that might be related to the development and maintenance of childhood anxiety, but few have unequivocally linked such risk factors to anxiety specifically, rather than to psychopathology more generally (Bögels & Brechman-Toussaint, 2006; Ginsburg et al., 2005). Moreover, reliance on main-effect models in this area of research, as opposed to conditional models, goodness-of-fit models (e.g., Chess & Thomas, 1989), or individual–environment interaction models, provides only a limited understanding of the relationship between dimensions of parenting and child outcome (e.g., Gallagher, 2002). Similarly, longitudinal studies that would speak to the causal mechanisms underlying the more robust associations that have been observed cross-sectionally are lacking (Rapee, 2012). Indeed, a meta-analytic review of the parenting literature specifically concluded that only 4% of the

variance in child anxiety can be accounted for by parenting (McLeod, Wood, & Weisz, 2007). However, as McLeod and colleagues (2007) and others have noted, the influence of inconsistent operational definitions, diverse measurement strategies, and varying populations examined across studies has made interpreting this literature challenging at best (e.g., Drake & Ginsburg, 2012). In spite of these challenges, however, numerous insights into the influence of family variables on childhood anxiety have been generated.

Temperament and Attachment

A recent meta-analysis of 46 studies examining the relationship between insecure attachment and anxiety reported a moderate association between these variables, with a medium effect size of 0.30 (Colonnesi et al., 2011). Insecure attachment, in addition to being associated with child anxiety, is also significantly related to high levels of BI, maternal anxiety, and parenting behaviors characterized by overcontrol and negativity, with evidence suggesting that each of these factors accounts for a unique proportion of variance in child anxiety (Hudson, Dodd, & Bovopoulos, 2011; van Brakel et al., 2006). Most recently, however, Hudson and Dodd (2012) examined a normal sample of 71 behaviorally inhibited and 89 behaviorally uninhibited children assessed initially at age 4 and again 5 years later; they found that although BI, maternal anxiety, and maternal overinvolvement significantly predicted child anxiety at follow-up even after they controlled for baseline anxiety, maternal negativity and attachment did not. These findings lend support to the predictive utility of behavioral inhibition with respect to later anxiety, but shed doubt on the role of maternal attachment. As the authors note, however, given that attachment was initially assessed at age 4, security of mother–child attachment at an earlier developmental stage might be a better predictor of anxiety later in childhood.

Several other studies have also examined BI in the context of attachment. However, whether child temperament characterized by BI interacts with insecure attachment to influence anxiety remains unclear. In addition, the distinction between temperamental and attachment variables has not been unequivocally demonstrated in the literature, and questions remain with respect to whether these variables are indeed casually related, caused by a shared third variable, or simply the same construct operationalized and assessed differently. In an investigation of BI and insecure attachment, van Brakel and colleagues (2006) reported a significant but small (accounting for less than 1% of the variance in child anxiety) interaction between these two variables, such that children classified as behaviorally inhibited and insecurely attached reported high levels of anxiety, whereas those classified as behaviorally uninhibited or securely attached endorsed low symptoms of anxiety. However, parental control also influenced this inhibition–attachment interaction (in a higher-order interaction), such that for those children classified as uninhibited and securely attached and those classified as inhibited and insecurely attached, high parental control predicted high anxiety levels; conversely, high levels of parental control were associated with low anxiety in children classified as inhibited and securely attached.

van Brakel and colleagues (2006) posit that parental control can play a positive role in child rearing by providing a child with needed structure in the context of a relationship in which the parent is sensitive to the child's needs (high BI, secure attachment). However, they also suggest that control can exert a negative effect (i.e., overprotective and restrictive parenting behaviors leading to reduced autonomy) when exhibited in the context of a relationship in which the parent is not sensitive and responsive to the needs of the child (high BI, insecure attachment) or when the child's behavior does not demand overly restrictive regulation (low BI, secure attachment). In sum, however, van Brakel and colleagues conclude that BI, attachment, and parental control appear to exert primarily additive effects upon the development of anxiety, with the observed interactions being relatively small in magnitude. Along these lines, neither Hudson and colleagues (2011) nor Hudson and Dodd (2012) observed any significant interactions between BI and specific aspects of the family environment; Hudson and colleagues suggest, however, that the effects of such an interaction might be detected only via longitudinal studies across the stages of development. Although not studied in the context of attachment security, Lewis-Morrarty and colleagues (2012) reported a significant interaction between BI and maternal overcontrol, such that high BI was associated with elevated symptoms of social anxiety only in the context of high maternal overcontrol and not under conditions of low maternal overcontrol. These results suggest that although temperamental variables can have a significant influence on the development of later anxiety, familial influences can moderate these relationships.

Parenting Behaviors

PARENTAL OVERCONTROL

Parental overcontrol has demonstrated one of the strongest links to childhood anxiety among the familial variables studied to date (Drake & Ginsburg, 2012). As noted above, in a meta-analysis of parenting variables, McLeod and colleagues (2007) found that across studies, parenting dimensions only accounted for about 4% of the variance in child anxiety. However, when they examined results at the construct level, they found that parental overcontrol accounted for 6% of the variance in child anxiety, with certain dimensions of control exerting a much larger effect on child anxiety (e.g., autonomy granting, which accounted for 18% of the variance in child anxiety). Although it is not clear whether parental overcontrol is a contributor to or a result of child anxiety (Bögels & Brechman-Toussaint, 2006), a strong relationship between these two variables has been noted from both the perspective of the child (e.g., Bögels & van Melick, 2004) and that of independent observers (e.g., Whaley, Pinto, & Sigman, 1999).

Chorpita, Brown, and Barlow (1998) sought to examine the role of children's control-related cognition in the relationship between parental control and child anxiety. Specifically, in a partial test of the model outlined in Figure 8.1, they examined whether a family environment characterized by a high degree of parental control predicted an increase in personal external locus of control, and whether that in turn predicted anxiety and elevations in the severity of anxiety. In a mixed sample of 62 children with anxiety disorders and 31 without, measures of perceived locus of control mediated between family environment and children's anxious emotion—a finding consistent with the model.

Four subsequent tests of the model proposed by Chorpita, Brown, and Barlow (1998) have been conducted to date (Affrunti & Ginsburg, 2012; Ballash, Pemble, Usui, Buckley, & Woodruff-Borden, 2006; Gallagher & Cartwright-Hatton, 2008; Nanda, Kotchick, & Grover, 2012). Although the developmental model proposed by Chorpita and Barlow (1998; Chorpita, 2001; see Figure 8.2) predicts that perceptions of control will shift from mediational to moderational in nature with advancing child age, Ballash and colleagues (2006) found support for a mediational model among a sample of young adults ages 18–25 in which perceived control acted as a mediator between family functioning and anxiety. Similarly, Affrunti and Ginsburg (2012) demonstrated that children's perceived competence partially mediated the relationship between parents' overcontrolling behaviors and the children's anxiety, suggesting that parental overcontrol might influence child anxiety by affecting the degree to which the children feel competent in their ability to successfully navigate the environment. Gallagher and Cartwright-Hatton (2008) found that, rather than parental control, overreactive parenting (a discipline style characterized as harsh, punitive,

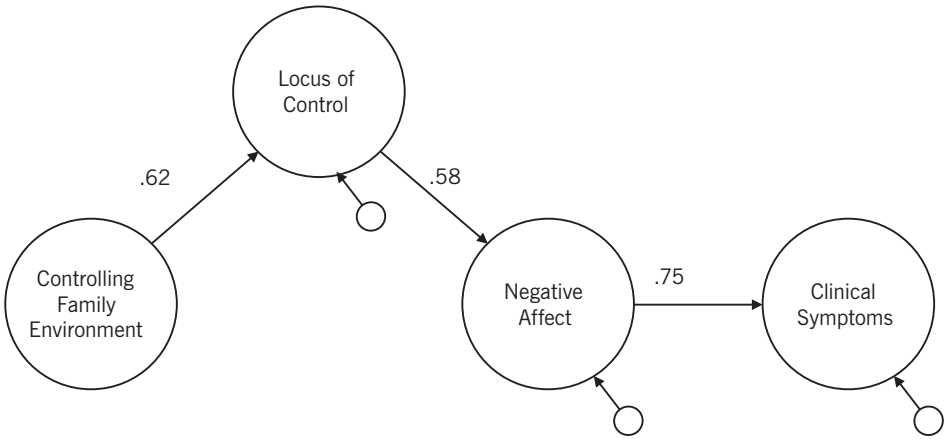

FIGURE 8.1. Model from Chorpita, Brown, and Barlow (1998): Perceived locus of control mediates parental control and child anxiety. From Chorpita, Brown, and Barlow (1998). Copyright 1998 by Elsevier. Reprinted by permission.

and inconsistent) was predictive of anxiety, and that this relationship was partially mediated by child cognitive errors, including catastrophizing, selective abstraction, overgeneralizing, and personalizing. In this study, although parental control significantly predicted child anxiety, it accounted for less variance than did overreactive parenting and was not a significant predictor when considered simultaneously with parental discipline style. Finally, Nanda and colleagues (2012) reported that children's perceived control fully mediated the relationship between parental psychological control and child anxiety, suggesting that the contribution of parental control to child anxiety is a function of its effects on a child's perceptions of control. Although supportive of not only the influence of parental control on a child's anxiety but also the importance of the child's own perceived control in this relationship, all of these studies were cross-sectional in nature and thus preclude inferences of causality.

Some more recent evidence, however, has begun to address the question of whether controlling parental behaviors generate anxiety in children, whether anxious children elicit controlling behaviors from their parents, or whether both may be true. In a longitudinal design, Edwards, Rapee, and Kennedy (2010) demonstrated that although maternal overprotection predicted later child anxiety, child anxiety also predicted subsequent maternal overprotection. In addition, evidence has suggested that it is not necessarily the anxiety status of the parent that determines whether overcontrolling behavior is emitted, but rather the anxiety status of the child. Gar and Hudson (2008) demonstrated that mothers of anxious children, regardless of whether or not they themselves had an anxiety disorder, were more overinvolved and overprotective in the context of a speech preparation task and a 5-minute speech sample; these results suggest that an anxious child might elicit certain parenting behaviors associated with overinvolvement and criticism, and that these parental factors might not be influenced by the parent's anxiety. In a subsequent test of this hypothesis, Hudson, Doyle, and Gar (2009) paired mothers of clinically anxious children and mothers of nonclinical children with a child (not their own) who was of the same anxiety classification as their own child (e.g., anxiety-disordered or not anxiety-disordered) and a child who was classified differently from their child. Mothers, regardless of their own child's anxiety status, exhibited greater levels of involvement with clinically anxious children than with nonanxious children, providing further evidence that a child's anxiety might elicit overinvolved and overcontrolled parenting behaviors. These findings suggest that future investigations of overcontrolling parental behaviors as they relate to child anxiety might be served better by examining anxious children and their parents, rather than anxious parents and their children. Interestingly, the type of task that parents and children are given to assess overcontrolling behaviors might also influence the results observed. Specifically, Ginsburg, Grover, Cord, and Ialongo (2006) noted higher levels of parental overcontrol, anxious behavior, and criticism when tasks were structured, suggesting that situational variables might also influence the interaction of parents and their anxious children.

PARENTAL REJECTION

In their meta-analytic review of the parenting literature specific to child anxiety, McLeod and colleagues (2007) conceptualize rejecting parenting behaviors as those comprising three distinct subdimensions: lack of warmth (e.g., negative and unpleasant interactions), withdrawal (e.g., an absence of involvement with or interest in the child), and aversiveness (e.g., hostility, criticism). Specifically, McLeod and colleagues ascertain that although research has historically relied upon the broad category of parental rejection to assess and define this constellation of behaviors, each subdimension might in fact be differentially related to child anxiety. Evidence from their meta-analytic review supported this notion, indicating that whereas warmth yielded a mean effect size of 0.06 (accounting for less than 1% of the variance in child anxiety) across the studies examined, withdrawal yielded a mean effect size of 0.22, and aversiveness yielded one of 0.23 (accounting for 4% and 5% of the variance in child anxiety, respectively). These results suggest that the presence of negative parenting dimensions of withdrawal and aversiveness is much more strongly associated with child anxiety than is the absence of the positive parenting dimension of warmth. Consistent with these findings, narrative reviews (e.g., Ginsburg et al., 2005) and empirical tests (e.g., Bögels et al., 2001; Lindhout et al., 2006) have also reported null findings for parental warmth, suggesting that contrary to parenting theories (e.g., Ainsworth, Blehar, Waters, & Wall, 1978; Baumrind, 1967), low parental warmth alone is not necessarily associated with heightened child anxiety. Indeed, Bögels and Brechman-Toussaint (2006) note that although low warmth itself might not be strongly associated with anxiety, the interaction of

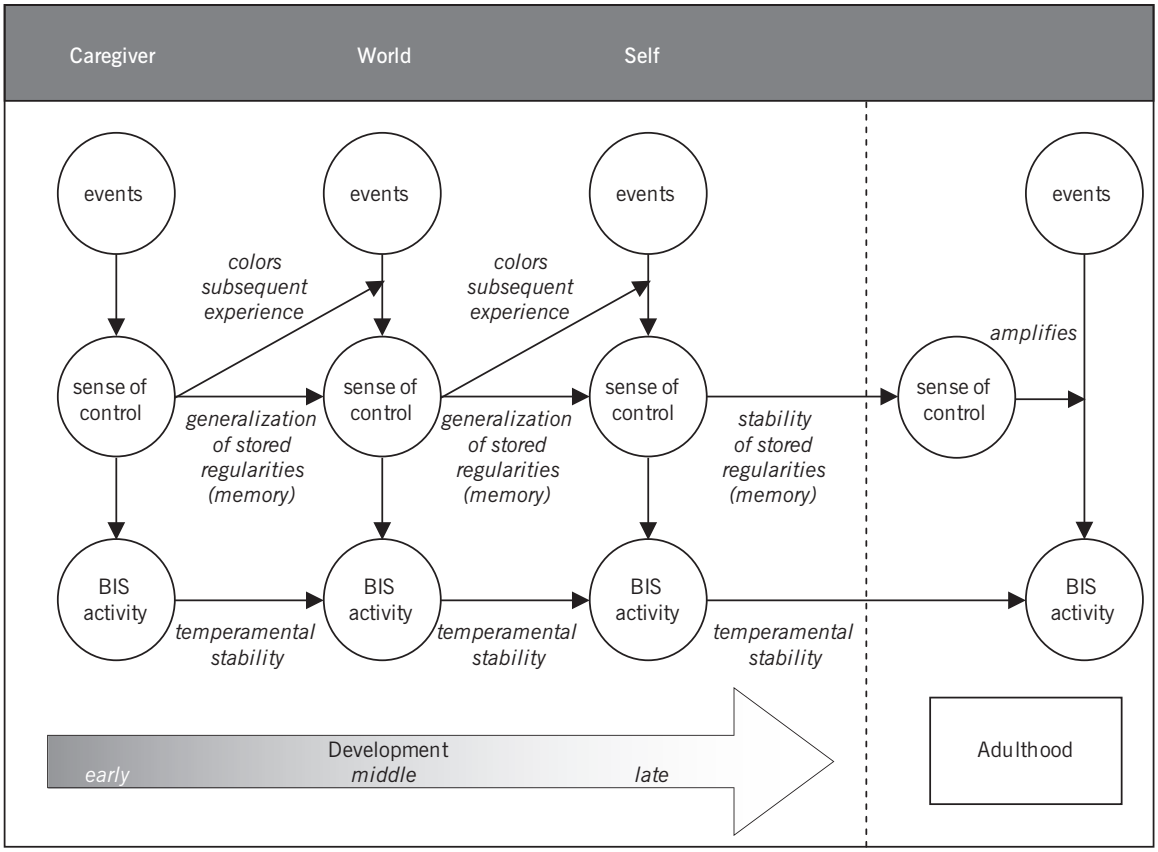

FIGURE 8.2. Model from Chorpita (2001): Perceptions of control across development. From Chorpita (2001). Copyright 2001 by Oxford University Press. Reprinted by permission.

low warmth and high control warrants further consideration in terms of its influence on child anxiety.

Consistent with McLeod and colleagues' (2007) conclusions regarding withdrawal and aversiveness, parenting behaviors defined as hostile, disapproving, and dismissive of a child (Drake & Ginsburg, 2012) have been associated with higher levels of child anxiety (e.g., Ginsburg et al., 2004). Indeed, one recent study found that not only did parents report more critical feelings toward their anxious children, but the children also perceived the parents as more rejecting, and independent raters found parents to be more critical of their anxious children than they were of nonanxious siblings (Lindhout et al., 2009). However, there is some question as to the specificity of this relationship with child anxiety rather than with psychopathology more generally (Bögels et al., 2001), and these parenting variables have been shown to account for a relatively small proportion of variance (McLeod et al., 2007). In support of the reciprocal nature of parent and child influences, however, Schrock and Woodruff-Borden (2010) reported that not only did the dyadic interaction change as a result of both partners' behavior and anxiety, but the anxiety of each partner had different effects on behavior. Specifically, they noted that whereas child anxiety would lead the child to become disengaged and interact negatively, parental anxiety prompted a more productive engagement between the dyad.

ANXIOUS MODELING

Although several studies have suggested a relationship between parental modeling of anxious and avoidant behavior and child anxiety (e.g., Barrett, Rapee et al., 1996; Chorpita et al., 1996; Dadds, Barrett, Rapee, & Ryan, 1996; Muris et al., 1996), it remains unclear whether this parenting variable actually contributes to the development of child anxiety (Rapee, 2012). Specifically, although one recent study demonstrated that anxious mothers reported high levels of anxious modeling, neither their children nor independent observers reported any differences in the anxious modeling behaviors displayed by these mothers and nonanxious mothers (Drake & Ginsburg, 2011). Yet, as Rapee (2012) notes, evidence from numerous sources has accrued to suggest a link between this parenting variable and child anxiety (e.g., Creswell, Schniering, & Rapee, 2005; Gerull & Rapee, 2002; Lester, Seal, Nightingale, & Field, 2010). This relationship has been demonstrated in the context of behavioral tasks, such that toddlers expressed more fear of a novel object after observing their mothers' negative reaction to the toy (Gerull & Rapee, 2002), as well as in questionnaire-based studies. Specifically, Creswell and colleagues (2005), among a sample of school-age children and their mothers, demonstrated that not only did mothers of anxious children endorse more threat-related interpretations to ambiguous situations, but their threat interpretations were more strongly correlated with their children's threat interpretations than with their own self-reports of general anxiety. Interestingly, subsequent to anxious children's receiving treatment for their anxiety disorders in this study, both maternal and child threat interpretations declined. In contrast to these results suggesting that mothers of anxious children endorse more threat interpretation biases, Lester and colleagues (2010) report data to suggest that children of anxious mothers also have a greater tendency toward threat interpretation. Moreover, these children also anticipated that their mothers would interpret ambiguous situations in a threatening manner and these expectations were related to the mother's anxiety levels rather than to those of the child (Lester et al., 2010). As is the case with other parenting variables, it is likely that anxious modeling interacts with child temperament (e.g., one characterized by high levels of behavioral inhibition) to influence child anxiety, such that children prone to fearfulness will experience higher levels of anxiety after being exposed to parental modeling of anxious behaviors (Barrett, Rapee, et al., 1996; Chorpita et al., 1996; de Rosnay et al., 2006).

PARENTAL COGNITIONS

Bögels and Brechman-Toussaint (2006), in their review of the parenting literature, suggest that research investigating the relationship between parents' beliefs about their children's coping abilities, anxious behaviors, and potential for success in challenging situations is in the early stages of its development, but has the potential to shape theories of anxiety and its transmission. Indeed, research from multiple sources has suggested that parents of anxious children perceive their children's ability across a variety of domains more negatively than do parents of nonanxious children (e.g., Micco & Ehrenrich, 2008). However, it has been hypothesized that such expectations might influence the children's anxiety only when they are directly and explicitly communicated to the children (Becker & Ginsburg, 2011), as has been demonstrated in previous investigations (e.g., Barrett, Rapee, et al., 1996; Chorpita et al., 1996).

PARENTAL ANXIETY AND PARENTING BEHAVIORS

Although anxious mothers report less warmth, more anxious modeling, and even heightened levels of distress when watching their children engage in "risky" play, these reports are not corroborated by either child reports or independent observers' ratings (Drake & Ginsburg, 2011; Lindhout et al., 2006; Turner, Beidel, Roberson-Nay, & Tervo, 2003). Indeed, recent evidence suggests that child anxiety, rather than parental anxiety, might elicit parenting behaviors that have been associated with anxiety (e.g., Hudson et al., 2009). Interestingly, Kiel and Buss (2010) observed that the relationship between toddlers' fearful temperament (e.g., seeking close proximity to their mothers, wanting to be held) and mothers' protective behaviors (e.g., shielding the children from an activity) was moderated by the degree of accuracy with which mothers predicted their toddlers' fearful behaviors. Specifically, toddler fearful temperament was associated with heightened maternal protectiveness when mothers had a high degree of accuracy in predicting, and thus were much attuned to, their children's behavior (Kiel & Buss, 2010). The authors conclude that high levels of fearful child behavior do elicit protective behaviors from mothers, but only in the context of mothers who are attuned to their children's behavior, suggesting that both child and

maternal characteristics play an important role in the dyadic interaction.

Family Environment

Numerous aspects of the family environment have been examined in relation to child anxiety, including cohesion, adaptability, and conflict. Although both high (e.g., Peleg-Popko & Dar, 2001) and low (e.g., Turner et al., 2003) cohesion have been associated with anxiety, there is little evidence for the specificity of this relationship (Bögels & Brechman-Toussaint, 2006). Similarly, both high (Teichman & Ziv, 1998) and low (Barber & Buehler, 1996) levels of adaptability have been associated with child anxiety, suggesting that the relationship between these family variables and child anxiety might be nonlinear or might interact with other parental, child, and familial variables to influence child anxiety. Ginsburg and colleagues (2004), in their review of the literature, reported that only two of five studies examining the influence of family conflict on child anxiety found positive associations. Rapee (2012) similarly notes that there is currently little evidence to support the specificity of this relationship, indicating that improved measurement and longitudinal studies are required to draw firm conclusions regarding the role of family conflict in child anxiety.

As a specific facet of the family environment, marital conflict and quality have also been examined in relation to child anxiety. Although some studies have suggested that marital satisfaction specifically predicts child anxiety over time (e.g., McHale & Rasmussen, 1998), others have reported no differences in parent-reported marital quality between parents with and without anxiety-disordered children (e.g., Siqueland, Kendall, & Steinberg, 1996). Although parental divorce has also been linked with child anxiety (Lansford et al., 2006), this association might be explained by interparental conflict, which can both precede and follow the separation (Rapee, 2012).

Cultural Variations

Investigations of the cultural aspects of childhood anxiety play an important role in determining which patterns of behavior are universal and which might be specific to particular groups or settings. By highlighting possible determinants of anxiety not accounted for by existing biological and psychosocial theory, cross-cultural perspectives help to clarify the underlying validity of our present conceptualization of childhood anxiety.

Cross-Cultural Differences in Self-Reported Anxiety

Among the self-report assessment measures studied most widely cross-culturally, two are more traditional measures of general levels of fear and anxiety, respectively (the Fear Survey Schedule for Children—Revised [FSSC-R; Ollendick, 1983] and the STAIC [Spielberger, 1973]). Three measures developed within the past 20 years and mentioned earlier in this chapter assess childhood anxiety dimensionally—two in a manner consistent with DSM-IV-TR diagnostic categories (the SCAS [Spence, 1998] and the SCARED [Birmaher et al., 1997]), and one designed to measure four theoretically derived dimensions of anxiety (the MASC [March, Parker, Sullivan, Stallings, & Conners, 1997]).

The FSSC-R, an 80-item inventory of different fear stimuli and situations, has been used to assess differences in patterns of childhood fears across numerous cultural groups. The FSSC-R has been translated into a variety of languages and administered to children and adolescents in the United States, Portugal, Italy, Turkey, Australia, the Netherlands, Northern Ireland, China, and the United Kingdom (see Fonesca, Yule, & Erol, 1994, for a review). Examination of the main differences across groups is limited to those groups that have received the same 80-item adaptation—that is, Australia, the United States, the United Kingdom, Portugal, China, and the Netherlands. Results showed relatively similar scores for most of these countries; however, the Dutch sample scored lower and the Portuguese sample scored higher than the other countries on total fear (Fonesca et al., 1994). One explanation offered to explain this difference is that the tendency for Latin cultures is to express fears more spontaneously, whereas Nordic cultures tend to control or conceal emotions (Fonesca et al., 1994). Across all groups, girls were found to score higher than boys. This does not necessarily imply a universal, "culture-free" gender pattern for fears, however, because the role of women in these cultures is fairly homogeneous and may involve a higher risk for the development of anxiety (cf. Nolen-Hoeksema, 1987).

Examination of the most common fears across cultures with the FSSC-R shows striking commonalities. Children in the United Kingdom, the United States, Turkey, Portugal, and Australia all shared the fear of being hit by a car as the most frequently endorsed childhood

fear. Fears of not being able to breathe, a bomb attack or war, fire, a burglar, falling from a height, and death ranked in the top 10 fears of at least four of these countries. In addition, items appended to the original 80-item measure revealed that fear of a parent's death was considerable in all countries tested (United Kingdom, Turkey, Portugal), with endorsement ranging from 73 to 84% (Fonesca et al., 1994).

In a manner similar to the work of Ollendick and colleagues, Spielberger and colleagues (Spielberger & Diaz-Guerrero, 1983; Spielberger, Diaz-Guerrero, & Strelau, 1990) have fostered research examining self-reported trait anxiety across different cultures. The STAIC measures general anxiety in school-age children and has two subscales—a Trait Anxiety scale, which measures general trait anxiety or proneness to negative affect, and a State Anxiety scale, which measures transient negative emotional state. At present, the majority of the cross-cultural research with the STAIC has involved validation of the instrument in a variety of countries. Currently, adaptations have been developed for Polish, Hungarian, Russian, Jordanian, Lebanese, and Bengali samples, most of which consisted of students in middle to late adolescence. In one comparative study, Ahlawat (1986) found similar factor structures between the Arabic STAIC and the American version (i.e., factor analysis supported a two-factor structure with the Trait Anxiety and State Anxiety scales in both samples). In addition, sex differences were similar to those found in the United States, with girls scoring higher on Trait Anxiety than boys. In general, support for the use of the STAIC across different cultures has been demonstrated.

The SCAS is a 38-item self-report questionnaire designed to assess DSM-IV-TR symptoms of GAD, SAD, social phobia, panic disorder and agoraphobia, obsessive–compulsive disorder, and specific phobia. The SCAS has been evaluated among numerous cultural groups, including Japanese, German, South African, Dutch, Hong Kong Chinese, Colombian, and Greek children and adolescents (e.g., Crane Amaya & Campbell, 2010; Essau, Ishikawa, & Sasagawa, 2011; Essau, Ishikawa, Sasawaga, Sato, et al., 2011; Essau, Leung, Conradt, Cheng, & Wong, 2008; Essau, Muris, & Ederer, 2002; Essau, Sakano, Ishikawa, & Sasagawa, 2004; Ishikawa, Sato, & Sasagawa, 2009; Li, Lau, & Au, 2011; Mellon & Moutavelis, 2007; Muris, Merckelbach, Ollendick, King, & Bogie, 2002; Muris, Schmidt, Engelbrecht, & Perold, 2002). Investigations using the SCAS across these cultural groups have yielded relatively consistent evidence with respect to sex differences (girls score significantly higher than boys on all scales), internal consistency (high and comparable to that observed in the validation sample), and factor structure (adhering to the six-correlated-factor structure initially obtained by Spence, 1998).

One group among whom the proposed SCAS factor structure was not supported was South African school children. Specifically, Muris, Schmidt, and colleagues (2002) reported that in their sample of South African children, three key differences in the factor structure of the SCAS were observed: (1) Items representing generalized anxiety and obsessive–compulsive symptoms loaded on the same factor; (2) items assessing separation anxiety loaded on multiple factors; and (3) a factor for school phobia was not identified. In addition, the levels of anxiety reported by South African children (in particular, those related to compulsive behaviors and physical separation from parents) were higher than not only those of the Dutch children to whom they were directly compared in this study, but also those of the Western children assessed in previous psychometric studies of the SCAS (Muris, Schmidt, et al., 2002). Greek children have also been observed to endorse markedly higher levels of anxiety than children in other cultures, with particularly high rates of endorsement for items pertaining to social phobia and obsessive–compulsive behaviors (Mellon & Moutavelis, 2007).

With respect to cross-cultural differences in the endorsement of specific SCAS items, Japanese children, relative to those in Western countries studied more often endorsed items related to obsessive–compulsive symptoms (e.g., checking to make sure things have been completed correctly) and specific fears (Ishikawa et al., 2009). In addition, the social phobia items most frequently endorsed by Japanese children in this study referred to fears of negative evaluation, whereas those most commonly endorsed by Australian children pertained to tests and speeches (Ishikawa et al., 2009). When compared directly with adolescents from England, Japanese adolescents, in two separate studies, scored significantly lower in self-reported anxiety (Essau, Ishikawa, & Sasagawa, 2011; Essau, Ishikawa, Sasawaga, Sato, et al., 2011). German children, when compared to Japanese children, have also been reported to endorse significantly greater levels of separation anxiety, social phobia, obsessive–compulsive disorder, and GAD, although Japanese children reported relatively more symptoms related to physical injury (specific) fears (Essau et al., 2004). Conversely, when com-

pared with Hong Kong Chinese adolescents, German adolescents reported significantly fewer symptoms of anxiety on the SCAS total anxiety scale as well as on each of the subscales (Essau et al., 2008). Finally, symptoms endorsed by Dutch children on the SCAS have been reported to be lower than those endorsed by Australian children (Muris, Schmidt, & Merckelbach, 2000), whereas those reported by Colombian children have been higher than those of their Australian counterparts (Crane Amaya & Campbell, 2010).

The SCARED, a 41-item self-report measure, was, (like the SCAS) designed to assess symptoms of anxiety consistent with DSM-IV-TR diagnostic categories, including GAD, SAD, social phobia, panic disorder, and school phobia. The psychometric properties of the SCARED have been evaluated among Belgian, Dutch, German, Italian, South African, and Chinese children and adolescents (see Hale, Crocetti, Raaijmakers, & Meeus, 2011, for a meta-analytic review of these studies). Across studies employing the SCARED, girls consistently score higher than boys on all scales, with the exception of the school anxiety scale on which sex differences are not observed. In addition, the four-factor structure of the SCARED, assessing symptoms of GAD, panic and agoraphobia, SAD, and social phobia, has been well supported in numerous cultures, although less consistent support has been obtained for the school anxiety factor of this scale. Indeed, Hale and colleagues (2011) suggest that the structure of symptoms of the DSM-IV-TR anxiety disorders is quite consistent cross-culturally when evaluated using the SCARED.

The MASC is a 39-item self-report instrument that was initially developed to assess four theoretically derived dimensions of child anxiety—namely, affective, physical, cognitive, and behavioral. Factor-analytic studies, however, have suggested that the items of this scale assess dimensions of physical symptoms, social anxiety, separation anxiety, and harm avoidance. The MASC has been translated and its psychometric properties evaluated among samples of Dutch, Taiwanese, Mexican, Chinese, and Icelandic children (Muris, Merckelbach, et al., 2002; Olason, Sighvatsson, & Smari, 2004; Varela, Sanchez-Sosa, Biggs, & Luis, 2008; Yao et al., 2007; Yen et al., 2010). Across the cultural groups studied using the MASC, the factor structure and reliability estimates observed have been consistent with those obtained in the initial validation sample. Similar to studies employing other measures of anxiety, girls consistently score higher than boys on the scales of the MASC. Although the mean levels of anxiety endorsed by Icelandic children (Olason et al., 2004) were similar to those reported by American (March et al., 1997) and Dutch (Muris, Merckelbach, et al., 2002) samples, specific differences have been noted for other groups. Specifically, Taiwanese children generally reported more social anxiety than their American counterparts, as well as higher levels of separation/panic; conversely, Taiwanese children generally reported lower levels of harm avoidance and physical symptoms than did American children (Yen et al., 2010). Both Mexican children and other Latino children residing in the United States more frequently endorsed worries and somatic symptoms than did European American children (Varela et al., 2008). Finally, Chinese children endorsed higher levels of social anxiety (on both the humiliation/rejection and public performance subscales) and separation anxiety/panic on the MASC than did the American normative sample (Yao et al., 2007).

Cross-Cultural Differences in Test Anxiety

Guida and Ludlow (1989) examined the phenomenon of test anxiety in children from different cultural groups; they evaluated the effects of SES, child gender, and cultural background on self-reported test anxiety. Using the Test Anxiety Scale for Children (Sarason, Davidson, Lightfall, Waite, & Ruebush, 1960), the investigators compared samples of low-SES urban African American children, middle-SES American children, upper-SES American children, and a large sample of Chilean students. In the comparative analyses, the Chilean students scored higher on test anxiety than the American samples. Across groups, children with high SES scored lower on the measure than children with low SES. Within low-SES children, there was also a tendency for girls to score higher than boys on the test anxiety measure.

Using the Spielberger Test Anxiety Inventory (Spielberger, 1980) and the FRIEDBEN Test Anxiety Scale (Friedman & Bendas-Jacob, 1997), Bodas, Ollendick, and Sovani (2008) evaluated test anxiety in a sample of Indian school children. They observed lower levels of self-reported test anxiety among these middle and high school children (ages 10–15), relative to American children as well as children evaluated in other cultures. In this sample, girls did not endorse higher levels of test anxiety than did boys, and no age differences were noted on the Test Anxiety Inventory (Bodas et al.,

2008). Although the absence of significant age differences is consistent with findings reported elsewhere with respect to test anxiety, the lack of sex differences is not (Bodas et al., 2008).

In a comparison of levels of test anxiety reported by Arab and Jewish students in Israel, using Friedman and Bendas-Jacob's (1997) Hebrew-language Test Anxiety Questionnaire, Arab 10th- and 11th-grade students were observed to report significantly higher levels of test anxiety than their Jewish counterparts (Peleg-Popko, Klingman, & Nahhas, 2003). Girls in both cultural groups endorsed higher levels of test anxiety on this measure than did boys, and a significant association between family environment and test anxiety was observed: More authoritarian styles of parenting were associated with higher test anxiety, and more supportive parenting styles were associated with lower test anxiety (Peleg-Popko et al., 2003). These authors indicated that the cultural differences observed with respect to test anxiety in this study mirror those reported elsewhere (i.e., individuals from Eastern cultures report more test anxiety than do those from Western cultures), suggesting that such differences might reflect cultural variations in the importance of tests for educational and professional advancement (Peleg-Popko et al., 2003).

Consistent with these findings, Essau and colleagues (2008) reported that whereas academic motivational goals (including competition to achieve good grades and a desire to be rewarded for good performance) were correlated with anxiety symptoms reported by Hong Kong adolescents, for German adolescents significant correlates of anxiety included being reinforced for anxious symptoms and parental communication about the potentially harmful nature of anxiety. Accordingly, these authors suggest that anxiety among Hong Kong adolescents appears to be related to extrinsic pressures to succeed, whereas for German children learning experiences within the family shape the experience of anxiety (Essau et al., 2008). Similarly, Greek adolescents self-reported significantly higher levels of anxiety and depression than Finnish adolescents, which the authors attributed to the high value placed on educational attainment and success in Greece (Kapi, Veltsista, Sovio, Järvelin, & Bakoula, 2007). However, although both of these studies suggest that perceptions of external pressure to meet familial standards of excellence might be associated with higher levels of anxiety, Essau, Ishikawa, Sasagawa, Sato, and colleagues (2011) suggest otherwise. Specifically, these authors found that although interdependent self-construal (i.e., perceiving oneself in a collectivistic sense and seeking to make one's behaviors and thoughts consistent with those of the group) was associated with higher anxiety for both English and Japanese children (and independent self-construal [i.e., perceiving oneself in an individualistic sense and pursuing autonomy and individual achievement] was associated with lower anxiety for both groups), this relationship was actually weaker for Japanese adolescents, suggesting that perceptions of connectedness to one's social group are not necessarily linked to poorer outcomes (Essau, Ishikawa, Sasagawa, Sato, et al., 2011).

Cross-Cultural Differences in Anxious Symptoms and Syndromes

In an investigation of cultural influences on general child pathology, Weisz and colleagues (1987) used the CBCL to compare American children with children living in Thailand. The general pattern suggested that the Thai children manifested more internalizing behavior (e.g., being withdrawn, anxious, or depressed) than did the American children. In a follow-up to this study, however, Weisz, Weiss, Suwanlert and Chaiyasit (2003) noted that the individual problems constituting the narrow-band factors of the CBCL were not perfectly comparable across cultures, particularly for the Anxious and Depressed scales, which were only moderately comparable across groups. Accordingly, the authors revised their original conclusions to indicate that Thai children have a higher prevalence of specific individual internalizing problems and certain narrow-band syndromes for which the items are highly comparable across cultures (e.g., the Somatic Complaints scale). The high degree of similarity with respect to somatic problems across cultures suggests either that these problems are quite consistent in these two different groups, or that physical problems might be in some way distinct from the psychological problems assessed by the other scales of the CBCL (Weisz et al., 2003).

With respect to somatic concerns, numerous recent studies have examined the prevalence and correlates of somatic complaints in Latin American children specifically. A potentially culture-bound syndrome, *ataques de nervios* (AdN), is a clinical presentation that in adults is comprised of symptoms closely related to panic attacks, including feeling out of control, trembling, crying, and fainting. An AdN is distinguished from a panic

attack by the fact that it is often preceded by an identifiable stressful event and is not typically associated with feelings of fear or apprehension (Guarnaccia, Martinez, Ramirez, & Canino, 2005). In an epidemiological study of Puerto Rican children ages 4–17, Guarnaccia and colleagues (2005) observed prevalence rates of 9% in a community and 26% in a clinical sample. In both groups, a higher prevalence of AdN was noted for girls than for boys; a family history of AdN was associated with a child's experience of an AdN (although a family history of mental illness was not); and children experiencing AdN were at greater risk of also meeting diagnostic criteria for a psychiatric disorder. Although it was hypothesized that the relationship between AdN and diagnoses of anxiety would be the strongest, given the resemblance of AdN to panic attacks observed in adults, in this study children experiencing an AdN had the highest odds of being diagnosed with any depressive disorder. However, among the anxiety disorders, the greatest risk for a psychiatric disorder was associated with panic disorder: Children in the community who had experienced an AdN were 31 times more likely to meet diagnostic criteria for panic disorder (Guarnaccia et al., 2005).

More generally, Latino children have been reported to experience higher levels of somatic symptoms than European American children, even after investigators have controlled for potentially confounding variables such as SES and family income (e.g., Pina & Silverman, 2004; Varela et al., 2004). Mexican and other Latino children in their own countries also report higher levels of anxiety symptoms compared with their European American counterparts in the United States, suggesting that heightened levels of anxiety observed among Latin American children are not simply a function of belonging to an ethnic minority group (Varela et al., 2004).

Finally, in an investigation of the cross-cultural applicability of the tripartite model of emotions (Lu et al., 2010), children and adolescents ages 9–18 of European American, Japanese American, Chinese American, and Chinese national descent received the Affect and Arousal Scale for Children (Chorpita, Daleiden, et al., 2000). Although no differences on any of the tripartite dimensions (NA, PA, PH) were noted for the American cultural groups, the Chinese national children reported significantly lower levels of NA and PA than did the American children. The authors concluded that the structure of emotions as posited by the tripartite model and measured by this scale was consistent across the cultures assessed.

Parenting Behaviors, Child Anxiety, and Cultural Differences

Several investigations have examined the role that parental practices might play in the expression of anxiety and somatic concerns among Latino children (Luis, Varela, & Moore, 2008; Varela et al., 2004; Varela, Sanchez-Sosa, Biggs, & Luis, 2009). Varela and colleagues (2004) reported that Mexican and Mexican American parents, relative to European American parents, verbalized more somatic, nonanxious interpretations of ambiguous scenarios during family discussions, and that Mexican parents made fewer anxious, nonsomatic interpretations than did European American parents. These results supported the hypothesis that somatic expressions of emotion might be more culturally acceptable for families of Hispanic descent (Varela et al., 2004). Luis and colleagues (2008) noted that although controlling parenting practices were associated with higher levels of child anxiety for Mexican and European American families, such practices were associated with lower levels of anxiety for Mexican American families. However, Mexican American parents made more controlling statements than Mexican parents and more statements associated with low warmth and acceptance than European American parents, suggesting that in this sample the relation between controlling parenting style and child anxiety was not culturally moderated (Luis et al., 2008). Varela and colleagues (2009) observed that maternal control was associated with higher levels of anxiety for both European and Latin American children (Mexican children were not included in this analysis), and that maternal acceptance was also significantly associated with high child-reported anxiety for European and Latin American children, but that the reverse was true for Mexican children. However, the relationship between maternal acceptance and child anxiety, when examined by cultural group, was significant only for the Latin American children, suggesting that Latin American mothers demonstrating high levels of acceptance might also offer reassurance to their children and potentially reinforce the children's expression of anxious symptoms (Varela et al., 2009).

In an investigation of the effects of parenting practices on anxiety among Japanese and English adolescents, Essau, Ishigawa, and Sasagawa (2011) observed no significant differences with respect to parental reinforcement or punishment for anxiety symptoms; in both countries, less parental punishment of anxious symptoms was associated with higher reports of

adolescent anxiety. However, whereas English parents were more likely to punish non-anxiety-related physical symptoms, Japanese parents were more likely to reinforce such symptoms, suggesting that the presence of somatic (in contrast to affective) symptoms are more easily tolerated in this Asian cultural group.

Finally, Muris and colleagues (2006) investigated the relationship among parental anxious rearing, overprotection, and rejection and child anxiety in a sample of South African children. This sample consisted of children and adolescents from the primary cultural groups of the Western Cape of South Africa and included white youth, black youth, and youth of mixed ethnic heritage. (Muris et al., 2006, labeled this third group "colored," as this term is still common in this region; they attribute this to South Africa's racialist past.) These authors observed lower levels of child-reported parental anxious, overprotective, and rejecting behaviors, and higher levels of parental warmth, for white children than for mixed-heritage and black children; for all groups, anxious rearing, overprotection, and rejection were associated with elevated levels of child anxiety. However, parents' occupational level fully accounted for group differences in perceptions of overprotective parental behaviors, suggesting that the family living conditions of low-SES families might be responsible for overprotective parenting behaviors, rather than cultural differences between these groups.

Cross-Cultural Differences in Anxiety Disorder Prevalence Rates

Cross-cultural prevalence estimates for the DSM-IV anxiety disorders have been reported in the context of epidemiological surveys of psychopathology more generally. Across these studies, anxiety disorders typically emerge as the second most prevalent diagnostic category in the population studied, following diagnoses of disruptive behavior disorders (e.g., Anselmi, Fleitlich-Bilyk, Menezes, Araújo, & Rohde, 2010; Fleitlich-Bilyk & Goodman, 2004; Gau, Chong, Chen, & Cheng, 2005). Specifically, among a sample of Brazilian children (ages 11–12), Anselmi and colleagues (2010) reported a prevalence estimate of 6.0% for any anxiety disorder; Fleitlich-Bilyk and Goodman reported a prevalence of 5.2%, also among Brazilian children (ages 7–14). Similarly, Gau and colleagues (2005) estimated the prevalence of any anxiety disorder among a sample of Taiwanese children to range from 9.2% for children in grade 7 to 3.1% for children in grade 9. Several additional investigations have reported comparable prevalence rates across a wide range of cultural groups, including Hong Kong Chinese adolescents (6.9%; Leung et al., 2008), Irish adolescents (3.7%; Lynch, Mills, Daly, & Fitzpatrick, 2006), Bangladeshi children (8.1%; Mullick & Goodman, 2005), Scottish adolescents (5.9%; West, Sweeting, Der, Barton, & Lucas, 2003), and Puerto Rican children and adolescents (6.9%; Canino et al., 2004). In those studies for which prevalence estimates for the individual anxiety disorders were reported (e.g., Canino et al., 2004; Fleitlich-Bilyk & Goodman, 2004; Gau et al., 2005; Heiervang et al., 2007; Leung et al., 2008; Mullick & Goodman, 2005; West et al., 2003), rates were relatively consistent across cultural groups.

In addition, across the cultural groups studied, girls have consistently been more frequently diagnosed with anxiety disorders than boys (e.g., Fleitlich-Bilyk & Goodman, 2004; West et al., 2003). Another common theme observed across these studies is the importance of using an impairment criterion in determining diagnostic status (e.g., Canino et al., 2004; Leung et al., 2008; West et al., 2003). Specifically, many studies reported elevated levels of anxiety disorders in certain cultural groups when questionnaire-based assessments were used. However, when researchers used diagnostic measures that apply an impairment criterion, the rates of anxiety disorders became markedly lower and more consistent with those reported in other cultural groups. For example, when relying simply on symptom counts using the computerized Voice version of the Diagnostic Interview Schedule for Children (Voice-DISC; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000), West and colleagues (2003) reported a prevalence estimate of 9.2% for any anxiety disorder among Scottish adolescents; this estimate was reduced to 5.9% when an impairment criterion was applied, however. Similarly, using only symptom criteria with the Spanish version of the DISC-IV (Bravo et al., 2001), Canino and colleagues (2004) reported prevalence rates for any anxiety disorder of 9.5%; when impairment criteria specific to each disorder were applied, the observed prevalence estimate was 6.9%.

THEORETICAL FRAMEWORKS AND POSSIBLE DEVELOPMENTAL PATHWAYS

Historically, models of childhood anxiety have tended to be unidimensional, focusing on only one aspect (e.g., learning theories, cognitive theories). Moreover, such

models were often adapted from models of adult psychopathology and failed to take into account the critical changes that occur during the course of children's physical, cognitive, and socioemotional development. More recent theories have become increasingly complex and integrate multiple interactive concepts, including biological, psychological, and environmental contributors to psychopathology. One example of such a theory is Barlow's (2002) triple-vulnerability model of anxiety, which posits that generalized biological, generalized psychological, and specific psychological vulnerabilities together place an individual at risk for developing an anxiety disorder. Similarly, models of psychopathology suggested by Pine (2009) incorporate data from genetic research, information-processing paradigms, cognitive and affective neuroscience research, and brain imaging studies to provide a framework for understanding anxiety disorders in children. Theories such as these recognize the transactional nature of the development of anxiety. They evaluate the contributions of not only the child and specific aspects of the environment (e.g., parents, peers, community), but also the dynamic interaction of these variables across the various stages of development (e.g., Vasey & Dadds, 2001). Indeed, it is now more generally acknowledged that rather than serving as causal variables, factors such as specific parenting practices exist in a bidirectional relationship with specific child characteristics such as temperament (e.g., Edwards et al., 2010; Gar & Hudson, 2008; Hudson et al., 2009).

As theories of child anxiety continue to emerge and evolve, it is imperative that they continue in the direction of integrating the findings currently being generated from the genetic, biopsychological, conditioning, and cognitive literatures. For example, in a review of the literature examining genetic contributions to environmental variables that influence psychopathology (including social support, parenting behavior, family environment, peer interactions, and stressful life events), Kendler and Baker (2007) report significant heritability estimates for parenting behaviors such as warmth. Moreover, this research suggests that both parent and child genes contribute to the parent–child relationship. Although such findings might suggest that parenting behaviors are genetically determined, they do not preclude the role of psychosocial variables. More specifically, a heritability estimate of 35% for parental warmth leaves room for other influences, including those from the environment, to affect outcomes.

Collectively, the literature supporting multidimensional theories of child anxiety not only illustrates the multiplicity of etiological influences contributing to childhood anxiety disorders (e.g., genetic, neurobiological, temperamental, psychosocial, familial), but also suggests numerous targets of intervention that change across time and with development. For example, although interventions aimed at parenting practices have demonstrated efficacy in the treatment of childhood anxiety disorders (e.g., Barrett, Dadds, & Rapee, 1996; Wood, Piacentini, Southam-Gerow, Chu, & Sigman, 2006), the impact of these interventions may change over time as peers become an increasingly important part of adolescence.

CONCLUSIONS AND FUTURE DIRECTIONS

More than 10 years have passed since the previous edition of this chapter was published, and in that time there has been a remarkable and unprecedented growth in the empirical knowledge regarding childhood anxiety disorders. Although the revisions to DSM that have been made during this period are important, they focus primarily on the symptoms and structure of the disorders, and thus significantly understate the wealth of new discoveries on this topic. We now have greater insight than ever before into the biological, genetic, conditioning, cognitive, familial, and ecological issues relevant to childhood anxiety and its disorders.

Many of these diverse findings organize themselves around two central themes. First, there is an increasing awareness of the importance of endophenotypes, intermediate dimensions or syndromes, and the hierarchical relations among the constructs relevant to anxiety. Much of the developmental continuity and discontinuity in anxiety syndromes and disorders can be best explained by understanding the risk and protective effects that involve such dimensions as BI, PA/NA, EC, and individual differences in conditionability and information processing. Second, current findings increasingly suggest that main effects are the exception rather than the rule, and that the development of anxiety and its disorders is frequently characterized by transactional effects (e.g., anxious children elicit different parenting styles than nonanxious children do), moderational models (e.g., individual differences in conditioning or baseline inhibition levels moderate the effects of experience on emotionality), feedforward models (e.g., hypercortisolism has long-term effects on neurohormonal regulation), or combinations of many of these.

Science often proceeds through cycles of generation and consolidation, and in our view, the field of child-

hood anxiety disorders has experienced an unprecedented generative period over the past 15 years. There are extensive and relatively independent literatures on cognitive, behavioral, biological, environmental, and genetic issues, among others. Going forward, research on childhood anxiety may be well served by attempts to consolidate and reconcile these varied and extensive new findings into parsimonious models or theories. Such attempts may foster integrative biopsychosocial experimentation that bridges what often remain independent literatures (e.g., genetic studies of intermediate dimensions other than end-state disorders; studies of the effects of culture on the interaction of cognition and affect). This work will likely require continued attention to understanding the basic constructs (and how best to measure them), as well as increased longitudinal research to tease out how these dimensions truly interact over development. Although our field does not have all the answers at the moment, the next decade's important questions—albeit more complex than we had hoped—are now at least clearly in sight.

NOTES

1. We use the terms "child," "children," and "childhood" throughout the chapter to refer to all children and adolescents, regardless of age, unless otherwise noted.

2. In DSM-IV, the former OAD (from DSM-III-R) was subsumed under the revised GAD, and hence our understanding of the symptoms and clinical presentation of GAD in children is based largely on studies of children with OAD. Research indicates minimal and nonsignificant differences between the DSM-III-R and DSM-IV criteria; experts have thus suggested that past research on OAD can be applied to understanding GAD in youth (e.g., Kendall & Warman, 1996; Tracey, Chorpita, Douban, & Barlow, 1997).

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CHAPTER 9

Obsessive–Compulsive Spectrum Disorders

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Obsessive–compulsive disorder (OCD) is a relatively common psychiatric disorder that typically has an onset in childhood or early adolescence. OCD symptoms ordinarily wax and wane over time, although the course is usually chronic. OCD can be associated with significant functional impairment in children and adolescents (Piacentini, Bergman, Keller, & McCracken, 2003; Storch, Larson, et al., 2010; Valderhaug & Ivarrson, 2005), and it is among the highest-morbidity disorders among adults worldwide (Kessler, Petukhova, Sampson, Zaslavsky, & Witchen, 2012; World Health Organization [WHO], 2008). Both cognitive-behavioral therapy (CBT) and selective serotonin reuptake inhibitor (SSRI) medications have demonstrated considerable efficacy (e.g., Franklin et al., 2011; Pediatric OCD Treatment Study, 2004; Piacentini et al., 2011) for the treatment of OCD in children and adolescents, although some degree of residual symptoms and impairment are not uncommon following treatment (Barrett, Farrell, Pina, Peris, & Piacentini, 2008; Watson & Rees, 2008).

OCD has long been considered as the modal disorder for a group of psychiatric conditions characterized by repetitive thoughts or behaviors (e.g., Cohen, Simeon, Hollander, & Stein, 1997). Spurred in part by the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5; American Psychiatric Association [APA], 2013) planning process, a significant body of knowledge examining potential similarities in the phenomenology, comorbidity, familial and genetic features, brain circuitry, and treatment response between OCD and these putatively related conditions now exists, supporting the concept of an OCD spectrum (e.g., Bienvenu et al., 2012; Hollander, Kim, Braun, Simeon, & Zohar, 2009; Lochner & Stein, 2010). This chapter focuses on the three spectrum conditions most commonly seen in children and adolescents: OCD, tic disorders, and trichotillomania (hair-pulling disorder).

OBSESSIVE–COMPULSIVE DISORDER

Historical Context

Prior to medical theories, obsessions were thought to be aberrant religious experiences, ("religious melancholy"), often believed to be the work of the Devil (Rachman & Hodgson, 1980). In the 18th and 19th centuries, several French physicians began describing symptoms and syndromes that are similar to the contemporary concept of OCD (Berrios, 1996). At the beginning of the 20th century, the French physician and psychologist Pierre Janet provided a detailed

clinical description of the disorder based on extensive clinical work with patients (see Pitman, 1987, for an account of Janet's work) and was one of the first authors to describe OCD symptoms in a child (Boileau, 2011). Freud (1909/2001), a contemporary of Janet, theorized that OCD was caused by unresolved conflict associated with aggressive and sexual impulses, resulting in regression to the anal stage of mental development. Lewis Judd (1965) described detailed criteria for the diagnosis of OCD in children; these criteria were quite similar to those currently in use.

Although psychodynamic therapy was the dominant approach in psychiatry in the first part of the 20th century, its efficacy for OCD was limited. During the late 1960s and early 1970s, effective treatment options began to emerge—both antiobsessional drugs (clomipramine), and behavioral treatment (exposure and response prevention). As a result, research interest into the etiology of OCD in adults grew substantially both within psychiatry and clinical psychology. This interest was further intensified by data documenting the significant disability associated with OCD, as well as large-scale epidemiological research showing that OCD is much more common than was previously believed. The publication by Judith Rapoport (1989) of *The Boy Who Couldn't Stop Washing*, which described a series of pediatric OCD cases treated by her clinical research team at the National Institute of Mental Health, led to dramatically increased public and professional awareness of OCD in children and adolescents.

Description of the Disorder

Core Symptoms

The core symptoms of OCD are obsessions and compulsions. *Obsessions* are recurrent, unwanted, and intrusive thoughts, images, or impulses that result in pronounced anxiety or distress. Common obsessions include fears about being contaminated or contaminating others (e.g., with pathogens or HIV); excessive doubt (e.g., uncertainly that a task has been completed); disturbing images/thoughts (e.g., violent scenes, blasphemous thoughts); sudden impulses to harm oneself or others (e.g., stab a family member with a knife); or an inexplicable experience of incompleteness, the feeling that things are not "just right" (e.g., unsymmetrical).

Compulsions are repetitive behaviors (or mental activities) typically designed to lessen the anxiety/discomfort associated with obsessions, or to neutralize the feared consequences of obsessions. Examples include repetitive and excessive washing rituals in response to contamination obsessions, checking compulsions related to excessive doubt, compulsive ordering or rearranging in response to symmetry obsessions, or idiosyncratic rituals associated with taboo obsessions (i.e., counting to 7 when thinking about the Devil). OCD symptoms tend to reflect an individual's developmental level and may therefore differ slightly among children, adolescents, and adults. For example, children are less likely than adolescents/adults to report sexual obsessions, but more likely to report obsessions about bad things happening to their parents (Geller, Biederman, Faraone, Agranat, et al., 2001).

Symptom Dimensions

There is a wide variety in thematic content of obsessions and compulsions, but symptoms tend to involve certain themes. A meta-analysis (Bloch, Landeros-Weisenberger, Rosario, Pittenger, & Leckman, 2008) of 21 factor-analytic studies of symptom checklists provided evidence for the following four-factor structure: (1) obsessions concerning symmetry, and ordering/repeating/counting compulsions; (2) obsessions with aggressive/religious/sexual content and related compulsions; (3) obsessions about contamination and cleaning compulsions; and (4) hoarding obsessions/compulsions. The factor structure was very similar across child/adolescent and adult samples.

Evidence from longitudinal studies suggests that these symptom dimensions are temporally stable (Fernandez de la Cruz et al., 2013; Mataix-Cols et al., 2002) and may reflect (partly) distinct underlying etiologies. Although further research is needed, preliminary data from genetic/twin studies suggest that some symptom dimensions have partly distinct familial/genetic underpinnings (Leckman et al., 2010). Imaging studies have also suggested that separate but overlapping brain systems mediate different symptom dimensions. For example, Mataix-Cols and colleagues (2004) used functional magnetic resonance imaging (fMRI) to examine brain activation of patients with OCD (who had mixed symptoms) in response to different symptom provocation. The findings showed that washing, checking, and hoarding dimensions had distinct (and overlapping) neural correlates. Another study found distinct (and overlapping) neural correlates of symmetry/ordering, contamination/washing, and harm/checking symptom dimensions (van den Heuvel et al., 2009).

For the past few decades, hoarding has been considered a symptom dimension of OCD. However, a mounting literature indicates that hoarding may be sufficiently different from OCD to be construed as a separable clinical entity (for a review, see Mataix-Cols et al., 2010). First, hoarding often occurs in the absence of other OCD symptoms. Second, there are phenomenological differences between hoarding and other OCD symptoms (e.g., hoarding is less characterized by repetitive, intrusive, ego-dystonic thoughts). Third, individuals with hoarding demonstrate different neurocognitive deficits and neural correlates. Fourth, compared to patients with other OCD symptoms, patients with hoarding symptoms are less likely to respond to SSRI medication or CBT. Given this evidence, hoarding is included as a separate disorder in the new DSM-5 chapter on obsessive–compulsive and related disorders (APA, 2013).

Subtypes

Tic-Related OCD

It has been suggested that patients with OCD who have a lifetime history of a comorbid tic disorder may represent a distinct subtype with (partly) independent etiology. Studies show that compared to patients with OCD but without a comorbid tic disorder, individuals with tic-related OCD are more likely to be males, to report antecedent sensory phenomena, to have attention-deficit/hyperactivity disorder (ADHD) and pervasive developmental disorders, and to have a family history of OCD (Hanna et al., 2002; Leckman et al., 2010; Rosario-Campos et al., 2005). Lewin, Chang, McCracken, McQueen, and Piacentini (2010) reported no significant differences in OCD or tic disorder severity, functional impairment, or risk for comorbidity in youth with both disorders as compared to those with either one alone. Evidence also suggests that individuals with tic-related OCD may have different developmental trajectories. For example, a longitudinal study following individuals with pediatric OCD for 9 years found that individuals with tic-related OCD were more likely to have remitted compared to individuals without tic disorder comorbidity (i.e., they showed a trajectory similar to that of individuals with tic disorders alone) (Bloch et al., 2009). In addition, it appears that children with tic-related OCD are less likely to respond to SSRIs alone (March et al., 2007), but may respond favorably to SSRIs augmented with an antipsychotic medication (Bloch, Landeros-Weisenberger, et al., 2006).

Early-Onset OCD

Early-onset OCD is another subtype of OCD, and it significantly overlaps with tic-related OCD. Taylor (2011a) performed a latent class analysis on nine existing data sets, and identified two separate age-at-onset groups: a group with childhood onset (mean age at onset = 11 years) and a group with adult onset (mean age at onset = 23 years). A meta-analysis (Taylor, 2011a) of studies comparing these groups indicated that patients with early-onset OCD were more likely to be male, to have a tic disorder, and to have a family history of OCD. Existing data also suggest that early-onset cases are less likely than later-onset cases to present with a chronic course (see below).

Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infection

Swedo and colleagues (1998) proposed that susceptible individuals (usually children) develop OCD or tic disorders because of a group A beta-hemolytic streptococcal infection that causes autoimmune inflammation in the striatum and other brain areas. In these cases, both onset of OCD and symptom exacerbation are believed to be temporally related to a streptococcal infection. Although some empirical evidence supports the validity of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) as an OCD subtype (Leckman et al., 2010), the concept remains controversial: Findings have been mixed, with important conceptual/definitional issues remaining unresolved (Oliveira & Pelajo, 2010). Importantly, given the difficulty in accurately establishing a PANDAS diagnosis, the true prevalence is likely to be much lower than estimates based on the purported number of cases presenting for treatment.

Common Comorbidities

Comorbidity among individuals with OCD is common, especially in treatment-seeking populations. Some evidence indicates that younger age at onset is associated with greater comorbidity, irrespective of chronological age (Geller, Biederman, Faraone, Bellordre, et al., 2001). Coskun, Zoroglu, and Ozturk (2012) investigated 25 preschool-age children referred to a university clinic and found that all had at least one additional DSM-IV (APA, 1994) diagnosis. The most frequent comorbid diagnoses were non-OCD anxiety disorders (68%), ADHD (60%), oppositional defiant disorder

(48%), and tic disorders (24%). Geller, Biederman, Faraone, Bellordre, and colleagues (2001) compared DSM-IV comorbidity rates among samples of children (N = 46), adolescents (N = 55), and adults (N = 100) with OCD. Non-OCD anxiety disorders (i.e., social phobia, specific phobia, panic) were prevalent in all three samples, and there was a significantly higher rate of separation anxiety among children (56%) and adolescents (35%) compared to adults (17%). As expected, the rate of Tourette's disorder was higher among children (25%) than among adolescents (9%) and adults (6%). Depression was less common among children (39%) than adolescents (62%) and adults (78%). Also, substance abuse/dependence was less common among children (0%) and adolescents (2%) compared to adults (16%). The adolescent and the childhood samples were characterized by high prevalence of both ADHD (children = 51%; adolescents = 36%) and oppositional defiant disorder (children = 51%; adolescents = 47%); however, these disorders were not assessed in the adult sample. Langley, Lewin, Bergman, Lee, and Piacentini (2010) compared youth with OCD who had primarily externalizing, primarily internalizing, and no comorbidities, and found those with internalizing comorbidities to have the highest level of OCD severity, whereas those with externalizing comorbidities evidenced the greatest functional impairment.

The OCD Spectrum

In the past two decades, as noted earlier, there has been growing research interest in the concept of an OCD spectrum—a concept that assumes relatedness among different psychiatric problems that share core features with OCD (Abramowitz, Taylor, & McKay, 2009; Stein, Fineberg, et al., 2010). A number of different psychiatric disorders have been implicated with the OCD spectrum, but the disorders most consistently noted are body dysmorphic disorder, eating disorders, tic disorders, hair-pulling disorder (trichotillomania), and excoriation (skin-picking) disorder (Bienvenu et al., 2012; Hollander et al., 2009). The notion of the OCD spectrum involves the assumption that these problems share phenomenological features (i.e., failure to inhibit repetitive thoughts/behaviors); respond to the same treatments; have similar comorbidity patterns; and have common genetic, neurobiological, psychological, and environmental underpinnings. Some disorders on the spectrum (e.g., tic disorders) are more clearly linked to OCD than others, and at present research on the etiology of these problems is too limited to permit a full understanding of how best to conceptualize them. Nonetheless, the OCD spectrum concept has been influential: In DSM-5 (APA, 2013), OCD is not classified in a category with anxiety disorders (as it was in DSM-IV), but in a category called obsessive–compulsive and related disorders, which includes OCD, body dysmorphic disorder, hoarding disorder, hair-pulling disorder (trichotillomania), excoriation (skin-picking) disorder, and more.

Definitional and Diagnostic Issues

According to the DSM-5 criteria for OCD (APA, 2013) an individual has to meet definition for either obsessions or compulsions (or both) (Table 9.1). Obsessions and compulsions are defined as indicated above under "Core Symptoms." The compulsions need to be either unrealistically related to what they are supposed to prevent/neutralize (e.g., avoiding the number 6 to prevent harm) or excessive (e.g., time-consuming washing rituals). The criteria require that the obsessions or compulsions occupy more than 1 hour per day, cause marked distress or impairment, and are not better explained by the effect of substances or symptoms of another mental disorder.

Patients differ in terms of how much insight they have into their OCD beliefs (e.g., the extent to which a patient really believes that compulsions prevent a feared outcome). Thus, in the DSM-5 criteria, users are asked to specify how much insight a patient has (good/fair insight, poor insight, or no insight/delusional beliefs). Children and adolescents are more likely than adults to have poor insight. As noted earlier, patients with a history of comorbid tic disorders often differ from other OCD patents in terms of course, comorbidity, family history, and so on. Therefore, the criteria also ask users to specify whether a patient has a current or past history of any tic disorder. In DSM-5, obsessions and compulsions related to hoarding should be diagnosed as hoarding disorder, not OCD. However, patients should be diagnosed with OCD if they present with typical OCD symptoms that lead to hoarding behaviors (e.g., not discarding things to avoid harm).

Developmental Course and Prognosis

Pediatric OCD usually exhibits a waxing and waning course and is typically considered a chronic disorder, although a substantial portion of sufferers may experience remission by early adulthood. Stewart and col-

TABLE 9.1. DSM-5 Diagnostic Criteria for Obsessive–Compulsive Disorder

A. Presence of obsessions, compulsions, or both:
Obsessions are defined by (1) and (2):

1. Recurrent and persistent thoughts, urges, or images that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals cause marked anxiety or distress.
2. The individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e., by performing a compulsion).

Compulsions are defined by (1) and (2):

1. Repetitive behaviors (e.g., hand washing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly.
2. The behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however, these behaviors or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent, or are clearly excessive.

Note: Young children may not be able to articulate the aims of these behaviors or mental acts.

B. The obsessions or compulsions are time-consuming (e.g., take more than 1 hour per day) or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The obsessive–compulsive symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

D. The disturbance is not better explained by the symptoms of another mental disorder (e.g., excessive worries, as in generalized anxiety disorder; preoccupation with appearance, as in body dysmorphic disorder; difficulty discarding or parting with possessions, as in hoarding disorder; hair pulling, as in trichotillomania [hair-pulling disorder]; skin picking, as in excoriation [skin-picking] disorder; stereotypies, as in stereotypic movement disorder; ritualized eating behavior, as in eating disorders; preoccupation with substances or gambling, as in substance-related and addictive disorders; preoccupation with having an illness, as in illness anxiety disorder; sexual urges or fantasies, as in paraphilic disorders; impulses, as in disruptive, impulse-control, and conduct disorders; guilty ruminations, as in major depressive disorder; thought insertion or delusional preoccupations, as in schizophrenia spectrum and other psychotic disorders; or repetitive patterns of behavior, as in autism spectrum disorder).

Specify if:

With good or fair insight: The individual recognizes that obsessive–compulsive disorder beliefs are definitely or probably not true or that they may or may not be true.

With poor insight: The individual thinks obsessive–compulsive disorder beliefs are probably true.

With absent insight/delusional beliefs: The individual is completely convinced that obsessive–compulsive disorder beliefs are true.

Specify if:

Tic-related: The individual has a current or past history of a tic disorder.

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leagues (2004) conducted a meta-analysis of 16 pediatric OCD treatment (primarily medication) studies that included posttreatment follow-up evaluations ranging from 1 to 9 years; they found 41% of participants to meet full diagnostic criteria for OCD at follow-up, with an additional 19% exhibiting subthreshold symptoms at this time point. Similar findings were reported by Micali and colleagues (2010) in their retrospective chart review of 142 pediatric patients seen at the Maudsley Hospital, London, for treatment of their OCD.

In contrast, OCD tends to be more persistent among individuals with adult onset. One study followed adults with OCD for more than 40 years (Skoog & Skoog, 1999) and found that even though 83% demonstrated some improvement in symptoms, 53% still had clinically significant OCD at the 40-year follow-up, and only 20% reported complete recovery. In addition, adults with OCD who participate in treatment trials often show a poor long-term outcome. For example, Bloch and colleagues (2013) reported 10- to 20-year

outcomes among patients participating in SSRI medication trials. At follow-up, almost half (49%) were still experiencing clinically significant OCD, and only 20% demonstrated remission of symptoms. Good initial response to SSRI treatment was a predictor of good long-term outcome.

Epidemiology

Prevalence

Lifetime prevalence estimates of OCD range from 1 to 2.3% among children and adolescents and from 1.9 to 3.3% among adults (Kalra & Swedo, 2009). The relatively minor discrepancy between rates for youth and adults may reflect the greater likelihood of remission in early-onset cases, which partially mitigates the rate of adult-onset illness (Stewart et al., 2004).

Sex Differences

Gender ratios in adult samples are relatively equal, possibly with a slight female preponderance; in childhood and adolescence, however, males are more likely to be affected than females (Geller, Biederman, Faraone, Bellordre, et al., 2001). Evidence suggests that males are more likely than females to have early-onset OCD and comorbid psychiatric disorders, especially comorbid tic disorders (Coskun et al., 2012). A review (Mathis et al., 2011) of research examining gender differences in OCD symptom dimensions concluded that males are more likely than females to report sexual–religious or aggressive symptoms, and females are more likely than males to report contamination/cleaning symptoms.

Cultural Variations

OCD occurs in all cultures around the world, and existing data suggest that prevalence is relatively similar across countries and cultures (Horwath & Weissman, 2000). Symptom presentation and clinical characteristics (e.g., gender ratio, comorbidity patterns) are also relatively stable across cultures (Fontenelle, Mendlowicz, Marques, & Versiani, 2004). Thus it appears that core features of OCD are mostly independent of culture. However, cultural factors can influence the content of obsessions and compulsions. For example, religious ideas in the culture may be reflected in OCD symptoms.

Theoretical Frameworks

Evolutionary Models

Evolutionary models of OCD typically assume that OCD symptoms reflect dysregulation in mechanisms that underlie normal evolutionarily conserved behavioral and cognitive repertoires. For example, Szechtman and Woody (2004) hypothesized that OCD represents a breakdown in a security motivational system. Other authors (Evans & Leckman, 2006; Feygin, Swain, & Leckman, 2006) have proposed a developmental evolutionary model emphasizing a dynamic interplay between threat detection and attachment. The model assumes that humans evolved psychological mechanisms focusing on external threats (e.g., predators, microbial disease) and formation/maintenance of relationships (e.g., parent–child attachment). According to the model, mechanisms involved in threat detection and attachment are intimately linked (e.g., on genetic and neurobiological levels), and a dysregulation in this general system underlies OCD symptoms. In healthy individuals, this system is presumed to account for (developmentally) normal rituals and preoccupation, such as childhood routines (e.g., bedtime rituals, collecting/storing objects), repetitive thoughts associated with romantic love (e.g., fixed preoccupation with one person), and preoccupation/fears that characterize new parents (e.g., checking behaviors, precautions). However, in individuals with OCD, the system has broken down for some reason—for example, because of genetic vulnerabilities, traumatic events, or brain injury.

Biological Models

Multiple pathophysiological models of OCD, some of which are more fully described below, have been proposed and investigated with varying degrees of success. However it is worth noting that a significant body of evidence has associated OCD with functional and structural abnormalities in cortical–striatal–thalamic–cortical (CSTC) circuitry within the brain (Insel & Winslow, 1992; Rosenberg, MacMaster, Mirza, Easter, & Buhagiar, 2007; Saxena, Brody, Schwartz, & Baxter, 1998). This circuitry (which involves portions of the orbitofrontal cortex, striatum [caudate, putamen], cingulate, and thalamus) is involved in response inhibition and planning, among other things, and it has been hypothesized that OCD symptoms result from an imbalance between production and inhibition of thoughts/

actions (Melloni et al., 2012). The model assumes that two neural pathways regulate output from the frontal cortex and function to modulate/control behavioral responses to external stimuli (e.g., make sure appropriate responses are executed). The "direct" pathway mediates thalamic stimulation of the frontal cortex, and the "indirect" pathway inhibits thalamic stimulation. It is believed that excessive neural tone in the "direct" pathway, relative to the "indirect" pathway, results in failure of the latter to inhibit inappropriate responses producing OCD symptoms (Rosenberg et al., 2007).

Animal Models

Several animal models have been used to study human OCD (Fineberg, Chamberlain, Hollander, Boulougouris, & Robbins, 2011), including ethological models (i.e., spontaneous behavioral problems in animals that resemble human OCD) and laboratory-based genetic or pharmacological models (i.e., genetic mutations or pharmacological agents that induce OCD-like behavior in mice). An example of ethological models is acral lick dermatitis in dogs, which is a condition characterized by excessive and repetitive licking, chewing, or scratching of the distal portions of the limbs, resulting in skin lesions. This condition shares some superficial characteristics with OCD in humans (e.g., both reflect excessive hygienic behavior) and responds to the same medication (i.e., clomipramine). Thus it has been used as a model for human OCD, especially excessive hand washing (Rapoport, Ryland, & Kriete, 1992).

Genetic animal models use genetically altered mice that exhibit behaviors resembling OCD (no genetic model exists in which mutations are based on knowledge of genetic underpinning of human OCD). For instance, it has been shown that mice with mutations of the Hoxb8 gene engage in excessive grooming behavior, resulting in hair loss and skin lesions. The excessive grooming is thought to mirror human OCD symptoms (e.g., washing rituals), and some evidence suggests that it is mediated by similar brain systems (Greer & Capecchi, 2002). Pharmacological models in which stimulants (acting on dopamine) are used to induce stereotyped or perseverative behavior in mice have also been used as models for OCD. In general, even though existing animal models have some face validity (the symptoms resemble human OCD symptoms), there is limited evidence demonstrating construct validity (e.g., shared underlying physiology) or predictive validity (e.g., similar response to treatment) (Fineberg et al., 2011).

Behavioral and Cognitive-Behavioral Models

BEHAVIORAL MODELS

The primary behavioral conceptualizations of OCD are based on Mowrer's (1956) two-factor conditioning theory. In the first stage, a neutral event or object becomes fearful or aversive to the individual as a result of its association with an unrelated fear-eliciting event through the process of classical conditioning. In the second stage, subsequent efforts to neutralize or avoid these feared events or objects (e.g., compulsions) become strengthened as a result of their anxiety-reducing properties (i.e., negative reinforcement). Since most individuals cannot recall specific fear-eliciting events associated with the onset of their OCD symptoms, more recent behavioral conceptualizations of OCD have incorporated other psychosocial acquisition mechanisms, including modeling, observation, and informational learning (e.g., Steketee, 1993) and/or biological etiologies as necessary precursors to the development of the disorder.

Regardless, behavioral principles provide a useful theoretical basis for understanding the maintenance of many OCD symptoms and form the basis for exposure plus response prevention (ERP), which is the most effective current intervention for OCD. ERP consists of systematic and graded *in vivo* exposure to feared situations and objects, paired with supervised response prevention of the relevant ritualistic behavior (Foa & Kozak, 1986). The most commonly proposed mechanism for ERP effectiveness is that over repeated exposures, associated anxiety dissipates through the process of autonomic habituation. In addition, successful completion of exposure facilitates the development and storage of corrective cognitive information pertaining to the feared situation (Foa & Kozak, 1986).

COGNITIVE-BEHAVIORAL MODELS

Cognitive-behavioral models of OCD (e.g., Salkovskis, 1996) assume that intrusive thoughts, impulses, and images are normal features of the human mind, but that certain dysfunctional core beliefs (e.g., inflated sense of responsibility) lead to maladaptive appraisals of intrusions. These appraisals evoke emotional

responses and counterproductive strategies, which in turn play a role in the development and maintenance of OCD symptoms. Survey studies (e.g., Freeston, Ladouceur, Thibodeau, & Gagnon, 1991) show that the majority of people in the general population occasionally experience intrusive thoughts with content similar to that of OCD symptoms (e.g., a thought of catching a disease from a public toilet or a sudden impulse to drive into oncoming traffic). Most people brush these off as irrelevant and meaningless intrusions into consciousness. According to cognitive-behavioral models, commonplace intrusions develop into obsessions when they are appraised as personally meaningful, threatening, unacceptable, immoral, or the like. The models assume that certain dysfunctional core beliefs (e.g. excessive responsibility, overestimation of threat, overimportance of thought, intolerance of uncertainty) lead to such maladaptive appraisals of intrusive thoughts. For example, excessive responsibility (i.e., the unrealistic belief of being responsible for, and having a power to prevent or cause, certain unwanted outcome) may lead an individual to appraise intrusive thoughts of harming another person as particularly threatening or unacceptable. In addition, such appraisal will lead to strategies aimed at avoiding, eliminating, or neutralizing the intrusion (i.e., compulsive rituals). The compulsions and other neutralizing/avoidant strategies are thought to be negatively reinforced because they temporarily reduce anxiety/distress associated with the intrusion. Furthermore, the anxiety reduction resulting from these strategies is counterproductive because it prevents the individual from learning that the appraisal is inaccurate or excessive.

Etiological and Risk/Protective Factors

Genetic/Familial Factors

Family history studies consistently support the notion of OCD as a familial disorder, with first-degree relatives of affected probands showing a 12% rate of OCD, compared to a 2% rate in first-degree relatives of normal controls (Alsobrook, Leckman, Goodman, Rasmussen, & Pauls, 1999). In addition, the finding that both generalized anxiety disorder and agoraphobia are found at higher rates in relatives of OCD versus normal probands suggests that observed genetic factors may not be specific to OCD per se, but instead may underlie a disposition towards the development of anxiety disorders (as defined by DSM-IV) in general (Nestadt et al., 2000). A meta-analysis of twin studies (Taylor, 2011b) concluded that most of the variance in OCD and obsessive–compulsive symptoms is explained by additive genetic factors, nonshared environmental factors, and interaction between them, but that shared environment or nonadditive genetic factors have few or no effects. Bloch and Pittenger (2010), in their review of the OCD genetics literature, reported the genetic heritability of OCD to be 26–61%. Grootheest, Cath, Beekman, and Boomsma (2005) suggested that genetic factors explain 45–65% of the variance in OCD symptoms among children/adolescents and 27–47% among adults.

Linkage and candidate gene studies have implicated a number of different genes in OCD with moderate to large effects, including genes that function within the serotonergic, dopaminergic, and glutamatergic systems (Hu et al., 2006; Nicolini, Arnold, Nestadt, Lanzagorta, & Kennedy, 2009; Samuels et al., 2011). However, failure to replicate findings has been common, and the exact genetic underpinning of OCD remains unclear (Pauls, 2010). It is believed that numerous genes play a role in OCD. Some have greater effects than others, and some represent a risk for specific symptom dimensions or subtypes, while others represent a more general risk for OCD and related disorders (or psychopathology more generally) (Taylor, 2011b).

Neurobiological Factors

NEUROCHEMISTRY

A growing body of evidence supports the role of glutamatergic dysfunction in OCD (Bhattacharyya et al., 2009; Carlsson, 2000; O'Neill et al., 2012; Pittenger, Bloch, & William, 2011; Rosenberg & Keshavan, 1998). Glutamate is one of the primary excitatory neurotransmitters in the brain, and glutamatergic projections are ubiquitous to most important cortical and subcortical circuitry in the nervous system. Relevant to OCD, glutamate is a critical mediator of *N*-methyl-*D*-aspartate (NMDA) receptor activity in the brain. NMDA receptor activity is thought to be critical in the formation of associative memory links (Meador, 2007), and this receptor has been referred to as the brain's "coincidence detector" (Pittenger et al., 2011). In a small pilot trial using magnetic resonance spectroscopic imaging, O'Neill and colleagues (2012) found significant

differences in glutamatergic metabolite concentrations in cortical areas associated with CSTC circuitry in five unmedicated youth with OCD, compared to matched healthy controls. Moreover, treatment with CBT resulted in significant changes in metabolite concentrations, with these changes both predicting response to treatment and correlating with the magnitude of symptom decrease. Given the role of NMDA receptor activity in facilitating associative learning, researchers have begun to pharmacologically target NMDA potentiation, most commonly using D-cycloserine, as a method to augment exposure-based behavior therapy for OCD (Rothbaum, 2008). Results to date for OCD have been mixed, with greater support for adult (Wilhelm et al., 2008) than for youth (Storch, Murphy, et al., 2010) studies. Although multilevel support for a glutamatergic hypothesis of OCD continues to accrue, significant knowledge gaps remain, and more definite research remains to be conducted.

The hypothesis that serotonin dysfunction plays a role in OCD is largely based on findings from controlled trials showing that SSRIs reduce OCD symptoms for both adults and children, as well as on candidate gene studies (e.g., Hu et al., 2006). Several platelet and cerebrospinal fluid studies have shown abnormal levels of this neurotransmitter in individuals with OCD; however, findings have not been consistent across studies (Rosenberg et al., 2007). Evidence for dysregulation in other neurotransmitter systems (including the dopaminergic system) has been found, although findings are preliminary and often mixed (Rosenberg et al., 2007).

NEUROIMAGING

Neuroimaging studies have generally supported the frontal–striatal–thalamic model, both in adults (Menzies et al., 2008) and in children (MacMaster, O'Neill, & Rosenberg, 2008). Although results are not entirely consistent, studies have found that, compared to healthy controls, patients with OCD show abnormal activation in these brain areas during rest or neutral tasks. Also, studies have found aberrant activity during symptom provocation. Furthermore, research suggests that abnormalities in some of these brain regions (e.g., the striatum) normalize after successful SSRI treatment (e.g., Rosenberg et al., 2000) and after successful CBT (e.g., Huyser, Veltman, Wolters, de Haan, & Boer, 2010; O'Neill et al., 2012, as noted earlier; for negative findings, see Benazon, Moore, & Rosenberg, 2003).

NEUROPSYCHOLOGY

Neuropsychological research has also produced evidence consistent with dysfunction in frontal–striatal–thalamic areas (Chamberlain, Blackwell, Fineberg, Robbins, & Sahakia, 2005). Results indicate that patients with OCD show dysfunction in visuospatial memory that is caused by an executive deficit in encoding strategies (Kuelz, Hohagen, & Voderholzer, 2004). A longitudinal study showed that poor performance in visual–spatial/visual–motor and executive domains at age 13 predicted OCD diagnosis at age 32 (Grisham, Anderson, Poulton, Moffitt, & Andrews, 2009), suggesting that such deficits may play a causal role in the disorder. Several other deficits in executive functioning have been documented, including problems with inhibition, set shifting, planning, and problem solving; however, findings have not been consistent (Kuelz et al., 2004).

For example, at least three research studies have attempted to assess response inhibition in pediatric OCD. One study using the ocular–motor paradigm found that participants with OCD more often than healthy participants demonstrated response inhibition failure (Rosenberg et al., 1997). In contrast, two neuroimaging studies using other types of inhibition tasks did not find a statistically significant difference between the performance of participants with OCD and controls (Rubia et al., 2010; Woolley et al., 2008). Similarly, research examining set-shifting abilities has been mixed, with some research showing deficits in patients with OCD compared to healthy controls and other psychiatric groups, but other studies showing no group differences (Kuelz et al., 2004). On balance, however, the overall evidence indicates that there is some dysfunction in executive functioning in OCD. Inconsistent findings in the neuropsychology literature may be due to small sample sizes in many of the studies, cognitive heterogeneity of the disorder (e.g., few studies link cognitive deficits with specific symptom dimensions), the use of tests that are not sufficiently sensitive, and failure to rule out possible confounding variables (e.g., medication use, comorbidity such as with ADHD).

Dysfunctional Beliefs

As described above, cognitive-behavioral models assume that certain strongly held beliefs may play a causal role in the development of OCD symptoms. Three types

of interrelated beliefs have been postulated to underlie OCD: (1) perfectionism and intolerance of uncertainty; (2) over-importance of thoughts and the need to control thoughts; and (3) inflated sense of responsibility and overestimation of threat (Obsessive Compulsive Cognition Working Group, 2005). In general, evidence has supported the notion that these beliefs, especially inflated responsibility, play a role in OCD. Scores on self-report scales assessing these beliefs (e.g., the Obsessive Beliefs Questionnaire) predict later OCD symptoms, after adjustments for baseline symptom severity (e.g., Coles, Pietrefesa, Schofield, & Cook, 2008). Evidence also comes from longitudinal studies (e.g., Abramowitz, Nelson, Rygwall, & Khandker, 2007) following first-time expecting parents from before and after the birth of their first child. (Becoming a parent is a known stressor that increases sense of responsibility.) Results show that dysfunctional beliefs before the birth of the child predict OCD symptoms at 3 months postpartum, after adjustments for baseline OCD severity. Also, negative appraisal of infant-related intrusive thoughts during the first month postpartum mediated the relationship between prebirth dysfunctional beliefs and OCD symptoms at 3 months postpartum. In addition, experimental studies have shown that manipulation of sense of responsibility increases compulsive-like behaviors in participants (Arntz, Voncken, & Goosen, 2007; Barrett & Healy-Farrell, 2003), although this increase has not been shown to influence treatment outcome in youth (Barrett & Healy-Farrell, 2003). These data are consistent with the notion that dysfunctional beliefs underlie appraisals of intrusive thoughts, which in turn influence OCD symptoms. Evidence also suggests that cognitive-behavioral models may apply to at least some children and adolescents with OCD, although research is scarce (Reynolds & Reeves, 2008).

Traumatic or Stressful Life Events

Clinical impression indicates that stressful or traumatic life events influence the development of OCD (de Silva & Marks, 1999). Studies using standardized questionnaires have shown that both children/adolescents and adults with OCD frequently report stressful life events prior to the OCD onset (Fontenelle, Cocchi, Harrison, Miguel, & Torres, 2011). For example, one study found that children/adolescents with OCD reported more negative life events and more life events in general in the year prior to OCD onset, compared to healthy controls (Gothelf, Aharonovsky, Horesh, Carty, & Apter, 2004). In addition, an epidemiological study following adolescents in the community for 1 year found that (1) a higher rate of undesirable life events and (2) a lower rate of desirable life events added to the prediction of later OCD symptoms (Valleni-Basile et al., 1996). Studies have also shown that adult patients with OCD report higher rates of childhood trauma than healthy controls do; however, the rates do not seem to be higher than in other psychiatric populations (e.g., Lochner et al., 2002). Overall, the evidence suggests that traumatic or stressful life events may influence development of OCD symptoms. Exactly how these stressors influence OCD is not well understood.

Events/Experiences Underlying Inflated Responsibility

Salkovskis, Shafran, Rachman, and Freeston (1999) hypothesized that certain types of life events and experiences can play a role in shaping and causing inflated sense of responsibility—a core belief thought to underlie OCD symptoms, as described earlier. These precipitating events/experiences included (1) excessive/inappropriate responsibility as a child (e.g., taking on responsibility for adult matters as a child); (2) a rigid and extreme code of conduct; (3) overprotective, indulgent, or critical parenting (thought to reduce exposure to responsibility as a child); (4) incidents where the individual's actions or inactions caused harm/misfortune; or (5) incidents where it appeared that the individual's actions or inactions caused harm/misfortune. Preliminary cross-sectional evidence from nonclinical populations suggest that responsibility attitudes mediate the relationship between these experiences and OCD symptoms (Smári, Þorsteinsdóttir, Magnúsdóttir, Smári, & Ólason, 2010), but more systematic longitudinal studies in clinical samples are needed to clarify their role in the development of inflated responsibility and OCD symptoms. Research also shows that pregnancy and the postpartum period increase the risk for development of OCD. Having a child and caring for an infant can increase a sense of responsibility, and it may be that this sense of responsibility mediates the influence of pregnancy on OCD symptoms (Abramowitz et al., 2007).

Possible Developmental Pathways

Multiple biological, intrapersonal, and environmental factors point to OCD as a neurodevelopmental disorder. From an epidemiological perspective, individuals

with early-onset illness (e.g., before age 10) are more likely to be male, to have a tic disorder, to have a family history of OCD, and to describe their symptoms as more sensory and less tied to concrete obsessional fears than those with later onset (Taylor, 2011b). This early preponderance of male cases decreases by adolescence, which is the more typical period for female onset (Ruscio, Stein, Chiu, & Kessler, 2010), yielding an equal gender ratio in adults. Poulton, Grisham, and Andrews (2009) posit that the relationship between onset age and gender may be mediated by androgen levels, which show a positive correlation with OCD symptom severity. In addition, up to one-half of adults with OCD report a childhood onset (Stewart et al., 2007). As compared to adult onset, individuals with childhood-onset OCD (before age 10) are more likely to have a familial (i.e., genetic) form of the disorder (Nestadt et al., 2000) and to demonstrate both poorer response to medication and overall prognosis (Skoog & Skoog, 1999). As noted by Pittenger et al. (2011), few cases have an onset after age 30 (Ruscio et al., 2010).

Further evidence for the conceptualization of OCD as a neurodevelopmental disorder comes from the fact that symptom presentation is, for the most part, phenomenologically similar across the lifespan. As such, Bolton, Luckie, & Steinberg (1995) suggested that risk for OCD may emerge during early childhood development. Although some age-related differences have been reported—for example, children and adolescents have been found to be more likely to experience harm obsessions and hoarding, whereas adults are more likely to experience sexual obsessions (Moore et al., 2007)—it bears noting that each of these symptoms can be present across the lifespan. As described earlier, in addition to tic disorders, other comorbidities show developmental trends (e.g., rates for ADHD are higher in children and adolescents, and depression and substance abuse are more common in adolescents and adults). However, it remains unclear whether these patterns are related to OCD pathogenesis, or simply reflect the natural history of the comorbid disorders as observed in the population at large.

From a biological perspective, Rosenberg and Keshavan (1998) found increased anterior cingulate (a structure in the CSTC circuit described earlier) volumes in pediatric patients with OCD compared to healthy controls. Anterior cingulate volumes were associated with obsessive, although not compulsive, symptomatology. Moreover, the age-related decrease in cingulate volumes found in controls was absent in the group with OCD. Interpretation of these findings suggested a neurodevelopmental model in which OCD is related to a maturational abnormality in the neuronal pruning of frontostriatal structures, elsewhere implicated in the etiology of OCD.

Collectively, the evidence presented above and elsewhere in this chapter suggests that some form of biological diathesis, initially evident in early development, underlies at least a portion of childhood-onset OCD cases. This diathesis is almost assuredly multidetermined and heterogeneous in nature. However, the likely biological underpinnings of the disorder do not negate the likely influence of environmental factors on the manifestation and course of the disorder. From a cognitive-behavioral perspective, the reduction in fear associated with efforts to avoid or neutralize the feared stimuli serves both to negatively reinforce performance of the compulsion and to forestall correction of the cognitive processes maintaining the obsessive belief. Over time, this can, and often does, lead to generalization of symptoms and worsening illness.

Family environmental factors, most notably symptom accommodation, have also been shown to maintain OCD symptoms, reinforce fear and avoidance behaviors, and undermine response to treatment (e.g., Peris et al., 2012; Renshaw, Steketee, & Chambless, 2005). In addition, the dilemma faced by many families of youth with OCD as to whether or not to burden family members by altering routines to accommodate OCD symptoms is considerable. Not addressing the increased anxiety and upset on the part of the patient by refusing to give in to his or her symptoms can have a negative impact on family functioning, resulting in increased feelings of hostility and blame toward the patient (Peris et al., 2008; Storch, Geffken, et al., 2007). Importantly, research has shown that directly targeting family environmental factors in treatment can lead to reductions in accommodation and enhanced child outcomes (Merlo, Lehmkuhl, Geffken, & Storch, 2009; Piacentini et al., 2011).

Current Issues and Future Directions

Among other things, future research on the etiology of OCD will involve clarifying the distinctiveness of individual symptom dimensions (e.g., hoarding), the validity of putative subtypes (e.g., early age at onset), and the nature of the relationship with other disorders (e.g., OCD spectrum disorders). OCD is a heterogeneous condition that has a complex etiology undoubtedly in-

volving numerous interacting factors. Some play a role in specific subtypes/dimensions, while others play a role in all OCD symptoms or in psychopathology more generally. Better understanding of the etiology of OCD subtypes/symptom dimensions may eventually facilitate treatment development or help optimize treatment effects by matching etiological subgroups and interventions.

Twin research shows that OCD is caused mostly by additive genetic factors, nonshared environmental factors, and interaction between them. However, the exact nature of the genetic architecture or environmental influences is not well understood. Several candidate endophenotypic markers of OCD have been proposed (for a review, see Taylor, 2012), and there is a hope that this work will facilitate discoveries of specific genetic underpinnings. Neurobiological research indicates that abnormalities in frontal–striatal–thalamic circuitry may mediate OCD symptoms. However, the causes of these abnormalities, although currently under study, remain elusive (e.g., the links with genetic underpinnings). Also, it is unclear to what extent such brain abnormalities reflect a core pathogenesis of the disorder and whether they represent a risk that could be detected before onset of the disorder (Rauch & Britton, 2010). Regardless, investigation of both biological (e.g., O'Neill et al., 2012) and environmental (e.g., Peris et al., 2012) predictors and correlates of treatment response will play a crucial role in developing more effective, personalized treatment protocols (Piacentini, 2008).

Given the substantial environmental influence in the etiology of OCD, it is clear that biological models are not sufficient to explain the disorder, and it will probably be informative to consider interaction between biological systems and environmental influence. It has been pointed out that a major limitation of biological models is the failure to explain the symptom heterogeneity of the disorder: Why, for example, does one individual develop checking compulsions, another contamination fears, and still another obsessions about harming others (Abramowitz et al., 2009)? By considering learning experiences, cognitive-behavioral models are able to capture the idiosyncratic nature of the symptoms. However, these models are limited, as they do not capture all OCD cases (Taylor et al., 2006) and explain only a small portion of the phenotypic variance in twin research (Taylor & Jang, 2011). It could be that refinement in conceptualization and assessment of dysfunctional beliefs will improve the explanatory power of cognitive-behavioral models. However, it seems likely that multiple explanatory models will be needed for a full understanding of OCD's etiology, including both biological models and cognitive-behavioral models. Evolutionary and developmental perspectives may also prove to be useful integrating frameworks (e.g., Evans & Leckman, 2006).

TIC DISORDERS

Historical Context

Gilles de la Tourette, a 19th-century French neurologist, published in 1885 a small case series of patients suffering from a disorder characterized by rapid involuntary motor movements, echolalia, hyperexcitability, and unusual vocalizations (see Lajonchere, Nortz, & Finger, 1996). His descriptions of the clinical features and associated characteristics, as well as his speculations about likely genetic underpinnings, childhood onset, and clinical course, were remarkably accurate and form the basis of the syndrome that today bears his name. Initial biological conceptualizations, however, quickly gave way to a psychoanalytic framework—given the lack of effective treatments in the field of neurology, coupled with the early successes of psychoanalysis in first half of the 20th century (Ferenczi, 1921). One unfortunate implication of the psychological model of tic disorders was the misperception that individuals with tics lacked willpower or possessed a character deficit, perhaps as a result of underlying psychic conflicts. The historical pendulum, however, swung back toward biologically based explanations with the discovery of antipsychotic medications and their efficacy for tic reduction, in conjunction with burgeoning research into the basic brain science of movement processes in the latter half of the 20th century (Kushner, 1999; Woods, Piacentini, & Walkup, 2007).

Recent years have witnessed a renewal of psychological approaches to tic disorders, but this time based on behavioral models that emphasize improved functioning and behavior change over relatively brief treatment periods. Moreover, the evolving conceptual model of Tourette's disorder/Tourette syndrome (TS) currently integrates both neurobiological and environmental factors in the understanding and treatment of the disorder (Himle, Woods, Piacentini, & Walkup, 2006). With

this brief historical context in mind, we now proceed to describe the symptom dimensions, diagnostic systems, developmental course, current theory, and proposed etiologies for chronic tic disorders from a developmental psychopathology perspective.

Description of the Disorder

Core Symptoms

Tics are defined as abrupt, rapid, recurring, and nonrhythmic motor movements or vocalizations involving one or more muscle groups that are usually experienced as outside voluntary control and often may mimic the appearance of normal movements or behavior (Robertson, 2012). Within this classification, they may be further defined as *simple* or *complex* tics and as *motor* or *vocal/phonic* tics. Simple motor tics involve isolated muscle group(s) and are manifested in a single anatomical location. They are characterized by fast, darting, meaningless muscle movements. Examples of simple motor tics include excessive eye blinking, nose twitching, shoulder shrugging, head jerking, or facial grimacing. By contrast, complex motor tics rely on the coordination of multiple muscle groups; are slower and more protracted in duration; appear more purposeful; and include movements such as touching objects or self, squatting, jumping, back arching, leg kicking, skipping, and facial and hand gestures. Simple vocal tics are typically inarticulate single sounds and include vocalizations such as throat clearing, coughing, sniffing or grunting. Complex vocal tics include intelligible syllables, words, or phrases; the words or phrases may include *echolalia* (repetition of others' words), *palilalia* (repetition of one's own words), and *coprolalia* (swearing). In other cases, they may involve animal noises such as chirping or barking, or spontaneous changes in the cadence, volume, or prosody of speech. Unlike simple tics, complex tics can often be mistaken for volitional behaviors and utterances (Coffey et al., 2000).

Definitional and Diagnostic Issues

In DSM-5 (APA, 2013), tic disorders have been newly classified under the umbrella of neurodevelopmental disorders, with the elimination of the DSM-IV section on disorders usually first diagnosed in infancy, childhood, or adolescence. It is grouped with other conditions characterized by onset in the developmental period, including ADHD and autism spectrum disorder. Tic disorders currently comprise four diagnostic categories: (1) Tourette's disorder, (2) persistent (chronic) motor or vocal tic disorder, (3) provisional tic disorder, and (4) other specified and unspecified tic disorders (Table 9.2). In DSM-5, a diagnosis of a chronic tic disorder can be made if tics persist for more than 1 year from the first tic onset, regardless of a tic-free period during that time. The removal of the DSM-IV maximum 3-month tic-free interval criteria in DSM-5 is largely consistent with clinical practice and simplifies the diagnostic process. Similarly, the DSM-IV diagnosis of transient tic disorder has been eliminated (along with its 4-week minimum tic duration) and replaced by provisional tic disorder in DSM-5, which is characterized simply by tics that have been present for less than 1 year since first tic onset. Chronic tic disorder may now be specified as with motor or vocal tics only. Generally, chronic motor tics are by far more common than a pure vocal tic disorder. The diagnoses of other specified and unspecified tic disorder are reserved for symptoms that are characteristic of a tic disorder but somehow do not meet full criteria for a tic disorder or any other specific neurodevelopmental disorder. Other changes in DSM-5 include the removal of the term "stereotyped" from the definition of tics, to minimize confusion in differentiating tics from stereotypic movement characteristics of conditions such as autism spectrum disorder.

Other DSM-5 criteria remain unchanged from DSM-IV. The diagnosis of Tourette's disorder requires multiple motor tics and at least one vocal tic to be present at some time during the illness, although not necessarily concurrently. While tic location, number, frequency, and complexity may fluctuate over time, the onset of the tics must be before age 18 to meet criteria for Tourette's disorder, chronic motor/vocal tic disorder, and provisional tic disorder. The tic occurrence cannot be attributable to substance intoxication, a general medical condition, or to a known central nervous system disease such as Huntington's chorea for the tic disorder diagnosis to be given. In general, DSM-5 offers a more unified definition of tics, more accurately reflects current clinical practice, and better captures the temporal pattern of tics while improving diagnostic reliability (Roessner, Hoekstra, & Rothenberger, 2011; Walkup, Ferrao, Leckman, Stein, & Singer, 2010). We hope that further research into clinical phenotypes and underlying neurobiological mechanisms will continue to advance diagnostic clarity.

TABLE 9.2. DSM-5 Diagnostic Criteria for Tic Disorders

Note: A tic is a sudden, rapid, recurrent, nonrhythmic motor movement or vocalization.

Tourette's Disorder

A. Both multiple motor and one or more vocal tics have been present at some time during the illness, although not necessarily concurrently.
B. The tics may wax and wane in frequency but have persisted for more than 1 year since first tic onset.
C. Onset is before age 18 years.
D. The disturbance is not attributable to the physiological effects of a substance (e.g., cocaine) or another medical condition (e.g., Huntington's disease, postviral encephalitis).

Persistent (Chronic) Motor or Vocal Tic Disorder

A. Single or multiple motor or vocal tics have been present during the illness, but not both motor and vocal.
B. The tics may wax and wane in frequency but have persisted for more than 1 year since first tic onset.
C. Onset is before age 18 years.
D. The disturbance is not attributable to the physiological effects of a substance (e.g., cocaine) or another medical condition (e.g., Huntington's disease, postviral encephalitis).
E. Criteria have never been met for Tourette's disorder.

Specify if:

With motor tics only
With vocal tics only
Provisional Tic Disorder

A. Single or multiple motor and/or vocal tics.
B. The tics have been present for less than 1 year since first tic onset.
C. Onset is before age 18 years.
D. The disturbance is not attributable to the physiological effects of a substance (e.g., cocaine) or another medical condition (e.g., Huntington's disease, postviral encephalitis).
A. Criteria have never been met for Tourette's disorder or persistent (chronic) motor or vocal tic disorder.

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Subtypes

Despite the suggestion from sources such as DSM-5 (APA, 2013) and the *International Classification of Diseases*, 10th revision (ICD-10; WHO, 1992) criteria that TS (as we henceforth refer to classic Tourette syndrome) is a unitary condition, there is growing evidence to the contrary. Recent research using sophisticated statistical modeling techniques such as hierarchical cluster analyses and principal-component factor analyses has indicated that TS is composed of multiple factors. Robertson, Althoff, Hafez, and Pauls (2008) reported five factors in a sample of 410 patients with TS: (1) socially inappropriate behaviors and other complex vocal tics, (2) complex motor tics, (3) simple tics, (4) compulsive behaviors, and (5) touching self. In the Robertson and colleagues (2008) sample, comorbid ADHD was associated with higher scores for Factors 1 and 3, while comorbid OCD was linked to elevated scores for Factors 1, 2, 3, and 4. Another large sample of 952 individuals from the Tourette Syndrome Association (TSA) International Genetic Consortium pool was analyzed via latent class analysis, with results indicating three primary classes: (1) TS + OCD symptoms, (2) TS + full-fledged OCD, and (3) TS + OCD + ADHD, with only the last class being heritable (Grados, Matthews, & TSA International Consortium for Genetics, 2008). The most recent factor analyses to date, using a sample of 639 patients with TS, revealed three factors accounting for 48.5% of the symptomatic variance: (1) complex motors tics and echo-pali phenomenon; (2) attention-deficit and hyperactivity symptoms plus aggressive behaviors; and (3) complex vocal tics and copro- phenomenon. OCD symptoms loaded significantly on the first two factors (Cavanna et al., 2011).

Such findings appear to support the clinical heterogeneity of TS, with all studies suggesting a solution of two or more factors. In general, research suggests that one consistent phenotype is composed of a "pure sim-

ple tics only" category, accounting for approximately 10% of all patients with TS. The remaining phenotypes involve a combination of complex tics, comorbid disorders, and other related psychopathology (Cavanna & Termine, 2012; Robertson, 2012). In light of such findings, research has begun to investigate whether different symptom dimensions of TS are associated with abnormalities in distinct cortical regions. In fact, recent work has already suggested that patients with TS who have only simple tics evidence cortical thinning mainly in primary motor regions, whereas those with a combination of simple and complex tics show cortical thinning, which extends into larger premotor, prefrontal, and parietal regions (Worbe et al., 2010).

Associated Characteristics

Tics characteristically wax and wane over time and have been described as fractal in nature, often occurring in bouts (Leckman, 2003; Leckman et al., 1998). Tic bouts are characterized by brief periods of stable intervals between tics, generally lasting 0.5–1.0 seconds, and intervals between bouts that last from minutes to hours (Du et al., 2010; Peterson & Leckman, 1998). An individual's tic profile (i.e., number, anatomical topography, and severity) may also change over time. As such, there is a great deal of inter- and intraindividual variability with respect to tic symptom presentation. Tics are also characterized by some degree of temporary suppressibility and are described as semi-voluntary to involuntary in nature (Jankovic, 1997). Suppressibility, suggestibility, and exacerbation with stress are some of the characteristics of tics that may lead to misdiagnosis. Although much diminished, tics can occur during all stages of sleep. Moreover, research indicates that sleep disturbance is frequently part of the TS picture, with decreased quality of sleep and increased arousal phenomena (Cohrs et al., 2001; Kostanecka-Endress et al., 2003).

Although tics are the central feature of TS, available research suggests that the vast majority of individuals with TS (93%) also report aversive sensory experiences (e.g., building tension, energy, pressure, itch, tingle, etc.), which typically precede tics and are partially and temporarily alleviated upon their expression (Banaschewski, Woerner, & Rothenberger, 2003; Kwak, Vuong, & Jankovic, 2003). These sensory experiences, labeled "premonitory urges," have been described by individuals with tics as more aversive than tics themselves; they can include a general sense of inner tension, or a more localized and focal sensation in the region of the tic. They can be experienced as nearly irresistible and associated with significant impairment (Swain et al., 2007). Although premonitory urges were not previously considered to be present in children below the ages of 9 or 10 (e.g., Leckman & Cohen, 1999), it is now clear that younger children do experience these phenomena, although not necessarily in as coherent a fashion as older individuals (Woods, Piacentini, Himle, & Chang, 2005). The ability of tic expression to alleviate discomfort associated with the premonitory urge suggests that the maintenance, and perhaps even progression, of the disorder may be related to a negative reinforcement cycle (Piacentini & Chang, 2006; Shapiro & Shapiro, 1992). In this regard, TS is probably similar to OCD, wherein compulsive behavior is negatively reinforced by its ability to reduce obsession-triggered distress (Piacentini & Langley, 2004).

Affective dysregulation, which can be manifested in patients with TS as recurrent episodes of anger or aggression (commonly termed "rage attacks"), can also be part of the TS profile (Budman, Bruun, Park, Lesser, & Olson, 2000; Freeman et al., 2000). Such explosive outbursts are more often present in children than adults; in one sample, 35% of children with TS were affected, versus 8% of adults (Budman et al., 2000). Clinically, explosive outbursts are recognizable by their stereotypic features, which include the abrupt onset of unpredictable and primitive displays of physical and/or verbal aggression that are grossly out of proportion to any provoking stimuli, often threatening serious self-injury or harm to others. Often the onset of explosive outbursts marks a dangerous course for children with TS, leading to deterioration in home functioning, severe demoralization, and school problems.

Studies have indicated that affective dysregulation may be particularly characteristic of a subpopulation of patients with TS and multiple comorbidities, including OCD, ADHD, mood and anxiety disorders, and oppositional defiant and conduct disorders, many of which also may be associated with aggressive behaviors (Hollander, 1999; McElroy, Hudson, Pope, Keck, & Aizley, 1992). One recent study indicated that severe forms of self-injurious behaviors were linked to the presence of episodic rages and risk-taking behaviors as well as greater tic severity, whereas mild to moderate self-injury was related more to the presence of OCD/OCD symptoms (Mathews et al., 2013). Although various studies have associated such affective dysregula-

tion with comorbid disorders (Budman, Park, Olson, & Bruun, 1998), other reports have also suggested that aggressive behavior is most closely related to tic severity (Nolan, Sverd, Gadow, Sprafkin, & Ezor, 1996). In support, a large cross-cultural sample evidenced a strong association between explosive outbursts and ADHD, greater tic severity, and lower age of tic onset (Chen et al., 2012).

Epidemiology

Prevalence/Incidence

For most of the past century, TS was deemed a rare and exotic condition—a view perpetuated by the fact that only the most severely affected patients presented for clinical or research study. In the last few decades, however, rigorous epidemiological studies have suggested otherwise. Epidemiological studies aimed at the full spectrum of tic disorders suggest that between 6 and 20% of school-age children may develop transient tics during childhood (Khalifa & von Knorring, 2003; Kurlan et al., 2001; Robertson, 2003). However, given the relatively common occurrence of transient tics, the clinical challenge resides with identifying when transient tics persist and develop into more chronic and complex tic disorders. The prevalence estimates of TS have been relatively consistent and range from 0.4 to 1% in mainstreamed school-age children between the ages of 5 and 18 (Robertson, 2008a; Scahill, Bitsko, & Blumberg, 2009). The prevalence of TS in community samples ranges from 0.1 to 1%, increasing to 1–2% when chronic motor or vocal tic disorders are included (Scahill, Sukhodolsky, Williams, & Leckman, 2005). It is worthwhile to note that most of these community cases were probably undiagnosed, mild, and without associated impairment or distress (Robertson, 2012). However, studies conducted in special education environments have found a higher prevalence of TS in populations with learning difficulties and autism spectrum disorder (Baron-Cohen, Scahill, Izaguirre, Hornsey, & Robertson, 1999; Kurlan et al., 2001). Although studies vary in sampling strategies and diagnostic procedures, the rate of 5–10/1,000, derived from population samples, is at least two orders of magnitude higher than estimated from clinical samples (Zohar et al., 1999). The magnitude of this difference underscores the unfortunate reality that a considerable number of individuals who meet criteria for TS may never present for treatment.

Sex Differences

It is likely that gender may influence the expression of TS. It is clearly more prevalent among males than females, with most epidemiological studies citing a male–female ratio of approximately 3:1 (Robertson, 2012; Zohar et al., 1999). Therefore, many studies of TS have been dominated by (if not limited to) male participants. It is unclear whether these rates are related to a higher prevalence of TS among males versus females or to greater symptom severity in males, which may in turn lead to higher clinic referral rates. The question of whether gender phenotypes involve differential clinical or neurobiological factors has been raised, but remains to be fully explored. One of the few studies to examine this issue reported that males had a more frequent history of simple tics in the absence of more complex tics than females, along with tic onset that was more often associated with rage (Santangelo et al., 1994). In contrast, tic onset in females was more closely associated with compulsive-type tics than in males. TS diagnosis was also found to occur at later ages among females than males. Although gender-related differences in the types of symptoms experienced at tic onset were found, the study concluded that the overall experience of TS appears to be similar for both groups.

Socioeconomic Status/Cultural Influences

Tic disorders do not appear to vary in clinical characteristics, course, or etiology by race, ethnicity, socioeconomic status, and culture, highlighting the biological underpinnings of the disorder (APA, 2013). The overall international prevalence of TS is approximately 1% in the majority of cultures of the world, with few exceptions (Robertson, Eapen, & Cavanna, 2009). Although TS has been extensively researched in Western populations, TS in non-Western cultures has received less attention. Based on the data available, however, it does appear that prevalence rates are much lower in African Americans in the United States, and TS seems to be extremely rare in sub-Saharan black Africans (Robertson, 2008b). Interpretations of prevalence rates across studies are complicated by the multidimensional nature of tics, their waxing and waning course, and the suppressibility of symptoms, all of which may provide challenges to accurate diagnosis. Possible explanations of the rarity of TS in the African American and sub-Saharan black African groups have included other medical priorities and less propensity to seek health

care; lack of awareness of TS; chance; ethnic and epigenetic differences; genetic/allelic differences between races; and an admixture of races (Robertson, 2008b). Research on clinical phenotypes and their genetic bases should contribute to clarifying the underlying reasons for such cultural differences.

Developmental Course and Prognosis

The onset of TS typically occurs between the ages of 6 and 7 and is marked by the emergence of simple tics, such as eye blinking, facial, or head/neck tics. Freeman and colleagues (2000) found that 41% of youth in an international study of TS reported that tics had emerged prior to age 6, and a full 93% reported tic onset prior to age 10. Following initial onset, studies of the clinical course of TS suggest a rostral–caudal progression of increasingly complex motor tics over the span of several years (Leckman et al., 1998). Typically, vocal tics appear at age 8 or 9, and complex tics and obsessive–compulsive symptoms (when present) at age 11 or 12. Although vocal tics generally emerge years after the initial motor tics, exceptions do exist in which a full complement of multiple motor and vocal tics will rapidly emerge over a brief period of a few weeks (McCracken, 2000). Complex vocal and motor tics such as coprolalia and copropraxia are relatively unusual and are only present in 10–15% of youth with TS (Robertson, 2012).

Children may present in early childhood with disruptive behavioral symptoms (such as motoric hyperactivity and inattention) prior to the onset of tics in as many as 50% of cases (Bruun & Budman, 1997). Although tics typically follow a fluctuating course, increasing age is associated with a greater degree of stabilization. It is not unusual for adolescent and young adult patients to report extended periods during which symptoms diminish or remit altogether. Indeed, longitudinal naturalistic studies of tic disorders suggest that tics may demonstrate persistence over time, but that impairment and tic-related dysfunction attenuate as youth age into adults (Coffey et al., 2004). Studies following youngsters with chronic tic disorder longitudinally have found that for most individuals, peak tic severity is reached in early adolescence, followed by a consistent decrease in symptoms across adolescence. By late adolescence or young adulthood, over one-third of patients with TS are virtually tic-free; fewer than half have minimal to mild tics; and fewer than a quarter have persistently moderate to severe tics (Bloch, Peterson, et al., 2006; Leckman et al., 1998).

Within an affected individual, tic frequency and severity are also likely to wax and wane over time. Symptom exacerbations are linked with common psychosocial stressors (e.g., peer and family conflicts, school difficulties, significant change in normal routines), as well as with such factors as illnesses, fatigue, and excitement. However, a degree of random symptom fluctuation is also typical of the condition (Coffey et al., 2000).

Although TS is usually considered a developmental disorder with childhood onset, it is apparent that tics can persist into adulthood. One study investigating the phenomenology of adult TS indicated that tics in adulthood were more likely to be characterized by facial and truncal tics, as well as a greater prevalence of substance abuse and mood disorders (Jankovic, Gelineau-Kattner, & Davidson, 2010). It appears that during the developmental course of TS, vocal and complex motor tics, self-injurious behaviors, and ADHD tend to improve, along with a decrease in overall tic severity. However, many adults with childhood tic onset still evidence mild tics, albeit with minimal impairment. In addition, they may experience an increase in related psychopathology such as OCD or mood disorders (Pappert, Goetz, Louis, Blasucci, & Leurgans, 2003).

Although TS is rarely associated with significant disability, in a minority of cases it can lead to significant functional impairment and even serious physical injury. Such cases of "malignant TS" have been linked to a history of OCD, complex vocal tics, coprolalia, copropraxia, self-injurious behaviors, mood disorder, suicidal ideation, and poor response to medication (Cheung, Shahed, & Jankovic, 2007).

Comorbidity

Tics rarely exist in isolation in individuals with tic disorders, and comorbidity is typically the rule rather than the exception. Approximately 90% of individuals affected by TS experience comorbidity and other psychiatric difficulties, as evidenced by studies in both epidemiological and clinic settings (Freeman et al., 2000; Khalifa & von Knorring, 2005). Youth with TS are likely to meet criteria for two additional psychiatric diagnoses (Freeman et al., 2000). The most predominant comorbidities in TS include OCD or OCD symptoms and ADHD. However, learning difficulties, mood disorders, and anxiety disorders are not uncommon.

The comorbidity of TS and OCD is bidirectional, such that approximately 23% of patients with TS meet criteria for OCD and up to 46% demonstrate OCD symptoms in the subclinical range (Piacentini & Graae, 1997; Robertson, 2000). By contrast, between 7 and 37% of individuals with OCD also meet criteria for TS (Miguel, de Rosario Campos, Shavitt, Hounie, & Mercadante, 2001). Family genetic as well as epidemiological studies have demonstrated a significant association between forms of TS and OCD, suggesting that they may share a common underlying etiology (Peterson, Pine, Cohen, & Brook, 2001). Indeed, it has been posited that OCD/OCD symptoms comorbid with tics can be distinguished from OCD or TS alone and may be an alternative phenotypic expression of TS (Miguel et al., 2001; Pauls, Leckman, Towbin, Zahner, & Cohen, 1986). Evidence from the OCD treatment literature supports this distinction. The presence of tics reduces the beneficial effects of SSRI treatment for OCD, but not those of CBT (March et al., 2007). Furthermore, Coffey, Miguel, Savage, and Rauch (1994) reported that individuals with both TS and OCD may have higher rates of affective, anxiety, and substance use disorders relative to those with either diagnosis in isolation. Individuals with comorbid TS and OCD typically endorse more aggressive and symmetry-oriented obsessions and touching, blinking, and counting compulsions, whereas OCD alone is typified by contamination fears and cleaning compulsions (Leckman et al., 1997; Sheppard, Bradshaw, Purcell, & Pantelis, 1999). In keeping with the findings from the OCD literature, patients with TS often indicate that a sensory-perceptual awareness that something is not "just right" precedes their repetitive behavior (Miguel et al., 1995, 2001). Indeed, when both disorders are present simultaneously, it can be challenging to differentiate the extent to which a symptom such as repetitive touching or tapping reflects a complex tic or a simple compulsion.

Comorbidity between TS and ADHD is also common (Termine et al., 2005). In clinical samples, 40–60% of children with TS meet criteria for ADHD, indicating possible shared neural circuitry deficits in response inhibition and impulse control (Sheppard et al., 1999). Even in mild cases of TS, the incidence of ADHD is seven to eight times that of the general population (Walkup et al., 1999). Similar to comorbid OCD and TD, clinical distinctions have been drawn between TS that co-occurs with ADHD and TS that presents in isolation. Compared to children with TS only, children with TS plus ADHD and those with ADHD alone share a similar profile of comorbid conditions including depression, anxiety, and disruptive behavior, along with deficits in executive functions (Kraft et al., 2012; Sukhodolsky et al., 2003). In contrast, youth with TS alone are often similar to their healthy control peers in their cognitive functioning, disruptive behaviors, and social functioning, although some studies indicate that they may have higher rates of internalizing symptoms (Robertson, 2011; Roessner et al., 2007). Such findings suggest that the presence of multiple comorbidities in TS is perhaps a function of the comorbid ADHD and not specific to TS itself (Spencer et al., 1998). Family genetic studies (Pauls, Leckman, & Cohen, 1993) have also distinguished between ADHD symptoms that appear before tic emergence and those that follow such onset, suggesting that TS and ADHD symptoms are genetically related when ADHD symptoms follow tic emergence but not when they precede tic onset.

Other common comorbidities include depression, non-OCD anxiety disorders (in earlier versions of DSM), and learning difficulties (Dykens et al., 1990; Freeman et al., 2000; King, Scahill, Findley, & Cohen, 1999). Despite challenges to the accurate ascertainment of comorbid learning difficulties, related to the presence of other comorbid psychopathology and the distracting effects of the tics themselves on attention, prevalence has been estimated to be approximately 22% (Burd, Freeman, Klug, & Kerbeshian, 2005). With regard to internalizing disorders, approximately 40% of youth with TS will experience depression or a non-OCD anxiety disorder—a rate significantly higher than that of healthy controls (Gorman, Plessem, Robertson, Leckman, & Peterson, 2010; Pitman, Green, Jenike, & Mesulam, 1987). Research has suggested that correlates of depression include tic severity, age, OCD, ADHD, and childhood conduct disorder (Robertson, 2006). One common explanation for the increased rates of comorbid affective disturbance and anxiety is the chronic debilitating burden of a disruptive and potentially socially stigmatizing tic disorder. In interpreting the high rates of overlap among affective disturbance, anxiety, and TS, many have noted that the chronic, impairing, and potentially stigmatizing nature of tic disorders may account for increased rates of anxiety and depression. Others have posited a biological explanation for this phenomenon, indicating that TD may be associated with increased stress-induced reactivity of the hypothalamic–pituitary–adrenal (HPA) axis and

increased central and peripheral noradrenergic sympathetic activity (Leckman, Walker, Goodman, Pauls, & Cohen, 1994; Lombroso et al., 1995).

Differential Diagnosis

Tics must be differentiated from abnormal repetitive movements including myoclonus, tremor, chorea, athetosis, dystonia, and akathisic movements, which may be related to other serious neurological conditions associated with a more insidious course such as Huntington's disease or Sydenham's chorea (Krauss & Jankovic, 2002; McCracken, 2000). Patients with TS appear normal on neurological examination, with the exception of tics, increased blinking rate, subtle ocular–motor disturbances, and mild graphomotor difficulties (Jankovic, 2001). Tic disorders are generally characterized by a combination of simple and complex tics, and vocal tics are uncommon in non-tic-related movement disorders. In addition, premonitory sensations described by patients with TS are rarely reported in other movement disorders such as Huntington's chorea; nor is the experience of tension relief after movement performance common in other conditions. The temporary suppressibility of most tics is also a unique aspect of tic disorders and is helpful in differentiating tics from other hyperkinetic movements (Towbin, Peterson, Cohen, & Leckman, 1999). Tic expression is also characteristically prone to suggestibility and has been related to a variety of triggers. Patients often report exacerbation during periods of stress, anxiety, or fatigue. Some individuals experience a decrease in tic symptoms during periods of intense focus.

Differentiating complex repetitive tics from OCD-related compulsions may prove challenging. However, OCD compulsions are probably characterized to a greater degree by a cognitive-based drive and may need to be performed in a particular fashion a certain number of times or until a "just right" feeling is achieved (APA, 2013; Miguel et al., 1995). Complex tics may also be difficult to distinguish from the repetitive stereotypical movements associated with some forms of intellectual disability, autism spectrum disorder, psychosis, and akathisia. The descriptor of "stereotyped" has been removed from the tic definition in DSM-5 to clarify the distinction between tics and stereotypies, as noted earlier. Motor stereotypies may be distinguished from tics on the basis of younger age of onset, prolonged duration, repetitive fixed form and location, absence of premonitory urge, and lack of associated neurological or developmental impairment (APA, 2013; Barry, Baird, Lascelles, Bunton, & Hedderly, 2011).

Situational and Contextual Factors

Despite the clear biological underpinnings of TS, mounting research has made clear the influential role of environmental and contextual factors in tic expression. Studies focusing on the impact of broad events and situations have demonstrated that tic severity tends to worsen during stress, anxiety, social activity, excitement, and fatigue (Conelea & Woods, 2008; Eapen, Fox-Hiley, Banerjee, & Robertson, 2004). In contrast, tic attenuation was associated with states of relaxation and calm, focused activities (Eapen et al., 2004; O'Connor, Brisebois, Brault, Robillard, & Loiselle, 2003). More rigorously designed experimental studies have also shown that specific antecedent factors can have an impact on tics. Exacerbating factors include the presence of others (Piacentini et al., 2006), academic tasks (Watson, Dufrene, Weaver, Butler, & Meeks, 2005), tic-related conversation (Woods, Watson, Wolfe, Twohig, & Friman, 2001), and overt observations (Piacentini et al., 2006). Events related to tic reductions include social interactions with familiar people (Silva, Munoz, Barickman, & Friedhoff, 1995), situations in which the individual is a passive participant (O'Connor et al., 2003), and leisure activities (Silva et al., 1995).

It is clear that emotional factors in particular can have a powerful influence on tic exacerbation. Findley and colleagues (2003) showed that youth with TS and OCD experienced a greater number of stressful events than healthy controls, with a significant relationship between tic severity and daily life stressors. Similarly, current psychosocial stress levels predicted short-term future tic severity in a group of youth with TS, independent of age (Lin et al., 2007). However, limitations of this research, including inconsistent definitions of emotional states, make it difficult to conclude what aspects of affective experiences are most closely linked to tic expression (Conelea & Woods, 2008). Involvement of the HPA axis has been posited as one potential mediating mechanism between stress and clinical symptoms of TS: A higher vulnerability to stress, secondary to genetic predisposition or early environmental exposure, may potentiate the effect of stressors on symptom severity through the HPA system to create a vicious

cycle (Hoekstra, Dietrich, Edwards, Elamin, & Martino, 2013).

Research has also explored the effect of contextual consequences on tic expression. Findings indicate that tics can increase when they are positively reinforced, as in the case of attention following a tic (Carr, Taylor, Wallander, & Reiss, 1996; Watson & Sterling, 1998), or negatively reinforced, as in the case of escape from demand situations (Carr et al., 1996; Scotti, Schulman, & Hojnacki, 1994). Moreover, reinforcement for tic-free periods has reliably been associated with tic reduction (Conelea & Woods, 2008; Himle & Woods, 2005; Himle, Woods, Conelea, Bauer, & Rice, 2007; Woods et al., 2008). Identification of contingencies influencing "voluntary" tic suppression would advance understanding of how suppression occurs and how it may be enhanced in the service of effective treatment.

Risk and Protective Factors

Many epigenetic factors have been implicated in the development of TS, including gender, prenatal and perinatal insults, exposure to androgens, and psychological stress (discussed previously), as well as postinfectious autoimmune mechanisms (discussed under etiology). A history of prenatal and perinatal difficulties (e.g, hypoxic–ischemic events) was significantly higher in children with TS and other chronic tic disorders (50%) than among controls (6%) (Saccomani, Fabiana, Manuela, & Giambattista, 2005). Additional factors related to higher incidence of TS in youth have included heavy maternal smoking, high prenatal levels of maternal stress, low birth weight, severe nausea/vomiting during the first trimester, and prenatal maternal smoking (Hoekstra et al., 2013; Mathews et al., 2006; Motlagh et al., 2010). Perinatal adversities are not only more prevalent in youth with TS, but are also associated with increased tic severity in affected individuals (Hyde, Aaronson, Randolph, Rickler, & Weinberger, 1992; Mathews et al., 2006).

Research has also examined the relationship between pre- and perinatal risk factors and the occurrence of common comorbidities such as OCD and ADHD in TS. Findings in this area indicate that pregnancy-related factors such as low birth weight and maternal smoking are linked to higher risk of ADHD and OCD comorbidity, whereas delivery complications such as the use of forceps are more associated with the emergence of comorbid OCD (Mathews et al., 2006; Santangelo et al., 1994).

Male gender is an established risk factor for TS, based on clinical observations of male dominance in the prevalence of TS (3:1 ratio). Given that an X-linked inheritance pattern is unlikely, due to evidence of common male-to-male transmission within families, it has been hypothesized that androgen exposure during critical periods in fetal brain development is a potential risk factor for the development of TS (Peterson, Zhang, Anderson, & Leckman, 1998).

Protective factors for TS have not been as well researched in the literature. However, one likely conclusion that can be drawn from the existing research on tic-related impairment is that tic severity and comorbidity profile exert a significant influence on overall functioning in affected individuals. A recent study indicated that young patients with severe tics associated with premonitory urges and a family history of tic disorders appear to be at a higher risk for poor health-related quality of life as adults (Cavanna, David, Orth, & Robertson, 2012). Another study examined the functional impact of tics among youth in a large Internet sample and found that greater functional impairment in children with chronic tic disorders was associated with one or more co-occurring psychiatric conditions and higher levels of tic severity (Conelea et al., 2011).

Temperature dysregulation involving some change in hypothalamic function has also been proposed as a potential risk factor in the pathobiology of some patients with TS (Kessler, 2001, 2004). In a case series, an increase in ambient temperature as well as core body temperature was associated with a transient increase in tics in some patients (Scahill et al., 2001). The increase in tics was correlated with their local sweat rate via a dopamine-mediated pathway in the hypothalamus.

Etiological Factors

Genetic/Familial Factors

The hereditary nature of TS is well documented in both family pedigree and twin studies of the condition. Family studies of TS indicate that tics occur in both parents and children in 25–41% of families with TS (Lichter, Dmochowski, Jackson, & Trinidad, 1999; Pauls, Raymond, Leckman, & Stevenson, 1991). Moreover, twin studies demonstrate that monozygotic twin pairs show much higher concordance rates for TS (53%) than do dizygotic twins (8%). When the entire spectrum of tic disorders is considered, concordance rates for monozygotic twins reach 77%, compared to

23% for dizygotic twins (Price, Kidd, Cohen, Pauls, & Leckman, 1985).

A growing body of research has pointed away from TS being a single-gene, autosomal dominant disorder, and toward a complex polygenic inheritance pattern where multiple genes interact with a variety of epigenetic factors to influence phenotypic expression. Linkage, association, and cytogenetic investigations have suggested the importance of several chromosomal regions in TS etiology, including 11q23, 4q34-35, 5q35, and 17q25 (Merette et al., 2000; TSA Consortium for Genetics, 1999). Several candidate genes have been assessed, including those for various dopamine receptor (DRD1, DRD2, DRD4, DRD5), dopamine transporter, noradrenergic (MAO-A, ADRA2a), and serotonergic (5-HTT) genes (Cheon et al., 2004; Comings, 2001; Du et al., 2010). More recently, rare sequence variants of gene—including SLITRK1 on chromosome 13q31.1 (which codes for a neuronal transmembrane molecule) and L-histidine decarboxylase (HDC, which codes for the rate-limiting enzyme in histamine biosynthesis)—have been associated with TS in some samples. However, these findings have yet to be consistently replicated (Abelson et al., 2005; Ercan-Sencicek et al., 2010). Although these genes appear to account for only a small number of TS cases, such rare variant findings have emphasized the relevance of investigating rare variations in common disease. Current genetic research in TS and other psychiatric disorders is moving toward the identification of shared genetic risk across diagnoses that have previously been conceived as entirely distinct entities (Bloch, State, & Pittenger, 2011). A growing number of studies highlight the possibility that specific genetic variations that disrupt critical molecular pathways underlying key neurodevelopmental processes may be manifested in a wide range of behavioral and cognitive phenotypes (Bloch et al., 2011; Stillman et al., 2009).

Neurobiological Factors

Tics have been conceptualized as pathological repetitive behaviors related to dysregulation of cortical–subcortical circuits (Graybiel & Canales, 2001; Mink, 2001). More specifically, tics are hypothesized to be the result of failed inhibition of CSTC associative and motor pathways. A growing number of neuroimaging studies show subtle but important differences in the structure and function of cortical and related subcortical regions in patients with TS compared to normal controls, including reduced volumes and abnormal asymmetries of the caudate, putamen, lenticular, and globus pallidus nuclei (Bloch, Lechman, Zhu, & Peterson, 2005; Lee et al., 2005; Peterson et al., 2003). A large structural imaging study of both children and adults demonstrated decreased caudate volume in patients with TS versus controls, whereas differences in the putamen and globus pallidus were limited to adults (Peterson et al., 2003). Smaller caudate volume in childhood has also been inversely correlated with greater persistence of tics and the presence of OCD symptoms in late adolescence and adulthood (Bloch et al., 2005). Children with TS have exhibited greater volume in the dorsolateral prefrontal cortex versus controls, though this effect was primarily present in children and was actually reversed in adults (Peterson, 2001). In contrast to adult TS, larger dorsolateral prefrontal cortical volumes in child TS was related to less severe tics, possibly indicating the influence of a compensatory neural process whereby synaptic plasticity develops over time from frequent efforts to suppress tics in various social contexts (Plessen, Bansal, & Peterson, 2009; Stern, Blair, & Peterson, 2008).

Although smaller in number, functional imaging studies of TS have shown abnormal activity (primarily decreased, some increased) in primary and associated sensory–motor cortex, as well as the lenticulate and paralimbic regions. The conscious suppression of tics in patients with TS has been shown to be related to decreased neural activity in subcortical regions including the ventral globus pallidus, putamen, and thalamus, along with increased activity in the prefrontal, parietal, temporal, and cingulate cortical areas normally involved in the inhibition of unwanted impulses (Gerard & Peterson, 2003; Peterson, 2001). Bohlhalter and colleagues (2006) found that the premonitory phase of tic generation was associated with increased activation in paralimbic, sensory association, and premotor cortical areas, with this activation pattern being similar to that seen in disorders involving the urge to itch or scratch. Based on their results, authors suggest that the involved neural regions might constitute a circuit linking unpleasant somatic sensations to an urge to move. Such studies suggest that the sensory–motor and limbic basal ganglia–thalamocortical circuits have the greatest relevance for TS pathophysiology.

A dopaminergic theory of TS is supported by multiple lines of research, including the apparent efficacy of dopaminergic antagonists such as haloperidol in the treatment of tics, as well as the exacerbating effects of

functional dopamine agonists such as amphetamines. Graybiel and Canales (2001) found that microinjection of amphetamine, a dopamine agonist, into animal striatum reliably induced stereotypies. Furthermore, severity (number and frequency) of stereotypies was highly correlated with the extent of gene expression in a specific compartment of the striatum, the striosomes, again implicating dopamine pathways in stereotypic behavior. Postmortem brain analyses of patients with TS have also demonstrated increased dopamine presynaptic carrier sites in the striatum (Minzer, Lee, Honig, & Singer, 2004; Yoon, Gause, Leckman, & Singer, 2007). Such findings provide evidence for the proposal that increased dopamine innervations in the brain play a key role in the pathophysiology of TS.

The cortical–striatal pathways implicated in TS appear to play some role in learning new motor sequences and a central role in retrieving these sequences in response to the appropriate stimuli. For the sake of efficiency, learned motor sequences are stored in the brain as "chunks" of behavior rather than bits. Graybiel (1998) argues that this capacity to compress bits of behavior into chunks may extend beyond simple motor tasks to more complex repertoires of action. Thus tics can be viewed as abnormal, repetitive action repertoires driven by premonitory sensations or urges.

A biological model for tic disorders has been proposed, based on past models of basal ganglia circuit function and dysfunction (Mink, 2001, 2006). According to the model, the normal, tonically active inhibitory output of the basal ganglia acts as a "brake" on motor pattern generators (MPGs) in the cerebral cortex and brainstem (Mink, 1996). For a desired movement controlled by a particular MPG, a specific set of striatal neurons is activated. The removal of tonic inhibition from the regions such as the globus pallidus and substantia nigra pars reticulata enables the desired motor pattern to proceed. In conjunction, the surrounding neurons project via the thalamus to competing MPGs, increasing their inhibitory output and applying the "brake" to competing MPGs. The net result is facilitation of intended movement with inhibition of competing movements. In tic generation, it is hypothesized that an aberrant focus of striatal neurons becomes inappropriately active, causing unwanted inhibition of a group of basal ganglia output neurons; these neurons in turn disinhibit a MPG, leading to an involuntary movement. Repetitive overactivity of a specific set of striatal neurons would result in recurrent unwanted movements (i.e., tics; Mink, 2006).

Possible Developmental Pathways

A growing number of imaging studies have begun to suggest that disrupted or immature brain maturational processes play a key role in the development of TS (Baym, Corbett, Wright, & Bunge, 2008; Jung, Jackson, Parkinson, & Jackson, 2012). Marsh, Zhu, and Wang (2007) studied cognitive inhibition differences in youth and adults with TS relative to controls, using a functional imaging paradigm. Findings indicated that although behavioral task performance was similar across groups, the participants with TS deactivated ventral prefrontal and posterior cingulate regions less with advancing age than healthy controls did. Greater activation of bilateral frontostriatal regions accompanied poorer performance in the group with TS. It was suggested that greater activation of the frontostriatal systems helps to maintain task performance in individuals with TS. The authors concluded that normative developmental correlates of frontostriatal activity that subserve self-regulatory control are disturbed in TS. However, patients with TS appear to co-opt normal developmental processes in circuits that subserve age-related improvement in self-regulatory control, while presumably struggling to maintain adequate task performance. Other studies have indicated an immature pattern of functional connectivity in patients with TS, characterized by stronger functional integration (more interaction among anatomical regions) and global functional disorganization of frontostriatal networks relative to controls; this pattern is consistent with a developmental hypothesis of TS (Church et al., 2009; Worbe et al., 2012). These functional abnormalities were correlated to tic severity in all frontostriatal networks.

A developmental model of TS based on current neurobiological research proposes that cortical reorganization of behavioral control neural circuits may operate to compensate for aspects of the disorder. Specifically, youth with TS may gain increasing control over their tics with age through the development of compensatory self-regulation mechanisms likely involving networks linking the prefrontal cortex with primary and secondary motor regions (Jackson et al., 2011; Serrien, Orth, Evans, Lees, & Brown, 2005). Paradoxically, children with simple TS (i.e., without comorbid conditions such as ADHD) have been shown to demonstrate enhanced inhibitory control over ocular–motor responses as well as motor output (Jackson et al., 2011; Mueller, Jackson, & Dhalia, 2006). Enhanced motor control in one study was predicted by white matter microstructure alterations in the prefrontal cortex; these neural changes

were related to neuroplastic functional adaptation, rather than a core component of the tic disorder (Jackson et al., 2011). The natural developmental course of tics, which is characterized by increasing remittance with age, appears to lend support for the neurodevelopmental immaturity model and the accompanying compensatory reorganization that is often observed in child TS.

The broad clinical phenotype and tic severity observed in TS are likely to be influenced by the extent and nature of genetically mediated neurodevelopmental disruptions in these brain regions. Epigenetic as well as genetic factors, along with stages of brain development, all play critical roles in the molecular pathways that become activated in TS. Increasingly, research suggests the presence of broad neurodevelopmental genes that increase susceptibility to a range of neuropsychiatric disorders, including TS, OCD, ADHD, autism spectrum disorder, and schizophrenia (Eapen, 2011; Robertson, 2012; State, 2010).

Immunological Factors

A postinfectious etiology for TS has long standing, with group A beta-hemolytic streptococcal (GABHS) infections posited to be the most likely candidates related to TS onset (Mell, Davis, & Owens, 2005). GABHS infections are known to trigger several immune-mediated diseases such as Sydenham's chorea and PANDAS, both of which involve symptoms similar to those seen in TS and OCD. In one study, youth affected with TS and OCD were significantly more likely than healthy controls to have had a streptococcal infection in the 3 months prior to symptom onset. Having multiple GABHS infections within a 12-month period was associated with a 13-fold increased risk for developing TS (Mell et al., 2005). Tic severity has also been associated with a variety of increased proinflammatory cytokines, decreased number of regulatory T-cells, and increased synthesis of antineuronal antibodies (Martino, Dale, Gilbert, Giovannoni, & Leckman, 2009). Of note, children with TS have also evidenced a higher risk of allergic diseases than controls (Ho, Shen, Shyur, & Chiu, 1999). Although such studies are intriguing, more studies are needed to resolve the relation among GABHS infections, antineuronal antibodies, and TS.

Psychosocial/Behavioral Factors

Although ample empirical literature documents that TS is a neurodevelopmental disorder with salient biological underpinnings, there is also mounting evidence that tics may be influenced by environmental variables (Himle et al., 2006; Woods & Himle, 2004). Indeed, Woods and Himle (2004) have found compelling evidence that tics may be responsive to reinforcement schedules. In their study, children with TS were assigned either to a condition in which they received a verbal instruction to "do whatever you need to do to keep your tics from happening," or to a condition in which they received both verbal instruction and differential reinforcement of their efforts. They found that differential reinforcement, via a token dispenser, produced significant decreases in tic expression: A 76% reduction in tics was observed in the reinforcement condition, versus only 10% in the instruction-only condition. These findings suggest that tics may be responsive to operant schedules. Although work to date has relied on small sample sizes and no doubt needs further replication, such work has provided a basis for further examination of environmental variables that may influence tic expression.

As noted previously, tic severity can be worsened or improved by antecedent variables (e.g., setting, emotions such as anxiety, and presence of others) and consequences (e.g., social reactions, tangible reinforcers). In an effort to optimize effective tic management, psychosocial and behavioral approaches attempt to identify and modify events or experiences associated with tic exacerbation and maintenance. Behavioral treatments have been shown to be effective in the treatment of various psychiatric conditions with underlying neurobiological abnormalities, such as OCD and anxiety disorders. Most behavioral treatments for tics have a limited evidence base, with the exception of habit reversal training (HRT). The effective core components of HRT have been identified as awareness training, competing response training, and social support. HRT has gradually accumulated a significant body of empirical support. The most rigorous and recent study, a randomized controlled trial of 126 youth with TS, found that HRT was associated with significant improvements in tic severity and impairment relative to a control condition consisting of psychoeducation and social support (Piacentini et al., 2010).

As behavioral approaches have gained more attention, concerns have been raised regarding their efficacy. One issue has concerned whether behavioral treatment aimed at reducing one tic might result in the emergence or exacerbation of another tic. Research has suggested that this form of symptom substitution does not occur during HRT (Numberger & Hingtgen, 1973;

Piacentini et al., 2010). Another question is whether tic suppression or behavioral treatments like HRT that use suppression-related techniques may lead to postsuppression exacerbation of tics. Findings have indicated that such a "rebound effect" does not occur after brief periods of suppression in children with tics (Himle & Woods, 2005). A third issue concerns whether increasing awareness of tics and associated urges may worsen their severity. Several studies have found, to the contrary, that awareness training alone may be helpful in reducing tics for some individuals. Self-monitoring of tics has not been associated with an increase in tic severity in several studies, and HRT has demonstrated itself to be generally acceptable to and well tolerated by families who receive the treatment (Billings, 1978; Sharenow, Fuqua, & Miltenberger, 1989; Woods, Miltenberger, & Lumley, 1996).

Theoretical Framework

TS can be considered a genetically complex neurodevelopmental disorder with clear biological and environmental influences. Although the exact pathophysiology of TS still remains to be elucidated, abnormalities in the CSTC pathways are undisputed. In general, tics have been proposed to represent a failure of cortical inhibition of unwanted MPGs in the subcortical regions of the basal ganglia (Mink, 2001). These circuits appear critical for the development of habits, as well as tics and other repetitive movements. Habits may be thought of as assembled routines that link sensory cues with motor action through a form of procedural learning (Swain, Scahill, Lombroso, King, & Leckman, 2007). Understanding the neural substrates of habit formation may clarify our understanding of TS. Indeed, research has already indicated that TS youth and adults both show impairment in habit or procedural learning relative to normal controls (Marsh et al., 2004; Marsh, Alexander, Packard, Zhu, & Peterson, 2005).

While fully acknowledging the neurobiological abnormalities implicated in tic etiology, the emerging neurobehavioral model of tic disorders suggests that tic expression is influenced by environmental events, which can worsen, improve, or maintain tics via a negative reinforcement cycle (Himle et al., 2006; Woods et al., 2005). From a functional/behavioral perspective, tic completion results in a temporary but often immediate and dramatic reduction in the intensity of an aversive sensation (Leckman, 2003). Operant conditioning principles suggest that any behavior that produces a subsequent reduction in an unpleasant state or condition will result in an increased probability of that behavior occurring when the unpleasant state recurs. This cyclic pattern has been described as a "negative reinforcement cycle." Evidence-based behavioral treatments for tic disorders, such as HRT, are theoretically governed by such operant conditioning principles. Based on behavioral theory, HRT teaches patients behavioral skills that enable them to resist and eventually habituate to the premonitory urge, thereby disrupting the negative reinforcement cycle. In this regard, HRT may work through a similar mechanism as exposure-based treatments for anxiety disorders and OCD (e.g., deconditioning). Although this proposed mechanism has not been directly tested, preliminary studies show that ERP treatment is effective for TS (Hoogduin, Verdellen, & Cath, 1997; Verdellen, Keijsers, Cath, & Hoogduin, 2004). Furthermore, studies have suggested that habituation to the premonitory urge does take place when suppression is in effect (Wetterneck & Woods, 2006; Woods, Hook, Spellman, & Friman, 2000).

Research suggests that the concept of "disinhibition" is a potentially important mechanism for tic expression—cognitively and clinically, as well as biologically—and may also partially account for poor impulse control and other behavioral problems associated with TS and related disorders such as ADHD. Increasingly, clinical translational research is exploring the potential mechanisms and predictors of evidence-based interventions such as HRT. Although few in number, studies examining neurocognitive predictors of behavioral treatment response indicate that adults with TS who evidenced better response inhibition on a visual–spatial priming task at baseline demonstrated greater response to HRT (Deckersbach, Rauch, Buhlmann, & Wilhelm, 2006). Largely consistent with these findings are pediatric studies indicating that problems in sustained attention are associated with greater difficulties in tic suppression (Himle & Woods, 2005; Peterson et al., 1998). Research aimed at exploring whether neurocognitive indices may function as stable trait-like phenotypic markers of TS or as malleable state variables, which may change with treatment, would be important in advancing etiological understanding. In addition, examination of potential baseline neurobiological predictors of treatment response would inform future efforts to optimize treatments for individual patients (Chang, 2007).

Current Issues and Future Directions

The clinical heterogeneity of TS speaks against the idea of its being a unitary disorder. Its phenotypic expression is varied, ranging from simple tics to a more complex profile of tics associated with a variety of psychiatric comorbidities. The underlying neurobiological basis of this heterogeneity has yet to be fully understood. Genetic research has highlighted a complex polygenic inheritance, and recent studies of rare copy number variations have emphasized the possibility of shared risks among TS and distinct diagnostic entities, including autism spectrum disorder and schizophrenia (Bloch et al., 2011). Another line of research has attempted to investigate the relationship between structural differences in distinct regions of the CSTC circuits and the clinical phenotype of TS. According to one model of basal ganglia organization, motor tics may result from dysfunction of the premotor and motor circuits, while behavioral disorders such as ADHD and OCD may be related to abnormalities in the associative and limbic circuits (Singer, 2005). Indeed, one study has demonstrated that comorbid TS and OCD were associated with reduced cortical thickness in the anterior cingulate cortex, whereas patients with only simple-tic TS evidenced cortical thinning mostly in the primary motor regions (Worbe et al., 2010).

Studies using data reduction methods to dissect the clinical phenomenology of tic disorders have generally suggested a two-factor model with "simple" and "complex" tic symptom factors/clusters when only tic symptoms are examined. However, when broader tic-related symptoms are included, a three- or four-factor solution appears; this includes factors such as inattention/aggression, compulsions, and perhaps self-injurious behaviors overlapping with the complex tic cluster (Grados & Mathews, 2009). Some comorbid conditions such as OCD and ADHD appear more integral to the TS phenotype, whereas others such as depression, anxiety, and conduct problems may be secondary to other psychopathology. Such attempts to identify more homogenous and etiologically meaningful subgroups within tic disorders are important and have potential relevance not only for etiology, but for our understanding of nosology, phenomenology, and treatment development.

Despite the clear advances in treatment made in both the pharmacological and behavioral realms in the past half century, many patients with TS only derive partial benefit from our best evidence-based treatments for TS (Cavanna & Termine, 2012; Robertson, 2012; Swain et al., 2007). Medication such as alpha-agonists (e.g., clonidine and guanfacine) along with neuroleptics have shown tic-suppressing efficacy. However, medications, particularly neuroleptics, are accompanied by significant side effects and are often not well tolerated by children (Jankovic & Kurlan, 2011; Pena, Yaltho, & Jankovic, 2010). Whereas many youth experience only mild tics with minimal functional impairment, which do not require treatment, other children experience a variety of negative consequences as a result of their tic disorder, including physical pain, social stigma, academic difficulties, and family conflict (Storch, Lack, et al., 2007). As such, further research into treatment development is needed to optimize intervention approaches available to affected youth. For severe cases of TS, a combination of medication with behavior therapy based on HRT principles may be the most useful. Despite the efficacy of medication and behavioral treatments, we have a relatively limited understanding of the underlying mechanisms of treatment response. Translational research aimed at elucidating the potential predictors and moderators of treatment response would help to advance TS intervention into an era of more personalized medicine. For example, it has been already shown in the OCD literature that OCD comorbid with tics responds worse to SSRI medication treatment, although the same does not hold for CBT (March et al., 2007). This line of research will aid us in better tailoring available treatments for those affected with TS and its related conditions. Information on the underlying biological mechanisms involved in treatment response would also aid us in further refining our interventions.

A greater understanding of normal brain development and the ways in which tic disorders may potentially derail this process is important to clarifying the complex pathophysiology of TS. The natural history of tics suggests that most youth experience significant improvement or resolution of their tic symptoms by early adulthood. The reasons underlying this developmental progression are still poorly understood, and answering this intriguing question may serve to explain why some adults continue to experience tics or have a recurrence of symptoms much later in life. TS is clearly a disorder of neurodevelopment, and better elucidating the structural and functional changes as well as neuroplasticity associated with TS at each stage of brain development may provide us with valuable clues into the underlying

mechanisms of the disorder and advance novel therapeutics for the condition.

TS in many ways can be considered a model neuropsychiatric disorder, which lends itself to the examination of the various interactions among genes, environmental factors, and neurobiological systems at play during the course of pediatric brain development. The future of TS research is promising, given the multidisciplinary collaborations that are possible among neurobiological, genetic, and behavioral domains of study. Most importantly, careful consideration of both biology and environment will best serve efforts aimed at effective prevention and treatment of the disorder.

HAIR-PULLING DISORDER (TRICHOTILLOMANIA)

Historical Context

Aberrant or emotionally triggered hair pulling has been mentioned in the Bible, early Greek literature, Shakespeare, and of course the medical literature (Christenson & Mansueto, 1999). In the 5th century B.C., the ancient Greek physician Hippocrates recommended routinely assessing excessive hair plucking when evaluating patients. At the end of the 19th century, Hallopeau (1889), a French dermatologist, coined the term "trichotillomania" and provided what is considered the first detailed description of excessive hair pulling in the medical literature. In the first half of the 20th century, dermatologists and psychodynamic therapists published a few case reports on trichotillomania, but little systematic research was conducted. By the early 1970s, behaviorists had developed treatment interventions for hair pulling and other habits (Azrin & Nunn, 1973). Despite a long history in the medical literature, hair-pulling disorder (HPD) was not included in official diagnostic systems until the publication of DSM-III-R (APA, 1987). In the past 20 years, research interest in trichotillomania (or HPD, the term used hereafter) has grown substantially, although this condition has received less attention than other OCD spectrum disorders (e.g., OCD and tic disorders).

Description of the Disorder

Core Symptoms

The core symptom of HPD is recurrent pulling out of hairs on the body. The behavior is typically habitual, and patients will often pull hair daily or almost daily. Both children and adults usually pull in episodes spread out throughout the day (e.g., before bedtime, during grooming routines, during times of stress).

Pulling Sites

Studies show that toddlers (Wright & Holmes, 2003) and preschool-age children (Walther et al., 2014) with HPD typically only pull hairs from the scalp, presumably because of a relatively low availability of hair in other areas. On the other hand, about half of school-age children (Walther et al., 2014) and adolescents (Franklin et al., 2008), and almost all adults (Woods et al., 2006), report pulling from more than one body area, suggesting that number of pulling sites increases with age or development. A survey among adolescents with HPD (ages 11–17 years; Franklin et al., 2008) showed that the most common pulling sites were scalp (85%), eyelashes (52%), eyebrows (38%), pubic region (27%), and legs (19%). In a similar survey among adults (Woods et al., 2006) the most common pulling sites were scalp (73%), eyebrows (56%), eyelashes (52%), pubic region (51%), and legs (22%).

Pre- and Postpulling Behaviors

Pre- and postpulling behaviors are common among children and adults with HPD (Mansueto, Townsley-Stemberger, Thomas, & Golomb, 1997; Tay, Levy, & Metry, 2004). Before pulling, patients may twirl the hair, stroke it, or look for the right hair to pull. Some prefer certain types of hairs, typically hairs that differ from the rest (e.g., a gray, coarse, or wiry hair). Others report special pleasure when they pull out a hair with a root at the end. Afterwards, some individuals will scrutinize the hair, play with it, roll it between the fingers, stroke it against the lips, smell it, or the like. Many will bite off the hair root, chew hairs, or swallow them. A survey among 68 adults with HPD (Grant & Odlaug, 2008) showed that 20% reported a current habit of swallowing the hairs (trichophagy), and an additional 13% episodically consumed the hair. Participants who reported trichophagy were more likely to be male and had more severe HPD than those who did not report this behavior. In a small minority of cases, the habit of consuming hair can lead to life-threatening complications if a "hair ball" (trichobezoar) clogs up the digestive tract (Gorter, Kneepkens, Mattens, Aronson, & Heij, 2010).

Proxy Pulling

Studies show that children (Tabatabai & Salari-Lak, 1981; Tay et al., 2004) and adults (Christenson, Mackenzie, & Mitchell, 1991) with HPD will sometimes habitually pull hairs from other people, pets, or dolls, in addition to pulling their own hair. Beattie, Hezel, and Stewart (2009) described two cases of mothers with HPD who reported shame, embarrassment, and substantial distress because of their inability to resist pulling hairs from their young children.

Affective Experiences

Sufferers of HPD often describe an overwhelming urge or desire to pull hair, and the behavior frequently produces relief, gratification, or pleasure. Pulling episodes are often triggered by negative affective states such as stress, boredom, tension, ambivalence, or frustration (Mansueto et al., 1997), and data suggest that pulling behavior may function to modulate negative states (Meunier et al., 2009; Shusterman, Feld, Baer, & Keuthen, 2009). Perfectionistic experiences are also sometime reported. For example, some individuals pull eyelashes evenly on both sides of the face. Some evidence indicates that affective experiences associated with hair pulling are less pronounced, or less commonly reported, among children compared to older individuals (Walther et al., 2014).

Automatic and Focused Subtypes

Many patients with HPD engage in hair pulling without reflective awareness of the act. They will pull and only notice afterwards what they have been doing. Some authors have suggested that it may be meaningful to distinguish between two styles of pulling: an "automatic" style, characterized by pulling without reflective awareness; and a "focused" style, characterized by pulling in full awareness, typically in response to internal events such as urge/arousal or negative affective states (e.g., stress or boredom). It has yet to be determined whether this distinction is clinically meaningful or has predictive validity, but it has been suggested that different treatment interventions fit these styles. HRT may be better suited for automatic pulling, and treatment focusing on emotion regulation may be better suited for focused pulling (Flessner et al., 2008).

The developmental trajectory of these pulling dimensions is not well understood. It appears that preschool-age children are less likely to be aware of hair-pulling behavior, or to experience a preceding urge, compared to older children and adults (Walther et al., 2014). However, preliminary data suggest that levels of automatic pulling remain stable once children are 10 years old. The focused pulling style, on the other hand, changes with age. Flessner, Woods, Franklin, Keuthen, and Piacentini (2009) examined cross-sectional survey data from females of a wide age range (10–69 years) with HPD. Automatic pulling remained stable across age groups, but focused pulling increased significantly during adolescence and other biological changes in adulthood (e.g., perimenopause). Panza, Pittenger, and Bloch (2013) reported similar findings in a sample of youth receiving treatment for HPD (8–17 years old). Results showed that the age of the patients had a significant positive correlation with levels of focused pulling, but no correlation with automatic pulling. These findings suggest that focused pulling may increase during adolescence, presumably because of greater emotional turmoil during that period, but that automatic pulling appears to be stable from late childhood to adulthood.

Common Comorbidities

Limited data exist on comorbidity in preschool-age children with HPD. A study of 10 toddlers with HPD showed that family problems or stressors were found in all cases (Wright & Holmes, 2003), that 50% had anxiety conditions, and that 20% had developmental problems. However, the study sample was drawn from an outpatient population, and structured interviews were not used. It seems plausible that comorbidity rates are inflated in outpatient samples, as young children who pull hair are presumably less likely to be seen by professionals if no other problems are present.

Several smaller studies utilizing semistructured interviews to assess comorbidity in outpatient youth with HPD reported consistently high comorbidity rates (60–70%), although the studies varied in terms of the most prevalent comorbid disorder (Hanna, 1996; King, Scahill, et al., 1995; Reeve, Bernstein, & Christenson, 1992). Tolin, Franklin, Diefenbach, Anderson, and Meunier (2007) assessed 46 youth ages 8–18 presenting for treatment in HPD specialty clinics and found that 18 (39%) met criteria for at least one comorbid disorder, with 14 (30% of the total sample) meeting criteria for an anxiety disorder. Panza and colleagues (2013) interviewed 62 participants ages 8–17 in a drug treatment trial for HPD. They reported the following comorbidity

rates: depression (31%), anxiety disorder (29%), ADHD (16%), tic disorder (6%), and OCD (5%). Finally, data from the Child and Adolescent Trichotillomania Impact Project (Franklin et al., 2008), an Internet-based survey of 133 youth ages 10–17 with HPD, found that over 45% of respondents endorsed depressive symptoms and 40% endorsed anxiety symptoms in excess of one standard deviation above published community scale norms (Lewin et al., 2009). Older age and age of onset predicted higher depression and anxiety scores, and depression, but not anxiety, symptoms partially mediated the relationship between severity of hair pulling and functional impairment. Studies of adults with HPD drawn from outpatient sources have also consistently shown high comorbidity rates, with anxiety and depressive disorders most commonly diagnosed (e.g., Odlaug, Kim, & Grant, 2010).

Obsessive–Compulsive Disorder

HPD has long been speculated to be a variant of OCD, and more recently it has been suggested that HPD belongs to the putative OCD spectrum (e.g., Lochner & Stein, 2006, 2010). HPD shares some phenomenology with OCD (e.g., both involve repetitive behaviors); however, these conditions also differ in important respects not only in terms of phenomenology (e.g., unlike OCD, HPD typically is not characterized by egodystonic intrusive thoughts), but also other clinical characteristics (e.g., gender ratio, course, comorbidity patterns, response to treatment). Nonetheless, OCD and HPD run in the same families and often co-occur (Bienvenu et al., 2012), and the two disorders may share some psychobiological underpinnings. One study found that HPD was more prevalent in an OCD sample than in samples of those with other anxiety disorders (Richter, Summerfeldt, Antony, & Swinson, 2003). Another study using a larger sample found numerically higher rates of HPD in a sample with OCD compared to samples with other anxiety disorders; however, the difference was not statistically significant (Lochner & Stein, 2010).

Body-Focused Repetitive Behaviors

HPD is often construed as one of several *body-focused repetitive behaviors* (BFRBs)—habitual behaviors that focus on the body. These include hair pulling, skin picking, nail biting/picking, cheek biting, thumb sucking, and more (Stein, Grant, et al., 2010). A review of the literature (Snorrason, Belleau, & Woods, 2012) showed that HPD and skin-picking disorder (SPD) have strikingly similar symptom presentation, frequently co-occur, and are likely to share important etiological factors. Studies show that the prevalence of SPD in outpatient HPD samples ranges between 10 and 34% (Snorrason et al., 2012). Preliminary data indicate that HPD, SPD, and pathological nail biting share genetic underpinnings (Bienvenu et al., 2009), and surveys among adults (Stein et al., 2008) and children (Walther et al., 2014) with HPD show high co-occurrence with other problematic BFRBs, including skin picking, nail biting, cheek biting, and nose picking. Clinical impression suggests that thumb sucking is common among young children with HPD. These children will frequently engage in hair pulling and thumb sucking at the same time, and treatment of thumb sucking may eliminate the hair-pulling habit (e.g., Friman & Hove, 1987).

Definitional and Diagnostic Issues

In DSM-III-R and DSM-IV (APA, 1987, 1994), HPD (or trichotillomania) was defined as recurrent hair pulling that results in noticeable hair loss and marked distress or functional impairment, and is not due to another mental disorder or medical condition. The definitions also included requirements of a mounting sense of tension prior to the act and gratification/relief while pulling hair. In DSM-5 (APA, 2013), however, the requirements of "noticeable" hair loss and a sense of tension–relief were changed, and the criteria now simply refer to hair loss. The reason for dropping "noticeable" was that hair loss in patients is often not clearly noticeable (e.g., when pulling is distributed over several areas) (Stein, Grant, et al., 2010). In regard to the other change, several research studies have shown that many individuals with HPD, especially children (Walther et al., 2014), do not endorse increased tension prior to pulling or gratification/relief during the act, despite a clinically significant hair-pulling problem (e.g., Conelea et al., 2012). Therefore, the DSM-5 criteria do not include these requirements. In short, the DSM-5 criteria define HPD as recurrent hair pulling resulting in hair loss, efforts to decrease or eliminate pulling, and significant distress or functional impairment. Exclusionary criteria include hair pulling due to another mental disorder (e.g., psychotic disorder) or a medical condition (e.g., dermatological illness).

Another change from DSM-III-R and DSM-IV to DSM-5 is that in the earlier DSMs, HPD was classified as an impulse-control disorder along with pyromania, gambling, intermittent explosive disorder, and others. It appears that HPD has little in common with some of these problems, and this conceptualization has had limited clinical utility. Thus, in DSM-5 HPD is included in the chapter on obsessive–compulsive and related disorders.

Developmental Course and Prognosis

Cross-sectional retrospective data from adult clinical samples show that HPD typically has a chronic course, with the most common age of onset in early adolescence (Snorrason et al., 2012). However, childhood onset is also common, and clinical impression suggests that early onset cases may have a less chronic course. Swedo, Leonard, Lenane, and Rettew (1992) examined children who were age 7 or younger and had HPD onset before the age of 5 years ($N = 10$), and compared them to a group of older children, adolescents, and adults with later onset ($N = 43$). The authors noted that the older sample typically had a chronic course, but the children in the early-onset sample often had an episodic course with complete remissions for a few months several times a year. The authors also reported that none in the older sample had onset before 5 years of age. Based on these data, the authors speculated that very early-onset cases (before 5 years) might represent a subtype with a distinct course and prognosis. However, there may have been important differences in how the two samples were recruited. All participants were recruited through advertisement in the media (e.g., newspapers), but the older ones were recruited for a drug treatment study, whereas the younger participants were recruited for a general pediatric consultation. Given that treatment-seeking populations often have more severe problems than non-treatment-seeking populations, it is unclear whether the findings reflect a real difference between the age-at-onset groups, or difference between the populations from which the samples were drawn. Also, later studies have shown that a significant proportion of adult samples report very early onset, indicating that the disorder is chronic at least in some early-onset cases. Prospective longitudinal research is needed to clarify the natural course of hair pulling in young children versus older individuals.

Epidemiology

Prevalence in the General Population

Christenson, Pyle, and Mitchell (1991) examined the prevalence of pathological hair pulling using self-report scales in a large university student sample ($N = 2,579$) with a high response rate (97.9%). The findings showed that 2.5% of the students endorsed a lifetime occurrence of hair pulling resulting in noticeable hair loss and distress or functional impairment, in the absence of an underlying skin condition. When a more restrictive set of DSM criteria was used (including requirement of preceding tension and subsequent relief or gratification), the prevalence rate was 0.6%. A survey study among adults in the general population also found a prevalence of 0.6%, using the strict DSM-IV criteria (Duke, Bodzin, Tavares, Geffken, & Storch, 2009). King, Zohar, and colleagues (1995) interviewed 794 adolescents (all 17-years-olds enlisted to a universal military service in Israel) and found 1% lifetime prevalence of HPD.

Prevalence in General Psychiatric Populations

Malhotra, Grover, Baweja, and Bhateja (2008) examined case files of all patients ($N = 1,610$) presenting to a child/adolescent psychiatric unit in India over a 5-year period, and found that 1.24% ($n = 20$) were diagnosed with HPD. However, HPD was not systematically screened for. A more systematic study using semistructured interviews to assess 102 consecutive patients admitted to an inpatient adolescent psychiatric unit found 3.9% prevalence of current HPD (Grant, Williams, & Potenza, 2007). Similar studies in adult psychiatric outpatient samples have shown lifetime prevalences of HPD ranging from 1.3 to 4.4% (e.g., Müller et al., 2011).

Sex Differences

Studies consistently show that a majority (approximately 90%) of adults who present for treatment or research on HPD are females (Snorrason et al., 2012). However, a few survey studies in community/student samples (Christenson et al., 1991; Duke et al., 2009; King, Zohar, et al., 1995) have reported an even gender ratio among those meeting strict criteria for HPD. This may indicate that the gender ratio in the general HPD population is more even, and that females are overrep-

resented in clinical/research samples because they are more likely to seek treatment or help. However, the low base rate of HPD in the survey studies (i.e., 0.6–1%) makes these findings difficult to interpret.

Findings concerning gender ratio among children in clinical/research populations are mixed. A few studies have found equal gender ratios in preschool-age children with HPD (Cohen et al., 1995; Muller, 1987; Tay et al., 2004); however, most studies have reported a preponderance of females in child and adolescent samples (Hanna, 1996; King, Scahill, et al., 1995; Malhotra et al., 2008; Meunier et al., 2009; Reeve et al., 1992; Santhanam, Fairley, & Rogers, 2008; Swedo et al., 1992), albeit lower than the percentages found in adult clinical samples (i.e., 57–87%).

Grant and Christenson (2007) interviewed adults with HPD/SPD and found that males were more likely than females to report a comorbid anxiety disorder, a later age of onset, and greater disability due to their problem. No other differences in phenomenology or clinical characteristics were found.

Theoretical Frameworks

Evolutionary Models

Several authors have conceptualized HPD and other BFRBs as pathological grooming behaviors (Feusner, Hembacher, & Phillips, 2009; Moon-Fanelli, Dodman, & O'Sullivan, 1999; Stein, Chamberlain, & Fineberg, 2006; Swedo, 1989), implying an evolutionary underpinning of these problems. Grooming serves an important function in a range of animal species, but it is unclear whether grooming serves this residual function in humans. An evolutionary approach would assume that BFRBs in humans reflect evolved grooming mechanisms, and perhaps that HPD and other "grooming disorders" reflect a breakdown in this mechanism. However, specific evolutionary hypotheses of HPD have not been formulated.

Animal Models

Ethological models involve studying naturally occurring (i.e., not artificially induced) behaviors or disorders that resemble and are assumed to reflect etiological mechanisms similar to those for human HPD symptoms. It has been proposed that "displacement behaviors" in animals may be a valid model for HPD in humans (Swedo, 1989). Such behaviors are actions that appear out of context or irrelevant to an organism's ongoing activities. These behaviors typically occur when a goal is thwarted (e.g., when a bird is prevented from approaching expected food or sexual partner, it may start preening its feathers) or when there is a conflict between two incompatible motivations triggered simultaneously (e.g., when flight and fight responses are in conflict, a bird may do neither and engage in grooming or nest-building behavior). Research suggests that displacement activities, like HPD, function to regulate arousal/stress in humans and nonhuman primates (Troisi, 2001); however, more research is needed to establish the validity of displacement behaviors as a model for human hair pulling.

Naturally occurring behavioral disorders in animals have also been proposed as models of HPD (Moon-Fanelli et al., 1999). For example, psychogenic feather picking in birds—a behavioral disorder characterized by excessive feather picking—shares many characteristics with human hair-pulling problems. Similar to excessive hair pulling in humans, birds afflicted with psychogenic feather picking will (1) excessively pluck out feathers; (2) tend to prefer plucking certain feathers over others (e.g., those that are different from the rest); and (3) often scrutinize, chew on, and play with plucked feathers (Zeeland et al., 2009).

Another animal model for HPD is *barbering* in mice (Dufour & Garner, 2010). Barbering is an abnormal behavior found in laboratory mice that is characterized by plucking of fur or whiskers from themselves or their cage-mates. It has been suggested that barbering behavior resembles human HPD with respect to phenomenology (repetitive hair removal behavior), demographics (adolescent onset and female preponderance), and genetic underpinnings (Dufour & Garner, 2010). Other behavioral disorders in animals (Moon-Fanelli et al., 1999) resembling HPD include psychogenic alopecia in cats (excessive self-grooming) and acral lick dermatitis in dogs (excessive licking and chewing of the limbs).

Researchers have also used genetically modified animals to model human HPD symptoms. For example, Greer and Capecchi (2002) showed that mice with mutations of the Hoxb8 gene engaged in excessive grooming behavior (compared to controls) that resulted in loss of fur and skin lesions. The authors ruled out dermatological causes of the behavior and pointed out that the Hoxb8 gene is expressed in brain areas (orbital cortex, striatum, and more) thought to be involved in human HPD.

In general, existing animal models of HPD typically have moderate to good face validity (e.g., similar phenomenology), but more research is needed to establish their construct validity (e.g., similarities in underlying physiology) and predictive validity (e.g., similar response to treatment).

Biological Models

Biological models of HPD assume that the disorder is caused by a dysregulation in some biological systems. Stein and colleagues (2006) proposed a neurocognitive model of HPD and other BFRBs, emphasizing deficits in mechanisms related to affect regulation, behavioral addiction, and cognitive control. The model was intended as a heuristic for research on psychobiological dysfunction in HPD. The affect regulation component assumes that the behavior has roots in brain systems involved in affective regulation. This is consistent with the observation that patients with HPD are frequently characterized by negative affect and emotion regulation difficulties, and that hair-pulling behavior appears to regulate negative affective states (e.g., Shusterman et al., 2009). The cognitive control component is based on the observation that patients with HPD have difficulty controlling the behavior, and postulates the role of brain mechanisms involved with control of cognitive and behavioral output (e.g., basal ganglia). The addiction/reward component assumes involvement of brain systems that have to do with reward processing and addiction. Because symptoms of HPD share many similarities with other addictions (e.g., appetitive urge or cravings), some authors have argued that it may be useful to characterize HPD as a behavioral addiction (Grant, Odlaug, & Potenza, 2007).

Behavioral Models

One behavioral model of HPD (Franklin & Tolin, 2007; Mansueto et al., 1997) posits that hair pulling is inherently reinforcing, at least for some individuals, and that the behavior is maintained through positive reinforcement (e.g., pleasure, gratification) and negative reinforcement (e.g., affect/arousal regulation). The model also assumes that other stimuli (e.g., external context or internal events such as urges or emotions) can become associated with the habit through classical conditioning. For example, if an individual usually pulls hair during the evenings, in front of the bathroom mirror, and when bored or anxious, contextual features such as the mirror in the bathroom, the implement used, or a state of boredom can over time acquire the ability to trigger or exacerbate the behavior. This model is supported by empirical evidence showing a range of idiosyncratic, individualized triggers of hair pulling (Christenson, Ristvedt, & Mackenzie, 1993) and consequences of the behavior that are pleasurable or affect-/arousal-regulating (Mansueto et al., 1997; Shusterman et al., 2009).

Implied in this behavioral model is the notion that behavior functions to regulate emotions. A few different emotion regulation models of HPD have been proposed. For example, Penzel (2003) has suggested that individuals with HPD and other BFRBs may have arousal regulation difficulties, and that the habit behavior functions to regulate high-arousal (e.g., tension, anxiety) and low-arousal (e.g., boredom) states. An experiential avoidance model more broadly assumes that hair pulling functions to help an individual avoid or escape aversive internal states (Woods, Snorrason, & Espil, 2012).

Etiological Factors

Genetics

HPD has been shown to run in families (Bienvenu et al., 2012), and a small-sample ($N = 34$) twin study showed that the HPD concordance rates were 38% for monozygotic twins and 0% for dizygotic twins, yielding a heritability estimate of 76% (Novak, Keuthen, Stewart, & Pauls, 2009). Specific genetic underpinnings of HPD are not well understood. Preliminary research has demonstrated that the Hoxb8 gene (Chen et al., 2010) and the Sapap3 gene (Welch et al., 2007) contribute to overgrooming in mice. Some evidence suggests a link between a variant of the Sapap3 gene and HPD in humans (Bienvenu et al., 2009; Zuchner et al., 2009), although these findings have not consistently been replicated (Boardman et al., 2011). Other candidate genes for human HPD have been suggested, including the slit and trl-like 1 (SLITRK1) (Zuchner et al., 2006) and a variation in a gene involved with a serotonin (5-HT_{2A}) receptor (Hemmings et al., 2006), but further research is clearly needed.

Neurobiological Factors

Brain imaging research in HPD is in its infancy and mostly limited to small samples of adult subjects. To

the best of our knowledge, only one neuroimaging study has been conducted in youth with HPD. Lee and colleagues (2010) conducted an fMRI study using whole-brain analysis. Nine youth (9–17 years old) with HPD and 10 matched healthy controls were scanned during two symptom provocation tasks (visual–tactile and visual only) and a neutral task. During the symptom provocation tasks, the youth with HPD showed increased activities in several brain regions, including areas involved in habit learning (i.e., striatum) and evaluation of emotional stimuli and rewards (e.g., posterior cingulate). Some imaging studies in adult samples (e.g., Chamberlain et al., 2008, 2010; Keuthen et al., 2007) have documented abnormalities in brain areas that support generation–suppression of motor responses (i.e., cortical areas), affect regulation (i.e., the amygdala–hippocampus complex), and habit learning (i.e., striatum). However, other studies using "region of interest" approaches have failed to find significant differences between brains of patients with HPD and control groups (e.g., Rauch et al., 2007).

Studies examining cognitive performance of youth with HPD are largely nonexistent, although limited data are available for adult samples. It has been suggested that inhibition deficits represent an endophenotype in HPD and other OCD spectrum conditions (Chamberlain et al., 2005). Some studies have shown poor motor inhibition (assessed with the stop signal task or the go/no-go task) in groups with HPD compared to control groups (Chamberlain, Fineberg, Blackwell, Robbins, & Sahakian, 2006), but other studies have failed to find significant differences (e.g., Bohne, Savage, Deckersbach, Keuthen, & Wilhelm, 2008). Adults with HPD have also been shown to have abnormalities in divided attention (Stanley, Hannay, & Breckenridge, 1997), visual–spatial learning (Chamberlain, Odlaug, Boulougouris, Fineberg, & Grant, 2009), and spatial working memory (Chamberlain et al., 2007). However, these findings need replication, and it is unclear to what extent these characteristics play a causal role in the development of HPD.

Affect/Arousal Regulation Difficulties

As mentioned above, some behavioral models assume that hair-pulling behavior functions to regulate affective states. Several research studies (reviewed by Snorrason et al., 2012) have asked children and adults with HPD to retrospectively rate affective states experienced just before, during, and immediately after pulling episodes. Findings have consistently shown that the intensity of negative affective states (e.g., anxiety or boredom) is typically highest before pulling and then decreases during and after pulling (although shame and embarrassment tend to increase after pulling). Results also show that pleasurable states (e.g., gratification or relief) tend to increase from before to during pulling and then decrease from during to afterwards. Diefenbach, Tolin, Meunier, and Worhunsky (2008) also found that adults with HPD reported reduction in negative emotions during an experimental hair-pulling task. Thus research suggests that hair-pulling behavior, at least for some individuals, serves the function of modulating negative states and producing positive feelings.

It may be that individuals with HPD are characterized by emotion regulation difficulties, and that these lead to the development of the hair-pulling habit as a dysfunctional emotion regulation strategy. Shusterman and colleagues (2009) asked adults with HPD to identify emotions they had difficulty regulating, and what emotions (if any) their hair pulling typically modulated. Results showed that the type of emotions an individual would report as difficult to manage tended to correspond with the type of emotions modulated by the hair-pulling behavior. For example, individuals who reported that hair pulling helped reduce boredom were likely to report difficulty with regulating boredom.

Preliminary data also provide support for the role of experiential avoidance in HPD (Begotka, Woods, & Wetterneck, 2004; Norberg, Wetterneck, Woods, & Conelea, 2007). First, levels of self-reported experiential avoidance are positively correlated with HPD severity; the more individuals avoid aversive internal events, the worse their HPD symptoms. Second, cross-sectional studies show that experiential avoidance statistically mediates the relationship between negative affect or thoughts and HPD symptom severity. In other words, negative affect or thinking influences HPD symptoms because of a general tendency to avoid or escape aversive internal events.

Environmental Stressors

Clinical impressions suggest that stress and trauma can exacerbate and possibly play a causal role in HPD. For example, Wright and Holmes (2003) examined 10 toddlers with hair-pulling problems and found family problems or stressors in all cases. Oranje, Peereboom-Wynia, and De Raeymaecker (1986) investigated case files of 21 children (2–15 years old) with HPD and

noted psychosocial stressors in most cases, ranging from mild (sibling rivalry) to more severe (hospitalization). Lochner and colleagues (2002) administered the Childhood Trauma Questionnaire to adult patients with HPD (n = 36), patients with OCD (n = 74), and healthy controls (n = 31). The findings showed that the clinical groups obtained higher scores than the control group on the emotional neglect scale and higher overall scores, but did not differ from each other. Even though clinical data suggest that stress/trauma may play a role in HPD for some people, further controlled or longitudinal studies are needed to determine the causal status of these stressors.

Activity restriction or understimulation has also been proposed as a potential risk factor for the development of HPD and other BFRBs. Studies show that a range of animal species can develop abnormal stereotypic behaviors, including overgrooming, in response to environmental restriction (Moon-Fanelli et al., 1999). However, studies in humans are scarce. As noted above, evidence shows that boredom often triggers hair pulling (Shusterman et al., 2009), and clinicians have reported cases where individuals developed HPD (Evans, 1979) after a period of severe activity restriction. Again, experimental or longitudinal evidence is needed to determine whether these types of stressors play a causal role in the development of HPD and other BFRBs.

Current Issues and Future Directions

Although research has increasingly provided a better understanding of HPD psychopathology, much work remains to be done. The association between HPD and several other related psychiatric problems requires further investigation. For instance, understanding the similarities and differences between HPD and SPD should help answer the question of whether they are better construed as different manifestations of the same disorder (Snorrason et al., 2012). Given emerging evidence for an association between SPD/HPD and other BFRBs (e.g., pathological nail biting and cheek/lip biting), and for the notion of the BFRBs as a diagnostic category (Stein, Grant, et al., 2010), research into shared etiological mechanisms of these problems and their comorbidity would be informative. Future research studies are also needed to clarify the relationship between BFRBs and stereotypic behaviors such as body rocking, head banging and hand flapping. Finally, the relationship between HPD (and other BFRBs) and OCD, or OCD spectrum conditions, warrants further research attention.

An important unresolved issue is the developmental course and distinctiveness of early-onset HPD. Even though clinical impressions and preliminary findings support the notion that early-onset HPD may represent a distinct subtype with a less chronic course, research with adequate methodology is required to answer this question. Longitudinal research following toddlers with HPD would be highly informative. Also, future researchers may want to examine the predictive validity and clinical utility of the distinction between automatic and focused hair pulling (i.e., pulling with or without reflective awareness of the act). Such work could potentially provide a deeper understanding of etiological mechanisms, and could enhance effectiveness of treatment by enabling clinicians to match treatment components to patient characteristics.

Existing research on the psychobiological dysfunction underlying HPD is limited and mostly restricted to adults. Further work in this area is warranted and should shed light on the underlying proximal etiology mechanisms. An evolutionary framework could also be useful for a better understanding of more distal (evolutionary) mechanisms underlying HPD, and could help guide research on psychobiological dysfunction.

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CHAPTER 10

Childhood Posttraumatic Stress Disorder

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Posttraumatic stress disorder (PTSD) is among both the immediate and long-term consequences of exposure to severe environmental adversity. Some evidence suggests that the perception of threat is as important as the external reality, if not more so. Exposure to traumatic events is related to a number of disorders that may occur in combination (i.e., comorbidity), and it may be a factor in the expression of disorders to which individuals are genetically predisposed. Early life stressors may cause enduring brain dysfunction (Anda et al., 2006), which, in turn, affects development, health, and ongoing life quality. Notably, common anterior cingulate/medial prefrontal cortex and hippocampal deficits. as well as decreased amygdala function, have been revealed for a number of disorders. Bremner (2006) has suggested including these disorders—PTSD, depression, borderline personality disorder, and dissociative disorders—among trauma spectrum disorders.

Adult stress reactions have been a major focus of study much longer than children's reactions have been. Some of the earliest accounts of children's stress reactions originated during World War I (e.g., Burt, 1943; Freud & Burlingham, 1943). However, such accounts were relatively infrequent during the war, and even less frequent during the 25–30 years after the war's end. Research on children's reactions to traumatic events did not begin in earnest until the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III; American Psychiatric Association [APA], 1980) was published, and children's PTSD reactions were not specifically mentioned in DSM until the revised third edition, DSM-III-R (APA, 1987). PTSD and other trauma-related disorders have often been defined and tested on the basis of adult reactions and assessment tools, or on that of specific trauma populations (Nader, 2008). More recently, researchers have demonstrated the importance of defining and assessing psychopathology from a developmental perspective (Costello, Foley, & Angold, 2006; Nader, 2008; Scheeringa, 2011). In addition, the need to distinguish among disorders such as PTSD, comorbid reactions, complex traumatic reactions, and traumatic or prolonged grief responses has become apparent in order to provide effective interventions (Ford, Courtois, van der Hart, Nijenhuis, & Steele, 2005; Nader, 2008; van der Kolk, Roth, Pelcovitz, Sun-

In Memoriam: This chapter is offered in memory of Kenneth E. Fletcher, who died in 2012 after a long battle with cancer. Ken was a brilliant statistician and researcher who made many contributions to the field of childhood traumatic stress. He provided assessment scales and published chapters and articles that influenced his colleagues in their pursuit of truth about childhood traumatic reactions. He was of great aid to and was greatly appreciated by his colleagues. Few knew the breadth of his many talents, however. For example, in addition to his academic work, he authored evidence-based books (such as an extensive story based on the life of Charles Manson) and children's stories. He will be greatly missed by his friends, colleagues, and family, as well as by the field of childhood trauma.

day, & Spinazzola, 2005). At least in part because of methodological differences, and in part because variables that influence posttrauma outcomes transact in complex manners, findings related to traumatic exposure and associated outcomes have often been mixed. Nevertheless, contrary to earlier beliefs, children do not simply grow out of their PTSD reactions, and they may have a more unremitting and chronic course than adults have (Scheeringa, 2011). Child-related changes in the DSM criteria for PTSD have been made and are likely in the future as researchers continue to fill in gaps in knowledge of risk and protective factors, the interrelatedness of variables, and developmental influences; recognize trauma's effects on neurobiology; neurobiology's (genetics) impact on trauma reactions; and the potential disruption of a youth's skill development (e.g., coping, self-regulation). This chapter focuses on PTSD. Trauma- and stress-related disorders other than PTSD (i.e., reactive attachment disorder, disinhibited social engagement disorder) are discussed by Lyons-Ruth, Zeanah, Benoit, Madigan, and Mills-Koonce in Chapter 15 of this volume.

EVOLUTION OF THE CONCEPT OF PTSD

Evidence that traumatic events can lead to psychological disturbance has been present in literature for centuries (Kinzie & Goetz, 1996). In *The Odyssey*, probably written down in the 8th century B.C. (Rieu, 2003), Odysseus is described as suffering from flashbacks (vivid reliving of aspects of the traumatic experience) and "survivor's guilt" (guilt over having survived when others did not) after fighting in the Trojan War (Figley, 1993). The study of human responses to traumatic events can be traced from the late 1800s. Posttraumatic conversion reactions were observed by investigators such as Charcot and Janet (see Veith, 1965) and by Breuer and Freud (1893–1895). After World Wars I and II and the Korean and Vietnamese wars, the terms "shell shock" and "traumatic neurosis" were used to describe soldiers' postwar syndromes. Civilians were studied as survivors of concentration camps or of civilian disasters. The study of traumatic stress expanded to include civilian crimes. Burgess and Holmstrom (1974) described the "rape response syndrome," and Mardi Horowitz (1979) studied symptom clustering and the impact of stressful life events. By 1980, Horowitz and colleagues provided early validation studies for adults of the symptoms listed in DSM-III as characterizing PTSD, which continue to be among its core symptoms: uncontrollable remembering of the original stressful events; efforts to forget about those events; avoidance of event reminders; social withdrawal; a flattening of affect that may lead to a sense of numbness; increased fearfulness and anxiety; fear of repetition of stressful events; and increased arousal and hypervigilance for other potentially threatening events.

DSM Perspectives on PTSD

Prior to DSM-III, the predominant view of traumatic stress reactions was based on the traditional psychoanalytic explanation. Freud argued that traumatization occurs when the ego's "stimulus barrier" is overwhelmed by a flood of unmanageable stimuli from external stressors; the breaking of the stimulus barrier disrupts the organism's functioning (Freud, 1920/1955; Wilson, 1994). Although in general, the removal of the external stressor was expected to lead to quick restoration of the organism's functioning, Freud did note that unmanageable stimuli can at times become so extreme as to overpower an individual's coping mechanisms, which leads to a sense of overwhelming helplessness. At this point the individual is thought to regress and begin resorting to a primitive defense, the repetition compulsion, in an attempt to gain mastery over the traumatic experiences by compulsively repeating them in dreams, memories, and reenactments (Freud, 1939/1964). When symptoms do not abate with time and distance from the trauma, the traditional psychoanalytic explanation is that current stress has revived infantile conflicts, which are the real cause of "traumatic neuroses" (Brett, 1993). This theory ascribes enduring traumatic reactions to premorbid characteristics of the victim, rather than to the threatening characteristics of the stressor.

The Definition of PTSD in DSM-III

Jones and Barlow (1990) suggested that symptoms of reexperiencing and overarousal could be accounted for by conditioned responses to internal or external cues that have become associated with a traumatic experience (Fletcher, 2003). Accordingly, learned alarms lead to anxious apprehension and reexperiencing of the traumatic experience. This is especially likely when the circumstances surrounding the traumatic event are perceived to be unpredictable and uncontrollable. The aversiveness can become emotionally overwhelming, which leads to avoidance of cues associated with the

trauma. Due to the processes of stimulus generalization and higher-order conditioning, cues can be difficult to avoid. As a consequence, traumatized individuals become inclined to withdraw from the world, numb their affective responses, and sometimes resort to dissociation. However, they are rarely able to avoid intrusive memories of their traumatic experiences for long. As a result, the characteristic "phasing" found in PTSD begins—alternation between reexperiencing and avoiding trauma-related memories and cues.

In DSM-III (APA, 1980), symptoms were clustered into three of the criteria that became the foundations of PTSD in DSM-III-R (APA, 1987) and DSM-IV (APA, 1994) (see Wilson, 1994). Perhaps the most radical change was Criterion A, which required exposure to "a recognizable stressor that would evoke significant symptoms of distress in almost everyone" (APA, 1980, p. 238). Contrary to previous formulations, this implied that PTSD is a normal reaction to abnormal circumstances, and no longer considered the result of the weakened nature of the victim. The intensity and scope of an individual's reactions could thus be expected to relate directly to the intensity and duration of exposure to the stressor, and symptoms might last indefinitely.

Refinement in DSM-IV

DSM-IV described PTSD much as DSM-III did, with some further refinements. According to DSM-IV, trauma survivors tend to experience recurrent distressing recollections (may be repetitive play for children), distressing dreams, behaviors reminiscent of the original traumatic experience, and physiological or psychological reactions to reminders of the event (Criterion B). Posttrauma arousal may disrupt sleep, sense of security, and concentration, and the traumatized individual may begin to anticipate further trouble (hypervigilance), be angry and/or irritable, and/or be easily startled (Criterion D). In an attempt to modulate the overwhelming feelings evoked by the recurring memories of the trauma, survivors avoid (or attempt to avoid) thoughts, feelings, and other reminders of the trauma (including memory for some aspect(s) of the event); they may "turn off" their feelings, leading to flat or a restricted range of affect, a sense of emotional distance and/or numbness, and social withdrawal; and they may have a sense of a foreshortened future (Criterion C).

Although a few child-specific alterations appeared in the perspective on PTSD in the 1990s, debate continued about the applicability of adult criteria to children. Some argued, for example, that three symptoms of avoidance might be too restrictive because it can be more difficult to recognize denial and numbing in children than in adults, and more difficult for children to report such symptoms (La Greca & Prinstein, 2002; Nader, 2008; Scheeringa, 2011; Schwarz & Kowalski, 1991). Additionally, symptoms vary across age groups; for example, some behavioral or emotional patterns, such as fearful inhibition, occur normally at certain developmental phases or in normal children with specific personality styles (Nader, 2008). Importantly, children with "subsyndromal" or "subclinical" PTSD have been found to be clinically and significantly impaired (Carrion, Weems, Ray, & Reiss, 2002; Daviss et al., 2000; Nader, 2008; Scheeringa, 2011; Scheeringa, Myers, Putnam, & Zeanah, 2012). Adolescents with partial or full PTSD have reported severe functional impairment in all domains of functioning (Abdeen, Qasrawi, Nabil, & Shaheen, 2008). Youth without PTSD who have reported few symptoms sometimes have had later emotional, behavioral, and functioning disturbances clearly associated with traumatic exposure (Greenwald, 2002; Nader, 2008; Yule et al., 2000). In fact, some individual symptoms (e.g., aggression, poor concentration) may significantly disrupt normal development and skill achievement (e.g., interrelating, self-control, self-image; Nader, 2008). A number of researchers have suggested that youth may alternate long periods of reexperiencing with extended periods of avoidance and numbing (Lubit, Hartwell, van Gorp, & Eth, 2002; Schwarz & Kowalski, 1991), making their assessment complicated. Some have argued that PTSD as described in DSM-IV and the 10th revision of the *International Classification of Diseases* (ICD-10) might not be inclusive enough, especially for children (Armsworth & Holaday, 1993). Others have argued for studying PTSD as a continuous variable rather than the dichotomous one described by DSM-IV and ICD-10 (Broman-Fulks et al., 2009).

Acute Stress Disorder

For a DSM-IV diagnosis of PTSD, duration of at least 1 month was required. Acute stress disorder (ASD; APA, 1994) was included in DSM-IV to reflect a significant reaction that lasted between a few days and 1 month. It included the PTSD symptoms of reexperiencing, avoidance and arousal as well as dissociative symptoms. Studies found ASD diagnoses for between 13 and 19% of adult posttrauma respondents and between 8 and

19% of youth (Bryant, Mayou, Wiggs, Ehlers, & Stores, 2004; Kassam-Adams & Winston, 2004; Meiser-Stedman, Dalgleish, Smith, Yule, & Glucksman, 2007; Meiser-Stedman, Yule, Smith, Glucksman, & Dalgleish, 2005). ASD was found for different types of traumatic exposure (Nader, 2008), such as burns (Saxe et al., 2005; ASD in 31% of 72 children), traffic accidents, assaults (Meiser-Stedman et al., 2005), and shootings (Hamlin, Jonker, & Scahill, 2004). Although studies demonstrated that adults with ASD were at greater risk of developing PTSD (Brock, 2002; Wilson, 2004), dissociative symptoms added little to ASD's predictive power for either adults or children (Kassam-Adams & Winston, 2004; Meiser-Stedman et al., 2005), and some argued that the dissociation requirement added little clinical utility (Harvey & Bryant, 2002). Tinnen, Bills, and Gantt (2002) suggested that dissociative PTSD is a subset of adults' complicated trauma reactions.

Changes in DSM-5 PTSD and ASD

DSM-5 (APA, 2013) includes changes in the structure of PTSD and in the exposure and symptom criteria. A separate diagnosis of PTSD for preschool children has been added. DSM-5 ASD now requires PTSD Criterion A exposure and any 9 (or more) of the following PTSD symptoms lasting between 3 days and 1 month: B1–B3, either B4 or B5, D7, either depersonalization or derealization, D1, C1, C2, E1, and E3–E6 (see Table 10.1 for these criteria).

THE STRUCTURE OF PTSD

Although findings, primarily for adults and adolescents, have been somewhat mixed (Armour et al., 2011; Elhai et al., 2009), research has provided little support for the three-factor DSM-IV PTSD symptom structure (Armour et al., 2011; Ford, Elhai, Ruggiero, & Frueh, 2009). The following proposed factor and no-factor models have proven successful (Elhai et al., 2009; Kassam-Adams, Marsac, & Cirilli, 2010): (1) four-factor models (e.g., emotional numbing [King, Leskin, King, & Weathers, 1998] and dysphoria [Simms, Watson, & Doebbeling, 2002]); (2) three primary factors plus a secondary factor (hierarchical; Anthony et al., 2005); (3) a two-factor model (Spitzer, First, & Wakefield, 2007); and (4) no factors (i.e., a dimensional or noncategorical model; Broman-Fulks et al., 2009). Some differences in findings may be related to whether the assessment was of global trauma versus a specific trauma (Elhai et al., 2009; Naifeh, Elhai, Kashdan, & Grubaugh, 2008). In a sample of 8- to 17-year-olds (Kassam-Adams et al., 2010), the DSM-IV three-factor model was a relatively good fit; however, other models tested were as good or better. DSM-5 PTSD includes four symptom-related criteria (B–E; Table 10.1) for adults, adolescents, and children over age 6: intrusion symptoms, persistent avoidance, negative alterations in cognitions or mood, alterations in arousal or reactivity. We discuss these next.

PTSD FOR CHILDREN OVER 6 YEARS, ADOLESCENTS, AND ADULTS

For children over the age of 6 years, adolescents, and adults, DSM-5 Criterion A (exposure) no longer requires a peritraumatic intense or observable reaction (i.e., the DSM-IV A2 requirement of fear, helplessness, horror, agitation). This is especially important for children, who may not be able to report their reactions or may not react visibly. It is also important for chronically traumatized youth, who may have learned not to react or are not able to identify their emotions. Instead, Criterion A lists the manner of possible exposure to life threat, serious injury, or personal violation (e.g., experiencing, witnessing, learning about; nonmedia repeated exposure to details). Clinician-researchers have observed that a child's accurate or inaccurate perception that a significant other has been endangered during a potentially traumatic event may be sufficient to result in PTSD or traumatic grief (Cohen, Mannarino, Greenberg, Padlo, & Shipley, 2002; Nader, 1997; Nader & Salloum, 2011). In DSM-5 Criterion A, indirect, nonmedia exposure—that is, learning of actual events with violent or accidental threat to a close relative or friend—is among exposures that may result in PTSD.

DSM-5 Criterion B (intrusion symptoms) is similar to DSM-IV B (reexperiencing). Wording changes in B3 make clear its dissociative nature. Such dissociative reactions may occur on a continuum, which at its most extreme includes a complete loss of awareness of present surroundings (e.g., "flashbacks"). As in DSM-IV, replications of traumatic event content—relevant to B1 and B3—may occur in play (or in other activities) for children. In DSM-5, DSM-IV Criterion C is divided into two criteria: C (avoidance of internal reminders—which may be manifested in children as numbing, denial, or distraction—and/or avoidance of external reminders) and D (changes in mood and cognition). While Criterion C is related to reminders

TABLE 10.1. DSM-5 Diagnostic Criteria for Posttraumatic Stress Disorder (PTSD) in Adults, Adolescents, and Children over 6 Years, Compared with DSM-IV Criteria

Criterion	PTSD: DSM-5 criteria (**Note:** The following criteria apply to adults, adolescents, and children older than 6 years. For children 6 years and younger, see corresponding criteria [in Table 10.2].)	Differences from DSM-IV criteria (There are now separate diagnoses for young children [see Table 10.2] and for everyone over age 6. The disorder may occur "with dissociative symptoms" and "with delayed expression" [see below)].)
A: Exposure	A. Exposure to actual or threatened death, serious injury, or sexual violence, in one (or more) of the following ways: 1. Directly experiencing the traumatic event(s). 2. Witnessing, in person, the event(s) as it occurred to others. 3. Learning that the traumatic event(s) occurred to a close family member or close friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental. 4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains; police officers repeatedly exposed to details of abuse). **Note**: Criterion A4 does not apply to exposure through electronic media, television, movies, or pictures, unless this exposure was work related.	• As in DSM-IV A1, the events that meet the exposure criterion include actual or threatened death or serious injury. In DSM-5, sexual violence is included as well. The ways of being confronted with the event that make one eligible for a PTSD diagnosis are described in A1–A4. • DSM-IV A2 is omitted. DSM-5 does not require an intense or observable reaction—fear, helplessness, or horror—at the time of the event(s). • Direct experience of the event and witnessing are described in A1 and A2. • A3 includes indirect exposure (i.e., learning that a significant other was endangered or killed by violence or an accident). • For adults and possibly older youth (e.g., rescue workers), A4 includes repeated nonmedia or work-related media exposure to the details of the event.
B: Intrusion symptoms	B. Presence of one or more of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred: 1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s). **Note:** In children older than 6 years, repetitive play may occur in which themes or aspects of the traumatic event(s) are expressed. 2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s). **Note:** In children, there may be frightening dreams without recognizable content. 3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.) **Note:** In children, trauma-specific reenactment may occur in play.	• DSM-5 B is similar to DSM-IV B, with some important wording changes—for example: • B1 refers to "memories" instead of "recollections," and defines the relevant recurrent, intrusive memories as those that are "involuntary." • Instead of recurrent distressing dreams "of the event," B2 broadens the dreams to include those related by content *or* affect to the event(s). • B3 specifically refers to dissociative reactions, which may occur on a continuum that includes varying degrees of dissociation. • B4 includes the possibility of prolonged psychological distress instead of intense distress. • B5 changes "physiological reactivity" to "marked physiological reactions."

(continued)

TABLE 10.1. *(continued)*

Criterion	PTSD: DSM-5 criteria	Differences from DSM-IV criteria
	4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s). 5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).	
C: Avoidance	C. Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following: 1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s). 2. Avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).	• DSM-IV Criterion C is now C and D. C is avoidance of reminders. • DSM-5 C includes actual avoidance as well as efforts to avoid. • C1 relates to internal reminders and includes memories as well as thoughts and feelings; it recognizes that avoidance behaviors may be directed toward memories, thoughts, or feelings closely associated with the event, as well as those about the event. • C2 includes external reminders, and also includes "closely associated" reminders.
D: Negative alterations in cognitions and mood	D. Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following: 1. Inability to remember an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs). 2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., "I am bad," "No one can be trusted," "The world is completely dangerous," "My whole nervous system is permanently ruined"). 3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others. 4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, or shame). 5. Markedly diminished interest or participation in significant activities. 6. Feelings of detachment or estrangement from others. 7. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).	• This is a new criterion that includes some of the symptoms from DSM-IV C. DSM-5 D states do not require traumatic reminders in order to occur. • This includes, with some wording changes, DSM-IV C3, C4, C5, and C6. • A total of three or more of the former combined C and D symptoms are still required for children over age 6. • D1 changes "inability to recall" to "inability to remember," and notes that this is typically due to dissociative amnesia rather than to injury or substances. • DSM-IV C7 (sense of foreshortened future) is replaced by D2—persistent, exaggerated negative beliefs or expectations about self, others, or the world. • D3, like D2, includes symptoms that have been included among complicated trauma reactions—persistent distortions related to blame of self or others. • Instead of DSM-IV C6 (restricted range of affect), D4 delineates persistent negative emotional state (also included in complex trauma symptom lists), and D7 notes a persistent inability to experience positive emotions.

(continued)

TABLE 10.1. *(continued)*

Criterion	PTSD: DSM-5 criteria	Differences from DSM-IV criteria
E: Arousal and reactivity	E. Marked alterations in arousal or reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following: 1. Irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects. 2. Reckless and self-destructive behavior. 3. Hypervigilance. 4. Exaggerated startle response. 5. Problems with concentration. 6. Sleep disturbance (e.g., difficulty falling or staying asleep or restless sleep).	• DSM-5 E symptoms are similar to DSM-IV Criterion D symptoms. They are listed in a different order. • E1 specifies that irritable and angry behaviors are not provoked or occur after little provocation. It notes that the anger and irritability are typically expressed aggressively. • E2 (reckless or self-destructive behavior) is added to the symptom list. • E6 (sleep disturbance) replaces DSM-IV D1 (difficulty falling or staying asleep), and adds "restless sleep" as an example of sleep disturbance.
F: Duration	F. Duration of the disturbance (Criteria B, C, D, and E) is more than 1 month.	
G: Impairment	G. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.	
H: Rule-out	H. The disturbance is not attributable to the physiological effects of a substance (e.g., medication, alcohol) or another medical condition.	Added within criteria list.
Specify whether:	*Specify* whether: **With dissociative symptoms**: The individual's symptoms meet the criteria for posttraumatic stress disorder, and in addition, in response to the stressor, the individual experiences persistent or recurrent symptoms of either of the following: 1. **Depersonalization**: Persistent or recurrent experiences of feeling detached from and as if one were an outside observer of, one's mental processes or body (e.g., feeling as though one were in a dream; feeling a sense of unreality of self or body or of time moving slowly). 2. **Derealization**: Persistent or recurrent experiences of unreality of surroundings (e.g., the world around the individual is experienced as unreal, dreamlike, distant, or distorted). **Note**: To use this subtype, the dissociative symptoms must not be attributable to the physiological effects of a substance (e.g., blackouts, behavior during alcohol intoxication) or another medical condition (e.g., complex partial seizures).	Added.
Specify if:	*Specify* if: **With delayed expression:** If the full diagnostic criteria are not met until at least 6 months after the event (although the onset and expression of some symptoms may be immediate).	Changes "delayed onset" to "delayed expression" and specifies that some symptoms may precede a full diagnosis.

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of the event, Criterion D does not require reminders to trigger the described emotional states (Scheeringa et al., 2012). D includes some of the symptoms described for complicated reactions (D2–D4 and D7). Sometimes with additional clarification, DSM-5 D retains DSM-IV C3 (inability to remember an important aspect of the trauma; now D1), C4 (diminished interest or participation; now D5), and C5 (detachment or estrangement; now D6). It has changed DSM-IV C6 (restricted range of affect) to pervasive negative emotional states (D4) and persistent inability to experience positive emotions (D7) for older children and adults (C3 and C6 for children 6 and younger; see below). C7 (foreshortened future) has been revised as D2, which better describes posttrauma pessimism: negative expectations of self, others, and the world. Discussed by clinicians as a part of complicated trauma reactions, distorted self-blame or blame of others has been added as D3. For adults, some evidence suggests that requiring both numbing and avoidance reduces the number of PTSD cases, probably by reducing spurious PTSD in those with depression (Forbes et al., 2011). In contrast to PTSD in children 6 years and younger, and contrary to some recommendations (Scheeringa, 2011), children ages 6–12 are still required to have a combined three symptoms from the DSM-5 C and D lists. Future research will determine whether this requirement results in underidentification of trauma-related impairment in youth. Arousal symptoms—DSM-IV Criterion D—are now DSM-5 Criterion E (arousal and reactivity). Criterion E clarifies that outbursts of anger and irritable behaviors are typically expressed as verbal or physical aggressiveness toward people or objects (E1). Reckless or self-destructive behavior—another symptom included in descriptions of complex trauma—is now included as E2. DSM-5 notes that auditory pseudohallucinations (e.g., hearing thoughts spoken in other voices) and paranoid ideation may be associated with PTSD. Repeated or severe traumas may result in difficulties with regulating emotions or maintaining stable interpersonal relationships, or in dissociative symptoms.

PTSD FOR CHILDREN 6 YEARS AND YOUNGER

Evidence has supported the inclusion in DSM-5 of a new diagnosis, PTSD for children 6 years and younger (hereafter abbreviated as PTSD-6; De Young, Kenardy, & Cobham, 2011; Scheeringa, 2011; Scheeringa et al., 2012; Table 10.2). PTSD-6 is an altered version of the criteria for adults, adolescents, and older children (Table 10.1), with differences in algorithms and some symptoms. In a study of preschoolers comparing DSM-IV PTSD, DSM-IV PTSD with an altered algorithm (Scheeringa, Zeanah, Myers, & Putnam, 2005), proposed DSM-5 PTSD-6, and DSM-5 proposed PTSD-6 plus other symptoms that were under consideration for inclusion, Scheeringa and colleagues (2012) found high agreement on the presence of PTSD, but low agreement on its absence. Misclassified cases were highly symptomatic. Using DSM-5 proposed PTSD-6 to assess preschoolers resulted in significantly more cases of PTSD than using DSM-IV PTSD did. The additional cases were all highly symptomatic and impaired (see also De Young et al., 2011).

As recommended by Scheeringa and colleagues, PTSD-6 requires only one symptom from the adult/adolescent/older child C and D lists. PTSD-6 primarily focuses on observable behaviors, rather than subjective symptoms that young children may not be able to report (see Table 10.2). The DSM-5 exclusion of DSM-IV Criterion A2 concerning intense or observable reactions is particularly important for this age group because such reactions are not always observable in very young children, who are often unable to report such reactions for themselves (Scheeringa, 2011). DSM-5 also recognizes the importance of caregivers to young children: Criterion A2 (witnessing) includes "especially primary caregivers," and A3 (learning of event) specifies that the event occurred to a parent or caregiving figure. Studies of cortisol have suggested that loss of or separation from a parent is particularly important to children ages 4 or under (see Nader & Weems, 2011). Intentional self-harm (Scheeringa et al., 2012); partial amnesia (DSM-5 PTSD D1); cognitions about self, others, and the world (DSM-5 PTSD D2); and blame (DSM-5 PTSD D3) are difficult to confirm in very young children and are not included in DSM-5 PTSD-6. Reckless and self-destructive behavior (DSM-5 PTSD E2) is also excluded from PTSD-6. Among associated features of PTSD, young children may experience developmental regression (e.g., loss of language), difficulties regulating emotions or maintaining stable interpersonal relationships, or dissociative symptoms.

Complicated Traumatic Reactions

Variously referred to as complex or complicated trauma, disorders of extreme stress not otherwise specified, or developmental trauma disorder (DTD), complex trauma is a form of post-trauma reaction that is

TABLE 10.2. DSM-5 Diagnostic Criteria for PTSD for Children 6 Years and Younger (PTSD-6)

Criterion	PTSD-6: DSM-5 criteria	Differences from DSM-5 PTSD criteria for adults, adolescents, and children over 6 years
A: Exposure	A. In children 6 years and younger, exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways: 1. Directly experiencing the traumatic event(s). 2. Witnessing, in person, the event(s) as it occurred to others, especially primary caregivers. **Note**: Witnessing does not include events that are witnessed only in electronic media, television, movies, or pictures. 3. Learning that the traumatic event(s) occurred to a parent or caregiving figure.	• A2 recognizes the importance of "primary caregivers" to young children. • For indirect exposure, A3 specifies that the event must have occurred to a parent or caregiving figure. • Although A4 is omitted for this age group, media exposure is excluded in a note after A2.
B: Intrusion symptoms	B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred: 1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s). **Note:** Spontaneous and intrusive memories may not necessarily appear distressing and may be expressed as play reenactment. 2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s). **Note**: It may not be possible to ascertain that the content is related to the traumatic event(s). 3. Dissociative reactions (e.g., flashbacks) in which the child feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.) Such trauma-specific reenactment may occur in play. 4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s). 5. Marked physiological reactions to reminders of the traumatic event(s).	• B1 (in note) points out that memories may not appear distressing in this age group. • B2 (in note) points out that dream content may not be ascertainable for this age group. • Slight wording differences exist in B4 and B5 ("reminders" in B5, "internal or external cues" in B4).
C: Avoidance of stimuli, or negative alterations in cognitions and mood	C. One (or more) of the following symptoms, representing either persistent avoidance of stimuli associated with the traumatic event(s) or negative alterations in cognitions and mood associated with the traumatic event(s), must be present, beginning after the event(s) or worsening after the event(s): **Persistent Avoidance of Stimuli** 1. Avoidance of or efforts to avoid activities, places, or physical reminders that arouse recollections of the traumatic event(s).	• For children age 6 or younger, C is not divided into C and D. Instead, it includes one symptom from either the avoidance or the negative cognitions/moods list. • Inasmuch as young children's memories, thoughts, and feelings may not be ascertainable, C1 and C2

(continued)

TABLE 10.2. *(continued)*

Criterion	PTSD-6: DSM-5 criteria	Differences from DSM-5 PTSD criteria for adults, adolescents, and children over 6 years
	2. Avoidance of or efforts to avoid people, conversations, or interpersonal situations that arouse recollections of the traumatic event(s). **Negative Alterations in Cognitions** 3. Substantially increased frequency of negative emotional states (e.g., fear, guilt, sadness, shame, confusion). 4. Markedly diminished interest or participation in significant activities, including constriction of play. 5. Socially withdrawn behavior. 6. Persistent reduction in expression of positive emotions.	refer to external reminders. C2 includes "people" and "interpersonal situations," in contrast to C1's "activities, places, or physical reminders." • Adult . . . PTSD D1 (amnesia), D2 (beliefs and expectations about self, others, and the world), and D3 (blame) are difficult to ascertain in young children and are omitted from the 6-years-and-under disorder. • C3 (adult . . . D4) specifies increased frequency (in contrast to persistence) of negative emotional states • C5 and C6 include observable behavior (social withdrawal and reduced expression of positive emotions), in contrast to adult . . . PTSD D6, which includes "feelings of detachment or estrangement," and D7, which includes "inability to experience positive emotions."
D: Arousal and reactivity	D. Alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following: 1. Irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects (including extreme temper tantrums). 2. Hypervigilance. 3. Exaggerated startle response. 4. Problems with concentration. 5. Sleep disturbance (e.g., difficulty falling or staying asleep or restless sleep).	• D1 adds temper tantrums to adult . . . PTSD E1. • Adult . . . PTSD E2 (reckless or self-destructive behavior) is omitted.
E: Duration	E. The duration of the disturbance is more than 1 month.	
F: Impairment	F. The disturbance causes clinically significant distress or impairment in relationships with parents, siblings, peers, or other caregivers or with school behavior.	For children age 6 and younger, the focus is on relationship impairment.
G: Rule-out	G. The disturbance is not attributable to the physiological effects of a substance (e.g., medication, alcohol) or another medical condition.	

(continued)

TABLE 10.2. *(continued)*

Criterion	PTSD-6: DSM-5 criteria	Differences from DSM-5 PTSD criteria for adults, adolescents, and children over 6 years
Specify whether	*Specify* whether: **With dissociative symptoms**: The individual's symptoms meet the criteria for posttraumatic stress disorder, and the individual experiences persistent or recurrent symptoms of either of the following: 1. **Depersonalization**: Persistent or recurrent experiences of feeling detached from, and as if one were an outside observer of, one's mental processes or body (e.g., feeling as though one were in a dream; feeling a sense of unreality of self or body or of time moving slowly). 2. **Derealization**: Persistent or recurrent experiences of unreality of surroundings (e.g., the world around the individual is experienced as unreal, dreamlike, distant, or distorted). **Note:** To use this subtype, the dissociative symptoms must not be attributable to the physiological effects of a substance (e.g., blackouts) or another medical condition (e.g., complex partial seizures).	There are slight wording differences in the first paragraph and the note.
Specify if	*Specify* if: **With delayed expression:** If the full diagnostic criteria are not met until at least 6 months after the event (although the onset and expression of some symptoms may be immediate).	

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considered more complicated than and can occur in the absence of full PTSD. Similarly, complicated grief reactions vary from normal bereavement in their intensity, duration, and/or interference with recovery from trauma. We discuss DTD and complicated grief below.

Developmental Trauma Disorder

Evidence suggests that the posttrauma reactions of a subgroup of children (Ford et al., 2009; Ford, Fraleigh, Albert, & Connor, 2010) and adolescents (Ford, Elhai, Connor, & Frueh, 2010) are not fully captured by PTSD (Ford, Grasso, et al., 2013). Such youth exhibit a range of cognitive, behavioral, and affective symptoms that may be impairing and long-lasting even if they do not meet full PTSD criteria (Danielson et al., 2010; Habib & Labruna, 2011). For example, in addition to or in the absence of a PTSD diagnosis, children who have been sexually abused have reported risky behaviors—drinking alcohol to intoxication, nonexperimental drug use, and delinquent behavior—and lifetime or recent major depressive disorder (MDD); Danielson et al., 2010). Such complex reactions may not respond to treatments for PTSD alone. Youth with multiple exposures and complicated reactions have benefited from treatments designed to enhance their ability to regulate emotions and impulsivity (Cloitre et al., 2010; Ford, Grasso, et al., 2013; Ford, Wasser, & Connor, 2011; Taylor & Harvey, 2010).

Originally represented in the DSM-III-R and DSM-IV PTSD associated symptoms, complicated trauma reactions have most often been studied in and associated with interpersonal, early, extreme, or prolonged stressors (e.g., abuse or other violence; APA, 1994; Pearlman, 2001; Pelcovitz et al., 1997; Ford, Grasso, et al., 2013; Ford, Nader, & Fletcher, 2013). A percentage of youth exposed to natural disasters and other "noninterpersonal" traumas have demonstrated the symptoms defined in the proposed definition of DTD. A body of evidence suggests that many of the symptoms are sig-

nificantly explained by polyvictimization (see Nader, in press). In 2005, clinician reports indicated that victims of prolonged interpersonal trauma, particularly early in life, had high rates of problems with (1) regulation of affect and impulses, (2) memory and attention, (3) self-perception, (4) interpersonal relations, (5) somatization, and (6) systems of meaning, which were identified as key elements in children's complex traumatic reactions (Cook et al., 2005; van der Kolk, 2005; van der Kolk et al., 2005).

The refined proposed diagnosis of DTD (van der Kolk, 2005)—which has evolved from case studies of chronically maltreated youth—is currently undergoing testing. Across development, self-regulation matures and assists prosocial relationships and productive goal-directed behaviors (Ford, 2011). Trauma, especially multiple, early, and severe traumas, may disrupt self-regulation. DTD can be understood as representing failures in self-regulation. The inventory used in the current field study to assess DTD includes impairment in developmental competencies related to affective and physiological dysregulation (tolerance/modulation of extreme affective states, sensitivity to sound or quiet and/or to touch, troublesome bodily states, dissociation, alexithymia [difficulty identifying and describing one's emotions]); attentional or behavioral dysregulation (bias toward or away from threats, lack of self-protection/looking for trouble, maladaptive attempts at self-soothing, self-harm, lack of goal-directed behavior); and self and relational dysregulation (negative self-perception, attachment and relationship difficulties, biased expectations, distrust or defiance, reactive aggression, boundary problems, dependence, lacking or excessive empathy) (Ford & Developmental Trauma Disorder Work Group, 2012). The proposed disorder may evolve over time and as we learn more about the child variables (e.g., genetic, personal history), event variables (e.g., intensity, chronicity, or multiple exposures), family variables (e.g., mental health, support giving, parenting), and other factors that may contribute to its occurrence. Some disagreement persists about the necessity of creating a disorder separate from PTSD (Scheeringa, 2011). As revised for DSM-5, PTSD includes symptoms that are included among proposed DTD symptoms. These include increased frequency of negative emotional states (e.g., fear, guilt, sadness, shame or confusion—D4); distorted blame of self or others (D3); exaggerated negative expectations (D2); reckless or self-destructive behavior (E2); and anger and aggression symptoms (E1).

Complicated Grief Reactions

Normal grieving may be complicated by a number of factors. Such factors generally disrupt, prolong, and intensify grieving, and/or grief symptoms may become intertwined with other symptoms (e.g., trauma symptoms) (Nader & Salloum, 2011). Different types of complicated grief reactions were originally proposed for study or inclusion in DSM-5, including adaptive versus maladaptive grief (Nader & Layne, 2009), bereavement-related depression (Corruble, Chouinard, Letierce, Gorwood, & Chouinard, 2009; Zisook et al., 2010), posthumous disillusionment (Stalfa, 2010), prolonged grief disorder (Boelen, van den Hout, & van den Bout, 2006; Prigerson et al., 2009), grief combined with other disturbances (Pearlman, Schwalbe, & Cloitre, 2010), and traumatic grief (Melhem, Moritz, Walker, & Shearer, 2007; Nader & Salloum, 2011). With the exception of traumatic grief and grief combined with other disturbances, most of these forms of grief have been studied primarily in adults. Each of the proposed forms may interfere with functioning, prolong grieving, and influence treatment needs (e.g., see Pearlman et al., 2010). Traumatic grief is associated with higher levels of posttraumatic symptoms, as well as with complicated or thwarted grieving (Nader & Layne, 2009). It focuses on the traumatic circumstances of a death and consequent trauma-related interference with adaptive grieving processes, whether or not the deceased is perceived as significant to the traumatized individual's survival or ability to function in life. The conceptualization of prolonged grief disorder, based primarily on the bereavement of adults who have lost a significant other, is focused primarily on the griever's attachment to the deceased. Reportedly, the individual may experience the loss as traumatic or devastating (Jacobs, 1999). It includes grief symptoms that are prolonged and intensified (Boelen et al., 2006; Prigerson et al., 2009; Shear, Jackson, Essock, Donahue, & Felton, 2006).

To a good extent in response to studies of proposed prolonged grief disorder (PGD) (Prigerson et al., 2009), a grief-related adjustment disorder has been added to DSM-5: persistent complex bereavement disorder, under the umbrella category of other specified trauma- and stressor-related disorder (309.89, example 5). The disorder is "characterized by severe and persistent grief and mourning reactions" (APA, 2013, p. 289). The disorder is additionally addressed in Section III of DSM-5 under "Conditions for Further Study" (APA, 2013, pp. 789–792). It requires that for at least 6 months for

children (12 months for adults) following the death of a close relative or friend, the individual experiences on most days, to a clinically important extent, at least one of the following: persistent longing or yearning for the dead person (which may be expressed by children in play or other behavior); severe sorrow and emotional pain; preoccupation with the dead person; and/or preoccupation with the circumstances under which the person died (which may be expressed by children in play or other behavior, or in preoccupation with possible deaths of other persons). The griever must also exhibit 6 of 12 symptoms indicating reactive distress or social/identity disruption. Symptoms must be out of proportion or inconsistent with cultural or religious norms and cause impaired functioning (see Table 10.1, G). The disorder includes specification if "with traumatic bereavement" (i.e., bereavement through murder or suicide, with continued distressing thoughts regarding the nature/circumstances of the death) (APA, 2013, p. 790).

THE STRESS RESPONSE SYSTEM

Current conceptualizations of posttraumatic reactions include a discussion of the neurobiological system. The stress response system involves a network of brain regions, including the hippocampus, amygdala, cingulate, and prefrontal cortex (PFC) (Bremner, 2006). This system also encompasses three anatomically distinct neuroendocrine circuits: the sympathetic nervous system (SNS), the parasympathetic nervous system (PNS), and the hypothalamic–pituitary–adrenocortical (HPA) axis (Del Giudice, Ellis, & Shirtcliff, 2011). A number of nontraumatic stressors may activate the SNS and the HPA axis. For example, studies of normal children suggest that prolonged or ongoing separations (e.g., foster placement, the death of a parent) may be traumatic for children under age 5, whereas intense shame and humiliation stressors may be more potent for older children and adults (Nader & Weems, 2011).

Research has demonstrated that childhood trauma influences stress reactivity in adulthood by altering HPA axis function (Heim, Plotsky, & Nemeroff, 2004; Roy, Gorodetsky, Yuan, Goldman, & Enoch, 2010). Allostasis (i.e., attaining stability through change) pertains to the body's response to internal or external, actual or threatened adverse/stressor events (Hulme, 2011). The allostasis model includes three systems that, when activated, generate the physiological adaptations required for protective behaviors: the monoaminergic neurons (serotonin, dopamine, acetylcholine, and norepinephrine), which increase arousal, vigilance, and external cue processing; the SNS, which releases epinephrine and norepinephrine to enhance cardiovascular performance, inhibit digestion, and make energy available for muscles; and the HPA axis, which produces physiological mediators—glucocorticoid hormones (cortisol in humans) that increase the conversion of proteins and lipids into the carbohydrates needed for restoring energy, increasing blood pressure and blood sugar, mobilizing amino acids, and reducing immune responses (Rodrigues, LeDoux, & Sapolsky, 2009). These physiological mediators remain elevated or lowered (in an allostatic state) in response to chronic, repeated, or severe stress (Hulme, 2011). Allostatic load (the condition of an individual's stress system) can escalate to overload characterized by stress system dysregulation and chronically high or low levels of one or more of the mediators (Hulme, 2011; McEwen & Wingfield, 2010; Seeman, Epel, Gruenewald, Karlamangla, & McEwen, 2010). This model attributes negative health states to the pathological harm from prolonged cellular exposure to altered levels of the physiological mediators (McEwen & Wingfield, 2010). For example, prolonged exposure to glucocorticoids is believed to exert a wide range of negative health effects, including effects on the brain's limbic system, which might explain many symptoms associated with PTSD and MDD (Hulme, 2011; Pruessner et al., 2010).

Trauma and the HPA Axis

The HPA axis initiates a long-term response to environmental challenges through the release of cortisol (Bremner, 2006; Del Giudice et al., 2011). Neurons in the hypothalamic paraventricular nucleus (PVN) secrete corticotropin-releasing hormone (CRH) and arginine vasopressin (AVP); in the anterior pituitary, these hormones trigger secretion of polypeptides, which then cleave into various other hormones (e.g., adrenocorticotropic hormone [ACTH] and beta-endorphin). When it reaches the adrenal cortex, ACTH stimulates cortisol release. As noted, cortisol leads to multiple, diverse physiological and metabolic changes in order to prepare the organism for optimal functioning under conditions of stress (Belsky & Pleuss, 2009). Feedback inhibition reduces stress-induced activation of the HPA axis and limits excess secretion of glucocorticoids effectively dampening the stress response (Gillespie, Phifer, Bradley, & Ressler, 2009; Jacobson & Sapolsky,

1991). Trauma may cause a disrupted feedback loop. Notably, HPA axis dysregulation includes dysregulation of CRH and AVP, resulting in increased release of plasma ACTH and cortisol, which may be coupled with glucocorticoid receptor (GR) insensitivity resulting in impairment of the negative feedback loop (Roy et al., 2010; see the discussion of genetic factors, below).

HPA axis dysregulation is implicated in a number of disorders (van Winkel, Stefanis, & Myin-Germeys, 2008). Psychosis may include increased baseline cortisol and ACTH levels (Walsh, Spelman, Sharifi, & Thakore, 2005). For those with a genetic vulnerability to depression, HPA dysregulation may compromise serotonergic system function, whereas among those with an inherited liability to psychosis, elevated cortisol may influence dopamine signaling (van Winkel et al., 2008). Some evidence suggests that social-evaluative stressors and/or their uncontrollability (Dahl & Gunnar, 2009; Jones & Fernyhough, 2007) may be important in cortisol overactivity, which may in turn mediate the effects of stress in either triggering or worsening symptoms of psychosis-vulnerable individuals (van Winkel et al., 2008; *Walker, Mittal, & Tessner, 2008).

Cortisol Response

Generally, fear and stress reactions are associated with elevations in the secretion of cortisol (Weems & Carrion, 2009). As noted above, prolonged activation may lead to sensitization or desensitization. Disturbances in reactivity may be upward or downward; that is, they may manifest as hyper- or hypocortisolism (McCleery & Harvey, 2004). The HPA axis responds to chronic stressors with sustained cortisol elevation, and thus a flattened diurnal pattern of release (Del Giudice et al., 2011; Miller, Chen, & Zhou, 2007). Chronic cortisol elevation is frequently followed by rebound below previous baseline levels after stressor termination (Koob & Le Moal, 2008). Consequent hypocortisolism may last for months. PTSD studies have shown lower, not different, or increased baseline cortisol levels. Both excessive and dampened cortisol reactivity to acute stress or neuroendocrine challenge have been associated with disease in humans (Carpenter et al., 2009).

Findings suggest different reasons for variations in cortisol reactivity following traumas: the type or nature of the trauma, a person's age, the length of time since the trauma, the time of assessment of cortisol, emotions elicited during the stressor, or the controllability of the stress, as well as comorbidity, attachment, personality/temperament, or other variables (De Bellis, 2001; Nader & Weems, 2011). For example, whereas lower cortisol levels have generally been associated with externalizing disorders, extraverted traits (in the absence of social stress), and years since trauma exposure, higher cortisol levels often have been associated with internalizing, inhibited, or introverted traits or types and with recent stress exposure, although with externalizing behaviors in preschoolers (Hulme, 2011; Nader & Weems, 2011; Young & Veldhuis, 2006).

For adults, cortisol is evoked when unpredictability, uncontrollability (i.e., over a situation or outcome), and social-evaluative threat (i.e., potential negative appraisal by others) combine (Dickerson & Kemeny, 2004). For children over age 4, as well, stressor paradigms are ineffective in elevating cortisol unless the task also evokes negative self-referent emotions such as shame or embarrassment (Gunnar, Talge, & Herrara, 2009). Although their baseline levels have been low, several studies have demonstrated exaggerated release of cortisol for women abused as children, in response to traumatic reminders and other stressors (Bremner, 2006). Some adult studies (e.g., of cortisol levels, using problem solving under stress) show that patients with PTSD have increased baseline cortisol levels in a prestress period consistent with anticipatory anxiety, and lower 24-hour cortisol during a resting period, compared to controls. Although both control groups and groups with PTSD have had increased cortisol during a challenge, levels were higher in the groups with PTSD. In response to traumatic reminders, adult female abuse victims with PTSD had fourfold higher increases in cortisol compared to female abuse victims without PTSD. Women abused in childhood who have depression have had an increase in cortisol response to stressful cognitive challenges compared to controls, as well as a blunted ACTH response to CRF challenge (Bremner, 2006). Child cortisol levels also have been correlated with the extent of maternal depressive symptoms (Lupien, King, Meaney, & McEwen, 2000) and with low SES while residing in urban areas with high trauma exposure beginning at an early age (Shonkoff, Boyce, & McEwen, 2009).

Brain Mechanisms

One of the mechanisms by which HPA axis dysregulation occurs is through glucocorticoid stimulation of the basolateral amygdala (in contrast to their inhibitory influence in the hippocampus and medial PFC) (Hulme,

2011). In turn, this process stimulates the HPA axis in a feedforward loop. Stimulation of the basolateral amygdala is anxiety-producing. The feedforward loop perpetuates anxiety (Mitra & Sapolsky, 2008; see the discussion below of the FKPB5 gene region).

BRAIN ACTIVITY AND VOLUME

Trauma has been associated with multiple brain-related influences, such as influences on brain activity (e.g., HPA reactivity), brain receptors (e.g., serotonin, gamma-aminobutyric acid receptors), and synaptic connectivity that contribute to cognitive functioning, regulation of mood and affect, and social attachment, among other aspects of behavior and emotional response (Anda et al., 2006; De Bellis, Baum, et al., 1999; Nader, in press). Prolonged or severe stress may affect the growth of brain regions (e.g., atrophy or death of neurons) and/or alter neurochemistry (Anda et al., 2006; Byrnes, 2001; Lupien, McEwen, Gunnar, & Heim, 2009; Sapolsky, 1998). It is associated with age-related reductions in brain volume for traumatized youth (Carrion, Weems, Richert, Hoffman, & Reiss, 2010; De Bellis et al., 2002). Stress-related brain changes, in turn, can alter physiological systems including immune response. Either overactivation (e.g., fear-inducing traumas) or underactivation (e.g., neglect) of important neural systems during critical periods may have a profound effect on child development (Perry, Pollard, Blakely, Baker, & Vigilante, 1995). Maltreated children with PTSD have had smaller intracranial and cerebral volumes than matched controls (De Bellis, Keshavan, et al., 1999). Brain volume has correlated positively with age of onset of PTSD and negatively with duration of abuse. Adults with early abuse-related PTSD have smaller hippocampal volumes than comparisons (Bremner, 2006). Although the hippocampus can grow new neurons (neurogenesis) even in adulthood (Bremner, 2006), childhood stressors can cause long-term increases in cortisol responses to stress, and stress and/or deprivation inhibits neurogenesis.

Studies suggest that childhood or adolescent PTSD may alter anterior cingulate neuronal metabolism. This structure is associated with attention (De Bellis, Keshavan, Spencer, & Hall, 2000) and is active during tasks involving conflict, which may suggest a means by which attentional disturbances arise in PTSD. Brain impairment in an infant's first 18 months of life is associated with abnormal social and moral development and with a later syndrome resembling psychopathy. During adolescence, the PFC and its connectivity to other brain regions may be particularly vulnerable to trauma (Blakemore & Choudhury, 2006). For children ages 10–17, Carrion and colleagues (2010) found that, compared to healthy controls, youth with PTSD symptoms had significantly decreased total brain tissue and total cerebral gray volumes. Even after the researchers controlled for total cerebral gray volume, the group with PTSD symptoms had decreased left ventral and left inferior prefrontal gray volumes. Disruptions to the functioning of the cortex, particularly the PFC, by exposure to extreme stress may influence the inhibition of the stress response as well as self-regulation, attention, organization, and planning (Rothbart & Rueda, 2005; Stein & Kendall, 2004; Stevens, Kiehl, Pearlson, & Calhoun, 2007).

GENETICS AND TRAUMA'S IMPACT ON COGNITIVE FUNCTIONING

In addition to a marked increase in risk of psychopathology (e.g., PTSD, depression, bipolar disorder, schizophrenia), exposure to early life trauma produces a cascade of neurobiological changes associated with adulthood cognitive deficits (Gould et al., 2012; Savitz, van der Merwe, Stein, et al., 2007). Age during trauma exposure may have critical implications for lifelong functioning, and results may vary by the type of trauma experienced. Gould and colleagues (2012) found that cognitive test performance (i.e., on tasks assessing visual memory and executive functioning) discriminated patients maltreated as children from healthy controls. For instance, emotional processing and processing speed deficits were seen in those with a history of neglect, and relatively more diverse executive functioning deficits (e.g., in spatial working memory) were seen in those with a history of sexual abuse. Visual memory deficits found in patients with histories of emotional abuse, physical abuse, and neglect may be partially explained by HPA axis alterations associated with early life trauma. Cognitive deficits have been associated with MDD (Castaneda, Annamari, Marttunen, Suvisaari, & Lonnqvist, 2008; Hasselbalch, Knorr, & Kessing, 2010) and with DSM-IV anxiety disorders including PTSD (Castaneda et al., 2008; Liberzon & Sripada, 2008).

Neurotrophins play an important role in mediating the relationship between stress and changes in HPA axis activity (Savitz, van der Merwe, Stein, et al., 2007). Studies suggest that the methionine (Met) allele

of a functional variant of the brain-derived neurotrophic factor (BDNF) gene (Val66Met) is associated with poorer memory and a disruption of a normal hippocampal disengagement pattern during memory task (Egan et al., 2003; Hariri et al., 2003; Savitz, van der Merwe, Stein, et al., 2007). The valine (Val) allele is believed to be associated with bipolar disorder, schizophrenia, and reduced cognitive performance. In addition to decreased executive and memory function, the low-activity Met allele has played a crucial role in mediating neural plasticity in response to aversive social experiences and neurotoxins (Berton et al., 2006; Tsankova et al., 2006). Both acute and chronic stress have been reported to inhibit hippocampal BDNF synthesis (Savitz, van der Merwe, Stein, et al., 2007; Tsankova et al., 2006). Savitz, van der Merwe, Stein, and colleagues (2007) found that after they controlled for other variables, the self-reported extent of childhood sexual abuse and of childhood neglect were weakly negatively associated with memory performance, but that the low-activity Met allele of the BDNF gene and the ε4 allele of the apolipoprotein E (ApoE) gene interacted with sexual abuse scores to result in reduced memory test performance. In their study, the Met allele was associated with a negative effect of sexual abuse on memory performance, in contrast to the Val allele, which had no effect. That is, the Val/Val homozygotes (with no Met alleles) demonstrated no decline in memory score with increases in sexual abuse scores, in contrast to the Met/Met homozygotes, whose memory scores decreased sharply with increasing sexual abuse scores. The effect of the Met allele appeared to be additive. For the ApoE *4* allele (a risk factor for Alzheimer's disease and later-life impaired cognition), memory scores were the same when there was no sexual abuse, but rapidly decreased with increasing sexual abuse scores in individuals with one ε4 allele. Savitz, van der Merwe, Stein, and colleagues (2007) suggest the possibility that when there is an environmentally or genetically induced HPA disturbance, the low-activity BDNF Met allele is a risk factor for memory dysfunction. In contrast, the high activity BDNF Val allele might partially counteract the stress-induced inhibition of BDNF synthesis and the adverse cortisol-related effects on hippocampal function.

In findings unrelated to abuse, the low-activity Met allele of the Val66Met polymorphism was associated with lower levels of self-reported dissociation (Savitz, van der Merwe, Newman, et al., 2007). The functional catechol-*O*-methyltransferase (COMT) Val158Met polymorphism interacted significantly with abuse scores to influence perceived dissociation. The Val/Val genotype was associated with increasing levels of dissociation in participants exposed to higher levels of childhood trauma. In contrast, the Met/Met genotypes displayed decreased dissociation with increasing self-reported childhood trauma. More study is needed.

OTHER CHANGES IN GENETIC EXPRESSION

Trauma may result in other changes that alter genetic expression. For example, altered GR gene expression influences stress-regulatory functioning, with resulting increased risk for psychopathology (McGowan et al., 2009). Exposure to stressful events during childhood development consistently demonstrates long-lasting alterations in the HPA axis, which in turn may increase vulnerability to disease and disorders, such as PTSD and other mood and anxiety disorders (Gillespie et al., 2009). These effects may be mediated in part by gene–environment interactions. From the brains of deceased suicide victims, McGowan and colleagues (2009) found that GR gene expression in the suicide victims' hippocampus decreased *only* for the group with abuse experiences. Sarapas and colleagues (2011) found that 25 gene sets—those generally involved in the HPA axis, signal transduction, or brain and immune cell function—were differentially expressed in PTSD. Among them were STAT5B (a direct inhibitor of GR sensitivity) and nuclear factor I/A, which showed reduced expression in PTSD (see also Yehuda et al., 2009).

THE FKBP5 GENETIC REGION

GR activation and ligand binding are moderated by a large molecular complex that includes FKBP5 (Roy et al., 2010). Although for individuals without PTSD, the alleles previously associated with high FKBP5 protein/messenger RNA expression are associated with GR resistance (i.e., FKBP5 inhibits GR), this association appears to be switched for patients with PTSD symptoms, who exhibit increased GR sensitivity (Binder et al., 2008). FKBP5 and major histocompatibility complex (MHC) Class II have state markers (Sarapas et al., 2011), with reduced expression in PTSD, consistent with enhanced GR responsiveness (Yehuda et al., 2009). When entered with PTSD severity, FKBP5 expression has been predicted by cortisol in regression analyses and has been reduced for individuals with PTSD (Yehuda et al., 2009). Similarly, STAT5B di-

rectly inhibits the nuclear translocation of activated GR and is also down-regulated in individuals with PTSD. Such decreased expression (both genes) is consistent with higher GR activity for PTSD. Reduced expression of MHC Class II genes is consistent with observations of abnormally reduced cortisol levels in these patients.

TELOMERE LENGTH

Telomeres are DNA repeats that cap the ends of chromosomes and promote stability. Inasmuch as they shorten progressively with each cell division, their length is a marker of biological aging (Tyrka et al., 2010). Recent studies have implicated advanced cellular aging as a potential mechanism by which psychological stress and trauma are linked to medical illnesses. Notably, Tyrka and colleagues (2010) found that participants with a history of childhood maltreatment (e.g., moderate to severe physical or emotional neglect) had significantly shorter telomeres—not explained by the effects of age, sex, smoking, body mass index, or other demographic factors—than comparison participants. Glucocorticoids have been shown to increase neuronal oxidative stress damage, which may explain the telomere shortening (Ceccatelli, Tamm, Zhang, & Chen, 2007).

THE NORADRENERGIC SYSTEM

The noradrenergic system also is involved in stress (Bremner, 2006) and in anxiety disorders (e.g., panic, DSM-IV PTSD, generalized anxiety disorder; Kalk, Nutt, & Lingford-Hughes, 2011). Stress exposure results in activation of the locus coeruleus and release of norepinephrine throughout the brain. Whereas acute stressors result in an acute increase in firing of neurons in the locus coeruleus and increased release of norepinephrine in the hippocampus and medial prefrontal cortex, chronic stress is associated with potentiated release of norepinephrine in the hippocampus with exposure to subsequent stressors. Epinephrine and norepinephrine increase SNS activity—heart rate, blood pressure, respiration, conversion of glycogen to glucose, lypolysis (conversion of fats to fatty acids), muscle tone, and alertness (Byrnes, 2001; Stein & Kendall, 2004). Attention narrows, and neurons become more sensitive to danger-related stimuli. PTSD symptoms have been stimulated through activation of the brain noradrenergic system (Bremner et al., 1997). Heightened norepinephrine may directly enhance memory for the traumatic event and contribute to hyperarousal, flashbacks, intrusive memories, and nightmares. Studies of individuals with PTSD have shown increased norepinephrine in blood and urine at baseline and in response to traumatic reminders (Bremner, 2006; Kalk et al., 2011). For PTSD, evidence suggests a peripheral alteration in the release of norepinephrine over time, reflected in increased excretion over hours (Kalk et al., 2011). Additionally, postmortem evidence from a small sample of veterans (Bracha, Garcia-Rill, Mrak, & Skinner, 2005) found noradrenergic abnormalities in vets with PTSD (evidenced by decreased cell numbers in the locus coeruleus), in contrast to vets with no psychiatric history or with alcoholism only.

EPIDEMIOLOGY

Prevalence/Incidence

Studies suggest that approximately 70–80% or more of individuals in the United States are exposed to one or more traumatic events in their lifetimes (Breslau, 2009; Gabert-Quillen, Fallon, & Delahanty, 2011). Millions of children each year (approximately two-thirds of children) are exposed to traumas such as maltreatment, war, other violence, accidents, natural disasters, and human-made disasters. In a longitudinal community sample of adolescents (N = 1,420), approximately 68% had experienced at least one traumatic event by age 16 (Copeland, Keeler, Angold, & Costello, 2007). In Ireland (Shannon, Maguire, Anderson, Meenagh, & Mulholland, 2011), 65% of adults reported moderate to severe childhood traumas. Multiple types of exposure (polyvictimization) are more highly associated with trauma symptoms than are repeated victimizations of a single type, and polyvictimization explains a large proportion of the associations between individual forms of victimization and symptom levels (Turner, Finkelhor, & Ormrod, 2010). In a San Francisco pediatric child health center, most of the low-income children assessed (67.2%) had experienced one or more adverse events (Burke, Hellman, Scott, Weems, & Carrion, 2011); 12% had experienced four or more such events. In a U.S. national sample of youth ages 2–17 (Finkelhor, Ormrod, & Turner, 2007a), 71% had experienced victimization, and 69% had experienced more than one type of victimization. For a larger national sample of youth (N = 4,053), Turner and colleagues (2010) reported that 66% of children and adolescents reported exposure to more than one type of victimization. Almost one-third reported at least five separate types, and 10% reported 11 or more types of victimization. For maltreatment alone,

in the U.S. federal fiscal year 2010 (U.S. Department of Health and Human Services, 2011), one-fifth of adjudicated maltreatment cases (3.6 million) were substantiated. Of substantiated cases, 78.3% were neglected, 17.6% physically abused, and 9.2% sexually abused.

Variations in Response to Exposure

As will be discussed, trauma or adversity has a role in the emergence of other disorders as well as PTSD. DSM-IV disorders are highly prevalent and persistent (e.g., in U.S. adolescents; Kessler et al., 2012). In the National Comorbidity Survey (N = 10,148 youth ages 13–17), more than half of adolescents met lifetime criteria for any DSM-IV disorder (Merikangas et al., 2010). Anxiety disorders were the most common disorder class, followed by behavior, mood, and substance use disorders (Kessler et al., 2012). There is generally a lower prevalence of a variety of disorders among adolescents with only one sibling versus two or more siblings; moreover, prevalence is lower in rural versus urban locations and lower in the U.S. South versus other regions of the country, although these latter findings are inconsistently related. Anxiety and behavior disorders tend to be more often chronic than mood and substance use disorders. Kessler and colleagues (2012) found that persistence is more prevalent for adolescents than for adults, apparently due more to recurrence than chronicity.

Only a minority of individuals exposed to a trauma develop PTSD, suggesting that vulnerability factors in addition to exposure increase the likelihood of the disorder (Adler, Kunz, Chua, Rotrosen, & Resnick, 2004; see "Risk and Protective Factors," below). The percentage of individuals who develop PTSD following traumatic experience varies by study and in relationship to type of event, nature of exposure, number of traumas, and other variables. Meta-analysis of 1990s studies of individuals exposed to specific traumas (Fletcher, 2003) found an overall PTSD prevalence rate of 36%: 39% of preschool children, 33% of school-age children, 27% of adolescents (2,697 youth from 34 samples; Fletcher, 1994), and 24% of adults (3,495 adults from five samples described in den Velde et al., 1993; Kilpatrick & Resnick, 1992; Smith & North, 1993). Pynoos and colleagues (1987) reported that children were at least as likely as adults to be diagnosed with PTSD (27% of children vs. 19% of adults met DSM-III-R criteria for PTSD—not a significant difference). Evidence also suggests a more unremitting course of PTSD for children compared to adults (Scheeringa, 2011; Scheeringa et al., 2005; see also our later discussion of delayed-expression PTSD). Additionally, Ford, Grasso, and colleagues (2013) relate that 10–30% of youth trauma victims who experience multiple victimizations are at risk of developing sequelae that are not fully captured by a PTSD diagnosis (see our earlier discussion of complicated traumatic reactions). In contrast to trauma-exposed samples, PTSD prevalence rates for national samples of adolescents were 4% (1.4% severe; Merikangas et al., 2010) and 8.1% (between ages 12 and 17; Kilpatrick & Saunders, 2003). This compares to 6.8% of adults (1.3% severe; Kessler, Berglund, Demler, Jin, & Walters, 2005). Lifetime prevalence of PTSD was 6.6% for females and 1.6% for males; 2.7% for 13- to 14-year-olds, 4.2% for 15- to 16-year-olds, and 5.8% for 16- to 17-year-olds.

Meta-Analysis of DSM-IV PTSD Symptoms in Children

Based on data from the 1990s, incidence rates for all DSM-IV PTSD symptoms among traumatized children were higher than 20% on average, with the exception of a pessimistic outlook on the future (16%; now revised in DSM-5 D2) and an inability to remember parts of the trauma (12%) (Fletcher, 2003). Seven of the 11 highest-ranked DSM-IV symptoms for children of all ages (excluding studies of 50 or fewer children) were symptoms of Criterion B, reexperiencing the trauma: feeling or showing distress at reminders of the trauma (51%); reenactment of significant parts of the event, such as actions, gestures, and sounds (40%); feeling as if the event were being reexperienced (39%); intrusive memories of the events (34%); bad dreams (31%); trauma-specific fears (31%); and talking excessively about the events (31%). Also included among the 11 symptoms with the highest incidence rates were 3 symptoms of the DSM-IV avoidance/numbing criterion (Criterion C): affective numbing (47%); loss of interest in previously important activities (36%); and avoidance of reminders of the events (32%). One symptom of the DSM-IV overarousal criterion (Criterion D) was included among the 11 most reported childhood symptoms: difficulty concentrating (41%).

Incidence rates for half of the 14 possible DSM-IV PTSD associated symptoms were greater than 20%: those for dissociative response (48%; now DSM-5 B3 and the "with dissociative symptoms" specifier), guilt (43%; DSM-5 D4), generalized anxiety or fears (39%; DSM-5 D4), low self-esteem (34%; included in part in DSM-5 D2), omen formation (26%), depression (25%; see DSM-5 D7), and separation anxiety (23%).

The least likely associated symptoms to be observed among traumatized children were self-destructive behavior (9%), panic attacks (8%), eating problems (7%), a warped time perspective (4%), and sleepwalking (1%). The associated symptoms of PTSD have been discussed as a part of more complex trauma reactions. Potential mediating and moderating variables that may influence symptom occurrence were not included in the percentages discussed above, and DSM-5 wording changes may alter prevalence in future samples. For example, aggressive or antisocial behavior is observed in 18% of traumatized children, on average. Regressive behavior is observed 13% of the time. However, symptom rates may be influenced by variables such as age and comorbidity.

Gender

Gender findings for PTSD and for disorders in general are mixed (Kessler et al., 2012; Nader, 2008). Some research shows increased trauma symptoms for girls (Abdeen et al., 2008) and a more consistent course for DSM-IV mood and anxiety disorders for girls (Kessler et al., 2012), whereas other research shows no posttrauma differences between the sexes (Carrion et al., 2002; Fletcher, 2003; La Greca, Silverman, Vernberg, & Prinstein, 1996; McFarlane, Policansky, & Irwin, 1987; Meiser-Stedman et al., 2007; Nader, 2008; Nader, Pynoos, Fairbanks, & Frederick, 1990; Pfefferbaum et al., 1999; Pynoos et al., 1987; Stallard, Velleman, Langsford, & Baldwin, 2001; Udwin et al., 2000). Occasionally, males have been found to have more symptoms than females (Seedat, Nyamai, Njenga, Vythilingum, & Stein, 2004). Some evidence suggests an increase in symptoms for females with age, but a decrease in symptoms for males with age (Korol, Green, & Gleser, 1999). When differences were found, they have often been modest (Silverman & La Greca, 2002). As will be discussed, some researchers suggest that the differences are related to differences in types of trauma or degree of exposure or methodological problems (e.g., asking all genders and cultures the same set of questions; Gross & Graham-Bermann, 2006).

General Gender Findings

In general, across cultures, evidence suggests that women are twice as likely to develop PTSD as men, and that their symptoms last up to four times longer than those of men (Norris, Foster, & Weisshaar, 2002). Gender differences are less apparent in young children. Studies of adults have confirmed the importance of perception. In addition to the effects of variables such as peritraumatic dissociation and distress, subjective perception rather than objective assessment of injury severity is a more consistent predictor of acute and chronic traumatic stress symptoms after a traumatic event (Gabert-Quillen et al., 2011). Adult studies suggest that, compared to men, women experience comparable threats as more threatening. Similarly, gender differences in perception of threat and danger have been found for children and adolescents (e.g., Brody, Lovas, & Hay, 1995; Muldoon, 2003). Some events may be more threatening for youth because of their reduced ability to protect themselves. Gender differences exist in help seeking and social support as well (Laufer & Solomon, 2009). For adults and children, social support can serve as a protective factor after a traumatic event (Gross & Graham-Bermann, 2006; Nader, 2008). For a large sample of war- and terrorism-exposed Israeli youth, Laufer and Solomon (2009) concluded that gender differences in PTSD are largely the result of differences in levels of fear, rather than differences in political ideology, religiosity, or social support. They found that gender was not a direct predictor of PTSD; however, it had an indirect effect, especially through fear. Although religiosity and ideological intolerance were positive predictors of PTSD, fear was the best predictor of PTSD. Similar to Abdeen and colleagues' (2008) findings, although girls reported higher fear levels and more posttraumatic symptoms than boys, more boys reported suffering from very severe symptoms. Girls tended to seek help from family and friends, while boys sought more professional help. Some studies have found more internalizing symptoms for girls (e.g., anxiety, depression) and more externalizing symptoms for boys (e.g., aggression, delinquency; Ho & Cheung, 2010). However, Ho and Cheung (2010) found a similar negative impact on adjustment outcomes for both genders.

Variables Implicated in Gender Findings

Studies of both adults and youth suggest that the higher female PTSD prevalence rates are due to differences in types of trauma experienced (e.g., girls' higher exposure to sexual assault, boys' higher exposure to community or wartime violence), in cognitive reactions (e.g., higher perceived risk and lack of control), or in psychological and psychophysiological reactions (e.g.,

stronger short-term reactions among women) (Abdeen et al., 2008; Catani et al., 2009; Goenjian et al., 2001; Olff, Langeland, Draijer, & Gersons, 2007). Other factors may include variations in exposure (e.g., more losses in secondary social networks, greater impact of secondary network losses for females; Hughes et al., 2011); differences in previous traumatic experience; differences in previous depression or anxiety; gender bias in reporting symptoms; or complex interrelationships of variables such as gender, socioeconomic status (SES), child traits/history, or race (Breslau, 2009).

For example, for a sample of Hong Kong youth, Ho and Cheung (2010) found that boys witnessed more community violence than girls, and girls witnessed and experienced more domestic violence than boys. In a study of Palestinian youth ages 14–17 (West Bank and Gaza; Abdeen et al., 2008), boys reported more direct exposure to violence, and girls reported more witnessing. Although no gender differences were found in the total Palestinian population, an interaction effect suggested that directly exposed boys had greater PTSD severity than girls, whereas girls who witnessed direct exposure had more PTSD than boys. No gender differences were found in severity of functional impairment or between exposure level and the severity of functional impairment. In general, social acceptance of experiencing and reporting distress and willingness to acknowledge and report distress is often higher for girls than boys, but may not necessarily reflect the actual level of experienced distress (Durakovic-Belko, Kulenovic, & Dapic, 2003; Laufer & Solomon, 2009). Other variables implicated in mixed findings for genders are age or differences in the timing for the genders of specific types of development—for instance, postpubertal peaks in synaptic proliferation (Blakemore & Choudhury, 2006), aspects of event-related potentials (an electroencephalogram index of attentional resources; Iacono & McGue, 2006), specific types of maturity such as sociocognitive and behavioral risk factors for aggression (Aber, Brown, & Jones, 2003; Rutter, 2003), and patterns of self-esteem (Twenge & Campbell, 2001; see Nader, 2008, in press).

Socioeconomic Status

Researchers have found that disadvantaged SES is a powerful correlate of deleterious effects on cognitive, intellectual, social, and emotional development (Nader, 2008; Yates, Egeland, & Sroufe, 2003), including a number of negative posttraumatic health and mental health outcomes in youth (e.g., PTSD; Han et al., 2011; Luthar, 2003; Nader, 2008; Yates et al., 2003). Multiple factors related to SES may increase the likelihood of traumatic reactions. For example, low SES may increase family stress, mobility, and psychiatric history, which have all been linked to children's stress reactions. Disadvantaged communities often struggle with higher unemployment rates (including fewer available jobs), access to fewer resources, declines in social organization, and a reduced sense of efficacy among residents (Deardorff, Gonzales, & Sandler, 2003). Family/neighborhood poverty/disadvantage, often found in U.S. inner cities, and family psychopathology appear to increase the likelihood of exposure to traumatic events (Brand, Schechter, Hammen, Le Brocque, & Brennan, 2011). More study is needed on the influence of specific and combined aspects of family demographics. For example, in contrast to the link between poverty and family violence (Tolan, Gorman-Smith, & Henry, 2006), in a study of Afghan war-exposed children, poverty did not significantly predict family violence (Catani et al., 2009). Additionally, although Kessler and colleagues (2012) found in common with other researchers that family SES was inversely related to disorder prevalence, in their research the association was significant for parental education, and the effects for SES disappeared after the investigators controlled for education.

Culture

Cultures vary, for example, in the beliefs and behaviors that are considered normal; in what is more or less accepted in girls versus in boys (Ahadi, Rothbart, & Ye, 1993; Heinonen, Räikönnen, & Keltikangas-Järvinen, 2003; Nader, 2008); and in socially expected and acceptable manners of expressing distress (Nader, Dubrow, & Stamm, 1999). Consequently, the form, frequency, and predictive significance of different child behaviors vary across cultures (Nader, 2008). For example, although in Western cultures shyness and oversensitivity in children have been associated with vulnerability, peer rejection, and social maladjustment, in some Eastern cultures (e.g., Shanghai Chinese children) these same traits are associated with leadership, school competence, and academic achievement (Ahadi et al., 1993; Chen, Rubin, & Li, 1995; Mash & Barkley, 2003; Mills, 2001). Because different cultures promote specific coping strategies to deal with stress (Shiang, 2000), culture is an important consideration in making assessments, interpreting findings, and creating

interventions. Pole, Best, Metzler, and Marmar (2005) observed that Puerto Ricans may be more vulnerable to PTSD than other Hispanic groups, as evidenced in studies observing no Hispanic effect that have tended not to include Caribbean Hispanics. Although the DSM-IV diagnosis of PTSD has been well validated in Western (e.g., U.S., Northern and Western European, Australian) cultures, some researchers question its applicability to non-Western cultures. For example, Rajkumar, Mohan, and Tharyan (2011) found a prevalence rate over 15% for PTSD in Indian villages following the 2004 Asian tsunami. PTSD symptoms were significantly associated with traumatic grief, female gender, physical injury, death of children, and financial losses, but not with functional disability or avoidance behaviors.

DEVELOPMENTAL COURSE AND PROGNOSIS

The developmental course and prognosis of childhood PTSD after exposure to single-occurrence, nonabusive stressors are not straightforward matters. Additionally, as time passes after traumatic events, some PTSD symptoms may subside while other mental health symptoms (e.g., depression) become more prominent (Kroll, 2003); or reactions may shift into patterns of thought and behavior or into vulnerabilities that do not appear as obvious PTSD symptoms (Nader, 2008). Follow-up studies of children's responses to single-occurrence, nonabusive stressors suggest that symptoms peak within the first year after the traumatic experience (Becker, Weine, Vojvoda, & McGlashan, 1999; Blom, 1986; Nader et al., 1990; Pfefferbaum et al., 1999), although a sizable number of children and adolescents are still symptomatic years later (Green et al., 1991, 1994; Terr, 1983; Tyano et al., 1996; Winje & Ulvik, 1998; Yule et al., 2000). PTSD symptoms may disappear after a few months, or symptoms may persist for more than 50 years (APA, 2013).

Duration of PTSD was examined in a well-designed longitudinal study of 217 survivors who had been children and adolescents at the time of the sinking of the ship *Jupiter* in Greek waters (Yule et al., 2000). Youth were intensively interviewed 5–8 years after the disaster, and their experiences were compared to those of a control group of 87 schoolmates. Of 111 who developed PTSD at some time during the follow-up period, the disorder lasted for less than 1 year in 30.1% of them; it lasted for 1–2 years for 16.4%, between 2 and 3 years for 12.6%, between 3 and 5 years for 14.4%, and for more than 5 years for 26.1%.

Delayed-Expression PTSD

Delayed-onset PTSD (now called PTSD "with delayed expression" in DSM-5) is the occurrence of diagnosable PTSD more than 6 months after an event when full PTSD criteria were not met before that time. Delayed-expression PTSD can be persistent and debilitating for children (Nader, 2008; Yule et al., 2000). In the *Jupiter* sinking study, Yule, Udwin, and Bolton (2002) found that 10% (11) did not develop PTSD until more than 6 months later. Onset was 7 and 10 months later ($n = 2$), 12 months later ($n = 4$), 15 months later ($n = 1$), or more than 18 months later ($n = 4$; 21, 39, 55, and 60 months later, respectively). Youth were symptomatic prior to onset of PTSD, with PTSD symptoms below diagnostic threshold and/or with another syndrome such as panic disorder. For the youth with most delayed onset, there was no clear trigger preceding the increase of PTSD symptoms. For some youth, a clear trigger emerged (e.g., death of a cousin, traveling through a train tunnel). PTSD was persistent rather than transitory with delayed onset (Yule et al., 2002).

Military studies also suggest that delayed onset of PTSD may be more chronic. Also, for military personnel, Fikretoglu and Liu (2011) found that delayed-onset PTSD was associated with early childhood trauma, repeated trauma experience, and type of exposure. For New York City adults after September 11, 2001, delayed PTSD was related to individual traits (e.g., lower self-esteem, mixed handedness/lower cerebral lateralization), culture (e.g., Latino, non-native-born), or adversity exposure (e.g., more negative life events, greater lifetime traumas) (Boscarino & Adams, 2009). Although there are rare cases in which no symptoms were reported prior to PTSD diagnosis delayed months to years after an event, most studied cases of delayed onset PTSD are preceded by some symptoms (Andrews, Brewin, Philpott, & Stewart, 2007).

Trauma and Other Stress Reactions in Relation to Normative Development and Context

It is essential to understand children's symptoms and reactions to adversity in relationship to normative adaptation at different developmental stages, as well as in relationship to context (i.e., biological, psychological, and social) (Costello et al., 2006; Nader, 2011).

Experts believe that early childhood trauma/maltreatment has a greater capacity to inflict significant and progressing dysfunction than a similar experience in adolescence or adulthood (Perry, 2006), when skills such as self-regulation are already established (Nader, in press). One of the reasons why trauma's interruption of developmental gains may have a cumulative effect is that youths take forward the skills, knowledge (e.g., biological, cognitive, social, and emotional), and other resources gained in earlier phases of development (Cicchetti, 2003a; Geiger & Crick, 2001; Nader, 2008; Price & Lento, 2001). Academic progress, interpersonal functioning, conscience building, and/or self-regulation development may be undermined by trauma and may progressively undermine or derail a youth's life trajectory. For example, posttrauma changes in a youth's mood and cognitive processing may lead to difficulties with school authorities and peers, negative school experiences, poor grades and/or dropout, and later lower occupational status (Caspi, 1998; Nader, 2008). Posttrauma personality change may influence interrelationships and selection for school and ongoing opportunities. For example, the dimension of agreeableness—prosocial traits such as politeness, cooperation, and compassion at one end of the continuum, and antisocial traits such as callousness and aggression at the other end (De Young et al., 2010)—is linked to the understanding of others' emotions, intentions, and mental states (e.g., empathy, theory of mind). Agreeableness may be undermined by trauma.

There is considerable variety in the rate and manner that developmental skills progress across time, and other variables complexly influence their progression. For example, observable developmental changes occur between ages 3 and 4 in self-regulation, theory of mind (i.e., the ability to recognize others' mental states—-e.g., beliefs, desires, emotions, intentions—and to use the information to predict and interpret behavior; Angold & Heim, 2007; Ferguson & Austin, 2010), and executive functioning (Cole, Dennis, Smith-Simon, & Cohen, 2009). Evidence suggests that 4-year-olds have a better grasp of strategies for regulating anger than 3-year-olds, although both 3- and 4-year-olds appear to understand equally strategies for regulating sadness (Cole et al., 2009). However, a changing understanding of death—which is limited for children under age 7—and the importance of the deceased to a child influence coping with sadness related to the loss of a significant other and influence the potential for traumatic impact (Nader & Salloum, 2011). Additionally, regression and loss of skills may follow traumatic experience and traumatic loss.

Age Group Effects and Critical Periods of Development

Extreme, repetitive, or abnormal stress during critical or specific periods of childhood brain development can impair the activity of major neuroregulatory systems, with significant and lasting neurobehavioral consequences (Anda et al., 2006; De Bellis & Thomas, 2003). Generally, pleasurable experiences and thoughts lead to positive emotions; painful ones trigger negative emotions (Gould et al., 2012). Stress during critical developmental time periods may produce severe disruptions in this relationship. Lasting changes in stress reactivity and in the limbic and paralimbic brain regions may result in psychiatric syndromes and associated cognitive dysfunction (Gould et al., 2012). For adults with trauma histories, variables such as age of exposure, traits, current stress level, and number of victimizations have influenced cortisol levels (see Nader & Weems, 2011). Research suggests that interactions between the developing amygdala and HPA axis underlie critical periods for emotional learning, which are modulated by developmental support and maternal care (Gillespie et al., 2009). That is, data suggest the existence of a critical period during which brain exposure to corticosterone influences fear learning, which is modulated by the quality of maternal care (Gillespie et al., 2009). With sufficient early parental support, an amygdala-dependent emotional circuit develops that can *appropriately* differentiate threatening from nonthreatening environmental stimuli. In contrast, when child abuse is combined with biological risk factors, amygdala development may be altered and perpetually *primed* for stress responsiveness. In addition, stable individual differences in stress response systems emerge with maturation (Del Giudice et al., 2011; Ellis & Boyce, 2008). When raised in adverse environments, highly reactive children sustain disproportionate rates of morbidity (Boyce & Ellis, 2005). Conversely, when raised in low-stress, highly supportive settings, they sustain unusually low rates. Importantly, exposure to stress hormones affects children differently at different developmental phases.

Prenatal and Infant Stress

Prenatal, infant, and childhood stress alter stress reactivity (Schneider, Moore, & Kraemer, 2003). Such in-

creases in reactivity have been linked to vulnerability to mood and anxiety disorders (Nemeroff, 2004). Prenatal exposure to cortisol has been linked to attention-deficit/hyperactivity disorder (ADHD), severe emotional disturbances, anxiety, social withdrawal, schizophrenia, and criminality. Effects may not emerge until adolescence (Halligan, Herbert, Goodyer, & Murray, 2007; Lupien et al., 2009). Exposure to cortisol in breast milk may influence infant personality toward inhibition (Glynn et al., 2007; Tyrka et al., 2008).

Stress Inoculation

Early life stress may foster adaptations that enhance interrelated aspects of emotion regulation, cognitive control, and curiosity, and that diminish the HPA axis activation induced by stress (Lyons & Parker, 2007; Nader & Weems, 2011). Animal studies have demonstrated that coping with early life stress increases prefrontal myelination and expands a region of the cortex that relates to arousal regulation and resilience (Katz et al., 2009). It is more likely for early life stress to result in stress resilience than stress vulnerability if the stressor is challenging enough to activate physiological and emotional coping processes, but is not overwhelming (i.e., is within an infant's coping capacity) (Gunnar, Frenn, Wewerka, & Van Ryzin, 2009). Otherwise, early life stress may increase risk for the development of mood, anger, anxiety, trauma-related, and substance use disorders. For human children, in accordance with stress inoculation theory is the finding that going to child care activates the HPA axis (Ahnert, Gunnar, Lamb, & Barthel, 2004), but that in the absence of factors that may maintain fearfulness (e.g., overprotective parenting; Gunnar, Frenn, et al., 2009; Rubin, 2002), day care reduces fearfulness in extremely fearful children (Fox, Henderson, Rubin, Calkins, & Schmidt, 2001).

Stress in Preschool Children

PTSD has been documented in preschool children with significant comorbidity, although more frequently with alternative diagnostic algorithms than with DSM-IV algorithms (Scheeringa, 2011; Scheeringa et al., 2012). De Young and colleagues (2012) found that in a very young age group, most children were resilient, 35% had at least one disorder, comorbidity was common, and distress was not reduced over 6 months. In studies controlling for comorbidity among disorders, specific phobias, PTSD, and selective mutism were associated with depression (Egger & Angold, 2006). A number of symptoms in addition to PTSD may result from trauma exposure. For children ages 3–5 exposed to a hurricane (Delamater & Applegate, 1999), in addition to a greater likelihood of PTSD symptoms compared to controls, there was a significant relationship between PTSD and developmental delays at 18 months but not at 12 months after the hurricane. Studies have shown internalizing or externalizing behavior problems (Wolfe, Crooks, Vivien, McIntyre-Smith, & Jaffe, 2003), low social competence (Cummings, Pellegrini, Notarius, & Cummings, 1989), and trauma symptoms (Levendosky, Huth Bocks, & Semel, 2002) for preschoolers exposed to domestic violence (Basu, Malone, Levendosky, & Dubay, 2009). As discussed, specific factors (e.g., dopamine polymorphism) may increase the likelihood of PTSD in young children.

Stress in School-Age Children

Although many studies have documented trauma in school-age children between the ages of 6 or 7 and 12 (Kamis, 2005; Nader et al., 1990; Pynoos et al., 1987), previous diagnostic algorithms for PTSD may have resulted in underestimates of children with PTSD (Scheeringa, Wright, Hunt, & Zeanah, 2006), as noted earlier. In addition, posttrauma outcomes may be manifested in other ways than in a diagnosis of PTSD. In response to domestic violence, although about one-third of school-age children have been resilient, such children also often exhibit increased levels of internalizing and externalizing behavioral problems (Basu et al., 2009; Grych, Jouriles, Swank, McDonald, & Norwood, 2000).

Traumatic exposure and PTSD in childhood are linked to a variety of negative outcomes in childhood and adulthood, including current and lifetime PTSD (Kulkarni, Graham-Bermann, Rauch, & Seng, 2011). A history of multiple trauma exposures is prevalent among adult women with disorders such as PTSD and MDD (Dennis et al., 2009). Women who in childhood were sexually abused, witnessed interpersonal violence, and/or experienced parent–child role reversal, as well as women with unresolved attachments, were more likely to be multiply interpersonally victimized (i.e., in multiple abusive relationships) as adults (Alexander, 2009). Notably, 77% of women who were multiply victimized had experienced multiple forms of childhood trauma; all had experienced some form of trauma in childhood. Allard (2009) found that for Japanese college students, a history of high-betrayal traumas (i.e., physical abuse, neglect, or sexual abuse by someone close) predicted

psychological distress—that is, PTSD and/or depression symptoms, but not anxiety—above and beyond distress predicted by medium-betrayal traumas (i.e., by someone who was not close) or any other type of trauma reported. A body of evidence suggests an association between bulimia nervosa and childhood trauma (Wonderlich et al., 2007). Dennis and colleagues (2009) found that adult physical assault exposure was significantly associated with more severe PTSD and depressive symptoms, whereas childhood violence exposure was most associated with increased hostility. Accident traumas were linked to depressive symptoms. Groups with PTSD and MDD reported more health conditions. Despite previous findings that violence and abuse are linked to worse outcomes than other types of trauma (e.g., Gill, Page, Sharps, & Campbell, 2008), Kulkarni and colleagues (2011) found that cumulative lifetime nonviolent traumas were the strongest predictors of both lifetime and current PTSD (see our discussion of polyvictimization, below).

Adolescent Stress

Biologically driven developmental differences emerge with the onset of puberty, characterized by increased sensation seeking and an increased desire for novelty (Steinberg et al., 2006). The ability to monitor and self-regulate behavior, via the PFC's regulatory functions, continues to develop across adolescence and typically does not reach full maturity until early adulthood (Steinberg et al., 2006). That is, adolescents are biologically prone to engage in greater sensation seeking, and they do not fully develop the capacity for impulse control until adulthood (Habib & Labruna, 2011; Steinberg, 2007; Stevens et al., 2007). Major developmental tasks in adolescence (e.g., separation and individuation) and adolescents' sense of invulnerability (which has been linked to increased risk taking; Alberts, Elkind, & Ginsberg, 2007), along with the onset of more adult behaviors such as driving, dating, and substance use, may result in increased exposure to potentially dangerous situations (Habib & Labruna, 2011). Developmental struggles with identity and self-perception may be compounded by the shame and secrecy associated with some traumatic experiences (e.g., molestation; Habib & Labruna, 2011). For adolescents, significant relational difficulties associated with trust are common and may be magnified by struggles to find purpose and meaning in life.

Self-regulation appears to serve as a protective factor against behavioral problems (Cruise et al., 2008), which are potential posttrauma outcomes. Youth with higher self-regulation have been less affected by the influence of deviant peers on levels of self-reported antisocial behavior (Dishion & Patterson, 2006). Higher levels of psychosocial maturity (i.e., temperance, perspective, responsibility) also are associated negatively with antisocial decision making (Cauffman & Steinberg, 2000; Cruise et al., 2008). Inhibiting emotional distraction is an aspect of emotional self-regulation. Wang and colleagues (2008) found that, in contrast to adults, healthy adolescents activated bilateral left posterior middle frontal gyrus (pMFG) in response to both attentional targets and sad distracters, indicating an inhibitory role for pMFG during emotional distraction in adolescents. De Bellis and Hooper (2012) found that maltreated youth with depressive disorders exhibited dysfunction in the process of inhibiting emotional distraction in the pMFG.

Suicide is the third leading cause of death among adolescents (U.S. National Library of Medicine & National Institutes of Health, 2004). Many studies of adult suicide risk have documented increased levels of suicidal behaviors in individuals exposed to trauma and diagnosed with PTSD (see Krysinska & Lester, 2010, for a review). Approximately 1 year after the terrorist attacks of 9/11, Chemtob, Madan, Berger, and Abramovitz (2011) found, for adolescents, that having a family member who was hurt but not killed and having partial or full PTSD were both significantly associated with increased risk for suicidal ideation in the last 4 weeks and in the last year. Knowing someone who was killed increased risk for partial or full PTSD, but not risk for suicidal ideation. Having a family member who was hurt but not killed increased risk for suicidal ideation, but not risk for partial or full PTSD.

OTHER RESULTS OF EXPOSURE TO TRAUMA

Other posttrauma disorders may predate, follow, or exist comorbidly with PTSD. That is, previous psychiatric history may be a vulnerability factor for developing PTSD, and youth exposed to traumas may have a variety of reactions in the absence of or in addition to PTSD (Ford, 2011; Morgan & Fisher, 2007). Additionally, trauma and PTSD symptoms may influence behavioral and emotional development, including the development of self-concept and skills that influence academic performance, interpersonal relating, and productivity (Carrion et al., 2002; Nader, 2008). As noted throughout this chapter, because DSM diagnos-

tic criteria prior to DSM-5's were developed for adults, these earlier criteria may have underdiagnosed children (Scheeringa, 2011). More changes may be needed to fully remedy underdiagnosis in children. Also, subsyndromal trauma symptoms are relevant to the emergence of dysfunction.

Comorbidity

PTSD is associated with significant comorbidity (De Bellis, 2001; Koenen et al., 2008; Nader, 2008). Comorbidity may have a substantial impact on the course and severity of PTSD (Kimerling, Prins, Westrup, & Lee, 2004; Nader, in press), as well as on the treatments that are effective following trauma (Ford et al., 2005; van der Kolk et al., 2005). Comorbidity is associated with worse prognosis, more severe symptoms, and lower social competence (Cerda, Tracy, Sanchez, & Galea, 2011; Schuckit, 2006). Additionally, comorbidity may indicate a more complicated form of trauma (Ford et al., 2005).

The timing of other disorders relative to PTSD is undergoing study. Some research now suggests that some disorders may predate PTSD. In an assessment of individuals across the first three decades of life, Koenen and colleagues (2008) found that at age 26, all adults with past-year PTSD and 93.5% with lifetime PTSD had prior mental health disorders between ages 11 and 21. The onset of most prior disorders (60–66%) was before age 15. Among new PTSD cases arising between ages 26 and 32, 96% had a prior mental disorder, and in 77% of these cases the disorder had begun before age 15. Some assessments of birth cohorts beginning in childhood that have evaluated a variety of mental disorders have found that PTSD is rare in prospective epidemiological community samples of children before age 15, whereas other mental disorders such as conduct disorder (CD) are common (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Koenen et al., 2008). It is unknown whether or not this finding is related to the failure of adequate adaptation of posttrauma diagnostic criteria for children. PTSD percentages are higher when a traumatic event is assessed. PTSD has been documented in very young, school-age, and older youth assessed in relationship to specific traumas.

Risk of Comorbidity

Personality traits such as neuroticism (Eysenck, 1967), parental psychiatric history (especially maternal; Milne et al., 2009), and childhood trauma are more strongly associated with comorbidity than with solitary disorders (de Graaf, Bijl, ten Have, Beekman, & Vollebergh, 2004; Kessler, Davis, & Kendler, 1997). Impairments in functioning are also more strongly associated with comorbid than with single disorders (de Graaf et al., 2004). Although factors such as parental history, the quality of parenting (e.g., warmth/support), peer influences (e.g., peer deviance), and stressful life events (e.g., loss of a parent, traumatic events) are associated with comorbidity (Cerda, Sagdeo, Johnson, & Galea, 2010), specific adverse events are not associated with any one class of disorders (Kessler, 2000; Kessler et al., 1997). As noted in our earlier and later discussions of genetics, trauma exposure may increase the likelihood of a number of disorders.

Common Comorbidities of PTSD

PTSD commonly occurs in association with anxiety disorders, depressive disorders, substance use disorders, and/or conduct disorders (APA, 2013; Koenen et al., 2008). Adults with PTSD evidence increased risk of MDD, substance dependence, impaired role functioning/reduced life opportunities (e.g., unemployment and marital instability), and health problems (Breslau, Davis, Peterson, & Schultz, 2000; Kessler, 2000; Koenen, 2007). Additional disorders, commonly comorbid or among long-term outcomes of trauma exposure, are antisocial behavior, personality disorders, psychotic disorders, bipolar and related disorders, and ADHD (APA, 2013; Breslau et al., 2000; Gold, 2004). For children, among the disorders found in association with PTSD (Nader, 2008) are attention deficit disorder (ADD) as defined in earlier DSMs, ADHD as defined by more recent DSMs, CD, oppositional defiant disorder (ODD), depressive disorders (e.g., MDD or depressive disorder not otherwise specified), phobias (e.g., social or specific), and anxiety disorders (e.g., separation, panic) (Carrion et al., 2002; Cicchetti, 2003b; Gilbert et al., 2009; Greenwald, 2002; Udwin, Boyle, Yule, Bolton, & O'Ryan, 2000; Weinstein, Staffelbach, & Biaggio, 2000). Studies have also shown increased health (e.g., somatic complaints) and emotional problems for youth with PTSD (Abdeen et al., 2008; Nader, 2008). The direction and nature of causality are not well understood for many associations. Future studies will need to examine the contributions of many variables (e.g., extent of comorbidity, genetics) in relationship to outcomes.

Other Trauma-Linked Disorders for Youth

A number of severe mental disorders associated with childhood trauma are discussed here.

Alexithymia

Alexithymia (i.e., difficulty identifying and labeling emotional feelings, and a tendency toward externally oriented thinking) is robustly associated with PTSD for chronically traumatized individuals (Frewen, Dozois, Neufeld, & Lanius, 2008, 2012). Alexithymia has been linked to physical violence, rape, and child abuse/neglect. Of the components of alexithymia, difficulty *identifying* emotions has been most strongly associated with psychopathology. Difficulty *describing* emotions may reflect a number of different underlying problems—for example, shame, fear of negative evaluation, cognitive difficulties, or cultural gender norms (Frewen et al., 2012; Suslow, Donges, Kersling, & Arolt, 2000; Wong, Pituch, & Rochlen, 2006). Instead of representing deficits in the emotional experiential range (DSM-5 PTSD, Criteria D4, D7), Litz and colleagues theorized that PTSD-associated emotional numbing symptoms that overlap empirically with those of alexithymia may be masking, by the magnification of negative emotions, a fuller range of emotional and expressive potential (Frewen et al., 2012; Litz & Gray, 2002). PTSD-associated alexithymic characteristics may also reflect information-processing deficits; greater difficulty putting positive feelings into words "relative to communicating emotions of negative valence" (Frewen et al., 2012, p. 157); deficits in emotional vocabulary and expressive skill (Frewen, Lane, et al., 2008); and identifiable maladaptive belief sets and secondary negative affective responses (e.g., anxieties) that are also likely to hinder emotional expressive potential in women with childhood PTSD.

Bipolar Disorder

Although bipolar disorder (BD) has a strong genetic basis, it has also been associated with early psychological trauma (Savitz, van der Merwe, Newman, et al., 2007). For BD, the rate of childhood trauma exposure ranges from 45 to 68% (15–21% exposed to sexual trauma, 21–28% to physical trauma) (Conus, Cotton, Schimmelmann, McGorry, & Lambert, 2010; Lysaker, Beattie, Strasburger, & Davis, 2005). For adults with BD in Northern Ireland, Shannon and colleagues (2011) found an approximately 62% prevalence rate of lifetime trauma, a 65% rate of moderate to severe childhood trauma, and a 35% rate of trauma related to civil unrest. Alvarez and colleagues (2011) reported that almost half of a sample of patients with BD, schizophrenia, or schizoaffective disorder had experienced some kind of child abuse. Hospital admissions were twice as high in this sample's victims of psychological abuse. Sexual abuse victims were more than twice as likely to attempt suicide. Groups with BD and recurrent unipolar depression have demonstrated higher levels of self-reported abuse and dissociation than their unaffected relatives (Savitz, van der Merwe, Newman, et al., 2007).

Childhood Behavioral Disorders

Morcillo and colleagues (2011) found a dose–response relationship between number of CD symptoms and risk for most psychiatric disorders. Conduct disturbances are among disorders associated with childhood trauma. Youth who join gangs have had significantly more violent victimizations prior to but not after joining a gang (Gibson, Miller, Jennings, Swat, & Gover, 2009). Trauma exposure is common (Abram et al., 2004; Greenwald, 2002), and there is a high prevalence of PTSD, in incarcerated youth (Brosky & Lally, 2004; Greenwald, 2002). For incarcerated juvenile females, evidence suggests that early exposure to traumatic events (e.g., maltreatment) is associated with a set of adverse outcomes, including delinquency, mood disorder, and self-injury (McReynolds & Wasserman, 2011). Additionally, a relationship between prior depression and CD has been demonstrated (Cerda et al., 2011). It may be that depression in adolescence hinders relationships with prosocial peers and contributes to interpersonal conflict, thereby reinforcing CD persistence into young adulthood (Ingoldsby, Kohl, McMahon, & Lengua, 2006). ADHD may precede or occur comorbidly with PTSD (Adler et al., 2004); it may also be a risk factor for PTSD. For a small sample of veterans, Adler and colleagues (2004) found that 36% with PTSD reported childhood ADHD, and 5% met criteria for current ADHD.

Depression

Posttraumatic depressive disorders have been found in children with PTSD or subthreshold PTSD symptoms (Carrion et al., 2002). Comorbid depression in the early phases of PTSD has predicted poorer treatment

outcomes (Nixon & Nearmy, 2011). Depressed patients with a history of childhood adversity have had elevated secretion of ACTH and cortisol in response to laboratory stress tests and neuroendocrine challenge tests (Gillespie et al., 2009; Heim, Mletzko, Purselle, Musselman, & Nemeroff, 2008). Elevated cerebrospinal fluid (CSF) concentrations of CRH have repeatedly been reported in patients with depression and with combat-related PTSD (Gillespie et al., 2009). Postmortem studies after suicides have found elevated CSF CRH, as well as increased CRH and decreased density of CRH receptors in the frontal cortex. A persistent finding for depressed patients is the elevation of CRH and AVP neurons in the PVN (Gillespie et al., 2009; see the earlier and later discussions of CRH). The strong relationship between depression and stressful life events appears to be moderated by genetic vulnerability (Gatt et al., 2009). For example, BDNF (particularly BDNF Met allele polymorphisms) is associated with increased risk for depression in abused children. Gatt and colleagues (2009) found that BDNF Val66Met polymorphisms combined with early life stress resulted in reduced hippocampal and prefrontal gray matter volume, as well as increased depression rates. These results were in turn associated with poorer working memory (see also Savitz, van der Merwe, Newman, et al., 2007; Savitz, van der Merwe, Stein, et al., 2007). Researchers have found increased emotion processing—evidenced in increased amygdala and subgenual cingulate activity—in depressed adolescents (De Bellis & Hooper, 2012; Yang et al., 2010).

Psychosis

Although multiple pathways are likely in the emergence of psychosis (Zelst, 2008), both recent and lifetime adverse life events have been associated with increased levels of psychotic symptoms in at-risk individuals (van Winkel et al., 2008). Psychosis-like symptoms or experiences in childhood increase the likelihood of adult-onset psychosis (Laurens, Hodgins, West, & Murray, 2007; van Os, Hanssen, Bijl, & Vollebergh, 2001). For a significant minority of 12-year-olds (about 6%), Polanczyk and colleagues (2010) found self-reported hallucinations and delusions associated with many of the same risk factors and correlates as adult schizophrenia (e.g., genetic, social, neurodevelopmental, home-rearing, and behavioral risks). Children's psychotic symptoms are familial and heritable, and are associated with a number of factors (Collip, Myin-Germeys, & van Os, 2008; Polanczyk et al., 2010). Whereas trauma may play a role for a subgroup with psychosis, many others have no history of trauma (Zelst, 2008). Nevertheless, adults with psychotic disorders report a high prevalence of childhood trauma (Conus et al., 2010).

Literature reviews report an excess of victimizing experiences, often occurring during childhood, in individuals with psychosis (Janssen et al., 2004; Morgan & Fisher, 2007; Zelst, 2008). Schreier and colleagues (2009) found that—whether informants were children, parents, or teachers—bullying victimization increased the risk of psychotic symptoms in early adolescence by twofold, independently of previous psychopathology, family adversity, or IQ. Associations were stronger when victimizations were chronic or severe (e.g., both relational and overt bullying). Using data from the National Comorbidity Survey, Shevlin, Dorahy, and Adamson (2007) found that after they controlled for depression, physical abuse was the only study variable (others included rape, physical attack/assault, and sexual molestation) that significantly predicted psychosis. However, findings did not rule out an association with the other types of trauma.

When restricting their analysis to patients with histories of sexual and/or physical abuse, Conus and colleagues (2010) found levels of trauma exposure to be closer to those found in other studies. Rates were higher for those suffering from long-term psychosis. Patients with such abuse histories were more likely to have a history of other psychiatric disorders (e.g., PTSD, substance abuse) before psychosis onset, more past suicide attempts, and poorer premorbid functional levels, as well as higher rates of comorbid diagnoses. They were also more likely to attempt suicide during treatment. Compared to those of controls, rates of psychosis in general and schizophrenia spectrum disorders in particular are higher among individuals with histories of child sexual abuse with penetration (Cutajar et al., 2010). Cutajar and colleagues (2010) found that risks were highest with penetration occurring after age 12 and with more than one perpetrator. Risk was 15 times greater than the general population for children molested in early adolescence by more than one perpetrator. Importantly, the number of types of trauma was associated with increased risk of psychosis. Odds ratios suggest an increased risk of psychosis for males who are raped (Shevlin et al., 2007).

Available data provides (weighted average) an approximately 29% prevalence rate of PTSD among patients with schizophrenia (Buckley, Miller, Lehrer, & Castle, 2009). PTSD is associated with more severe

psychopathology, more suicidal ideation and behavior, and increased physical health problems for such patients. Studies suggest that in those with schizophrenia spectrum disorders, the childhood sexual trauma prevalence rate ranges from 30 to 60% for women and from 25 to 30% for men.

STRESS SENSITIVITY

Exposures to severe stress, such as childhood trauma or other stressful life events, can increase sensitivity to daily and other life stresses (Collip et al., 2008; see also the discussion of genetic factors below). van Winkel and colleagues (2008) suggest that the association between stress and psychosis also may reflect an underlying vulnerability, characterized by elevated emotional and psychotic reactions to stress. Evidence suggests that individuals with greater than average liability to psychosis are overreactive to small stressors (Myin-Germeys & van Os, 2007; Myin-Germeys, Van Os, Schwartz, Stone, & Delespaul, 2001; van Winkel et al., 2008). Myin-Germeys, Marcelis, Krabbendam, Delespaul, and van Os (2005) found that dopaminergic hyperresponsivity was associated with increased psychotic reactions to daily life stress in first-degree relatives of psychotic patients. Some evidence suggests that environmental exposures, in interaction with (epi) genetic factors, may induce psychological or physiological alterations traceable to a common pathway of cognitive biases and/or altered dopamine neurotransmission (broadly termed "sensitization"); such changes may facilitate the onset and persistence of psychotic symptoms (Collip et al., 2008). Stress reactivity was found to be unrelated or inversely related to cognitive impairment (also associated with genetic risk for schizophrenia), suggesting independent stress- and non-stress-related pathways to psychosis. The administration of corticosteroids, and illnesses associated with elevated cortisol (e.g., Cushing syndrome), have both induced psychotic symptoms.

RISK AND PROTECTIVE FACTORS

No single, environmental, genetic, or other personal factor is responsible for symptoms of PTSD. Some variations in prevalence rates of PTSD and other trauma-related disorders are associated with, for example, characteristics of the traumatic event itself (e.g., its nature, cause, severity, duration); youth characteristics such as cognitive, emotional, psychobiological, and behavioral responses to the event, as well as biological vulnerabilities, developmental stage, gender, and coping skills; and characteristics of the social environment (e.g., family support and cohesion, SES, community support) (Fletcher, 2003; Nader, 2008). A meta-analysis of PTSD risk factors revealed that child or family psychiatric history and reported childhood abuse uniformly increased the likelihood of developing PTSD after traumatic exposure (Brewin, Andrews, & Valentine, 2000). However, certain risk factors (e.g., gender, age during trauma, education, previous trauma, and childhood adversity) were only significant in certain populations and could not be generalized to all patients with PTSD (Adler et al., 2004).

Event-Related Risk and Resilience Factors

Exposure (e.g., to direct, witnessed, or perceived threat, as well as to intense concern for another) has been a consistently robust predictor of posttrauma symptoms (Abdeen et al., 2008; Breslau, 2009; Finkelhor et al., 2007a; Murthy, 2007; Nader, 2008). A body of evidence has shown that intense subjective experiences or peritraumatic emotions (e.g., fear, panic) are important predictors of traumatic reactions as well (Ahern, Galea, Resnick, & Vlahov, 2004; Andrews, Brewin, Rose, & Kirk, 2000; Laufer & Solomon, 2009; Nader, 2010; Pfefferbaum, Stuber, Galea, & Fairbrother, 2006). Age may influence the likelihood of exposure to particular events. For example, infants and very young children are at greatest risk of burn injuries (De Young, Kenardy, Cobham, & Kimble, 2012).

PTSD cannot be diagnosed unless someone has first been exposed to a traumatic event. Events that qualify as traumatic according to DSM-IV or DSM-5 standards can differ greatly from one another—for instance, vehicle accidents, natural disasters, fires, dog bites, severe illnesses, war, domestic violence, school shootings, terrorist attacks, bullying, physical abuse, and sexual abuse—and such differences probably contribute to the course of each child's individual posttraumatic reactions. Although some events (such as emotional abuse or neglect) have not been clearly defined as DSM PTSD Criterion A events, such events have been associated with deleterious and traumatic effects. Below, we discuss some of the event-related variables that influence posttrauma outcomes including exposure variables, immediate and ongoing post-disaster interventions, and number of past and subsequent trauma exposures.

Physical and Subjective Proximity

Degree and nature of exposure are important factors influencing prevalence rates and symptomatic reactions. Proximity has been found to be associated with higher levels of posttraumatic stress. A number of combined or individual, direct, and subjective proximity variables—such as proximity to threat of physical harm to self or others, worry about others, and loss—have been associated with increased symptomatology. For instance, children who were on the school playground (where most of the shooting was directed) during a sniper attack displayed a greater incidence of PTSD symptoms than did children inside the school; and children at school, whether on the playground or not, displayed higher rates than children not at school that day (Nader et al., 1990; Pynoos et al., 1987). Children and adolescents exposed to the 1995 Oklahoma City bombing reported more symptoms of PTSD than those who had minimal exposure to the bombing (Pfefferbaum et al., 1999).

The type of event and the nature of exposure may combine to influence outcomes. After the 2007 Virginia Tech campus shootings—an event where thousands of older youth and adults were indirectly exposed, and a small percentage were directly exposed (Hughes et al., 2011)—increased PTSD symptoms were related to exposure levels, especially inability to confirm friends' safety (30.7%), death of at least one friend/acquaintance (20.3%), and death of a close friend (10.1%). Symptom levels were unrelated to age, gender, or ethnicity/race. Highest youth risk categories (5% of total) had a more than 45% prevalence of probable PTSD (31.7% and 23.2% in the next two categories of risk). Ma and colleagues (2011) found an overall PTSD prevalence of 2.5% (N = 3,208 adolescents) in youth in regions surrounding the epicenter 6 months after an earthquake. Risk factors included being female, being buried/injured, having parents who were severely injured, death of one or more classmates,having a house that was destroyed, and witnessing someone buried/wounded/dying during the earthquake.

Type of Trauma

Some discussion suggests differences in reactions related to the type of trauma experienced (see Nader, 2008, Ch. 10, for a summary; Briere et al., 2001), as well as to the duration and intensity of trauma (Briere et al., 2001; Clinton & Jenkins-Monroe, 1994) and/or age at onset of trauma (Herman, 1992). For example, studies have shown that early and/or prolonged trauma (e.g., maltreatment) is associated with more problems (Bolger & Patterson, 2003). In the past, clinical observations suggested two main types of trauma: (1) acute, nonabusive stressors that occur only once (disasters such as floods, fires, transportation accidents, etc.); and (2) chronic or abusive stressors, which encompass ongoing or multiple stressors (war, chronic illness, repeated surgeries, etc.) and/or incidents of physical or sexual abuse, whether of single or repeated occurrence (Terr, 1991). It was believed that Type 2 traumas were associated with more complex traumatic reactions (see Fletcher, 2003). However, evidence has demonstrated that a percentage of Type 1 traumas are linked to complicated reactions (van der Kolk et al., 2005), and polyvictimization has explained much of the variance in anxiety, depression, and aggression symptoms for youth exposed to more than one type of trauma, including sexual abuse (Finkelhor, Ormrod, & Turner, 2007a, 2007b, 2009).

The literature suggests that specific dimensions of stressors are associated with increased stressfulness of events. Events that are perceived as uncontrollable (by children and/or their parents) appear to lead to worse stress reactions afterwards (Weigel, Wertlieb, & Feldstein, 1989). Meta-analysis of 96 studies of children's exposure to distinct, identifiable disasters revealed that disasters had a significant effect on youth PTSD symptoms (small to medium magnitude) (Furr, Comer, Edmunds, & Kendall, 2010). The more personal the impact of a traumatic event is, the worse a child's reactions appear to be. Children who were exposed to more damage to their homes in Hurricane Hugo were more likely to have symptoms of PTSD afterward (Shannon et al., 1994). Separations from the family during a crisis can have devastating consequences (Freud & Burlingham, 1943; Yule & Williams, 1990), as can the death or injury of a parent or sibling (Pfefferbaum, et al., 1999). Social stigmatization of victims can also worsen reactions to traumatic events (Ayalon, 1982; Frederick, 1986; Nir, 1985). Children with cancer, for instance, may be more likely than children exposed to other traumatic events to experience feelings of estrangement and social isolation, resulting in part from the stigma of their disease and in part from the side effects of therapy (e.g., loss of hair, prolonged absences from school; Nir, 1985). Children in war-torn countries may be more likely to have their social development inhibited, due partly to the greater sanctioning of violence in their

social environment and partly to their greater fear of others (Thabet, Ibraheem, Shivram, Winter, & Vostanis, 2009). For example, violence exposure is associated with increased odds of CD and substance abuse (Cerda et al., 2011). Although event differences have been highlighted, discovery of the impact of multiple traumas suggests the need to reassess differences while controlling for polyvictimization or cumulative trauma.

Cumulative Trauma or Polyvictimization

When assessments include more than one type of traumatic event, many survivors report exposure to multiple categories of trauma (Finkelhor et al., 2007a, 2007b; Green et al., 2010; Kessler, 2000; Martin, Cromer, DePrince, & Freyd, 2013). Cumulative trauma or polyvictimization—in which individuals with one type of victimization (e.g., assault) also have high numbers of additional different kinds of victimizations (e.g., assault, plus theft, bullying, and/or witnessing traumas)—is frequently reported among survivors of traumas such as child maltreatment, domestic violence, and genocide or war (Cloitre et al., 2009; Finkelhor et al., 2007a). In a community representative sample (N = 1,420 children; Copeland et al., 2007), 37% of youth had been exposed to more than one event. Children ages 2–17 who experienced four or more different kinds of victimization in a single year accounted for 22% of a national sample (N = 2,030 children; Finkelhor et al., 2007a, 2007b; see also the discussion on prevalence, above).

REVICTIMIZATION

Revictimization is common after traumas (Finkelhor et al., 2007b; Nader, in press). Exposure to one type of violent experience is strongly associated with additional violence exposures. Exposure to multiple forms of childhood trauma is associated with increased risk for multiple adulthood victimizations. Although other variables (e.g., attachment status) may influence revictimization, Alexander (2009) found that multiple victimizations were unrelated to assessed demographics (e.g., education, income, ethnicity). Type of revictimization may or may not match original victimization. Childhood physical abuse has predicted adult physical assault and crime victimization (Hosser, Raddatz, & Windzio, 2007). Although studies have consistently found that childhood sexual abuse increases risk of adult sexual victimization (Zurbriggen, Gobin, & Freyd, 2010), other traumas (e.g., childhood emotional abuse) have also been associated with adolescent sexual aggression victimization and perpetration, even after researchers have controlled for childhood sexual and physical abuse and tendency for socially desirable-responses. Pathways to revictimization may involve impairment in the ability to recognize risky situations and betrayal (Gobin & Freyd, 2009; Zurbriggen et al., 2010), or may involve dissociation. Although dissociation may successfully protect against incorporation of overwhelming information into conscious awareness, it can become automatic and generalize to other dangerous situations, resulting in an inability to detect danger (Noll, Horowitz, Bonanno, Trickett, & Putnam, 2003; Zurbriggen et al., 2010). Additionally, childhood sexual abuse may damage mechanisms for saying no or increase the likelihood of freezing.

EFFECTS OF POLYVICTIMIZATION

Compared to individuals exposed to a single trauma type, survivors of multiple trauma types, particularly intrafamilial childhood traumas, are more likely to experience chronic mental and physical health problems (e.g., aggression, anxiety, depression, sleep disturbance, severe obesity, somatic complaints, and substance abuse) (Anda et al., 2006; Finkelhor et al., 2007a, 2007b; Green et al., 2010). Similarly, Ford and colleagues (2011) demonstrated that polyvictimized adolescents were more likely than those with no trauma or with trauma histories without polyvictimization to meet criteria for psychiatric disorders. Polyvictimization has been highly predictive of levels of anxiety, depression, and anger/aggression outcomes (Finkelhor et al., 2007a, 2007b), and, when accounted for, it greatly reduces or eliminates the association between individual types of victimizations (e.g., sexual abuse) and symptoms.

Studies have demonstrated that adults with an accumulation of more than five types of trauma (Nijenhuis, van der Hart, & Steele, 2002) or more than four types of adversity (Anda et al., 2006) evidenced increased risk of psychopathology and more symptoms (e.g., PTSD, dissociation, substance abuse) than those with fewer such experiences. After controlling for traumas that also increased complexity, Briere, Kaltman, and Green (2008) found that the total number of different types of childhood traumas was related to symptom complexity in adulthood. For youth, the

number of negative life events has correlated positively with depression and conduct problems (Haine, Ayers, Sandler, Wolchik, & Weyer, 2003). Fergusson and Horwood (2003) reported that youth exposed to six or more stressors had 2.4 times more externalizing and 1.8 times more internalizing disorders than youth with low adversity. For an outpatient clinic population (N = 295), Ford and colleagues (2011) found that parent-reported severe externalizing problems, clinician-rated psychosocial impairment, and PTSD were associated with interpersonal polyvictimization, independently of demographics and psychiatric diagnoses. PTSD was associated with severe impairment. The adverse effects on functioning of polyvictimization in childhood may be due to a number of factors—for instance, biological dysregulation, altered cognitive processing, peer group influences, clustering of behavior problems, engagement in violent behavior, or combinations of these outcomes (Finkelhor, Shattuck, Turner, & Ormrod, 2014).

Disaster Response

When events affect multiple individuals (e.g., natural disasters, war, terrorism), the immediate response to the event has influenced psychological outcomes to exposure (Nader, 2012). In the early aftermath of events, interventions that focus on emotional processing may be contraindicated (Hobfoll et al., 2007; Ørner, 2007). During the first 2–4 weeks after an event, trauma survivors may not be cognitively or emotionally prepared to engage in intensive emotional processing of traumas. Some early interventions have had negative effects that may be related to timing and/or to inexperienced interveners/interviewers (Nader, 2008; Raphael & Wilson, 2001; Ruzek & Watson, 2001). Evidence suggests the importance of reestablishing safety, calming elevated emotional reactions, rebuilding a sense of personal and community efficacy, enhancing connectedness, and restoring hope (Hobfoll et al., 2007); a return to normality (e.g., a return to routine, even if return to a location is not possible) is also important (Woolsey & Bracy, 2010).

Environmental Risk and Resilience Factors

Environmental factors also influence youth outcomes. For adults, across populations and study methods, early adversity (e.g., trauma), psychiatric history (e.g., anxiety, depression), and family psychiatric history are risk factors for PTSD (Brewin et al., 2000).

Parenting

Parenting is influenced by multiple factors (e.g., SES, depression, daily stress), including genetics (Bakermans-Kranenburg & van IJzendoorn, 2010); in turn, parenting influences youth resilience and vulnerability. Notably, parents with apparently less efficient variants of the serotonergic and oxytonergic system genes have exhibited lower levels of sensitive responsiveness to toddlers (Bakermans-Kranenburg & van IJzendoorn, 2008). Parents with two dopamine-related genes (COMT and DRD4) demonstrated less parenting responsiveness when confronted with daily hassles, but greater levels of responsiveness when hassles were low, suggesting greater susceptibility to daily stress levels (i.e., to favorable and unfavorable environmental influences; van IJzendoorn, Bakermans-Kranenburg, & Mesman, 2008). In addition to the influence of family environment on posttrauma outcomes (e.g., after war; Kamis, 2005), attachment, support, and parental mental health are among influencing factors.

ATTACHMENT

Although genetic factors may influence children's susceptibility to parenting behaviors (Bakermans-Kranenburg & van IJzendoorn, 2010), a substantial body of evidence has demonstrated the importance of sensitive parenting to a youth's resilience or vulnerability to psychopathology (Breidenstine, Bailey, Zeanah, & Larrieu, 2014; Munafo, Yalcin, Willis-Owen, & Flint, 2008), as well as to a youth's coping styles (e.g., strategies of adaptation under stress) and interacting styles (Bakersman-Kranenburg & van IJzendoorn, 2010; Moss, Bureau, Béliveau, & Lépine, 2009; Nader & Nader, 2012; Ozen & Atkan, 2010). By school age, early attachment classifications/relationships influence such child characteristics as sense of security, readiness to engage others, and patterns of emotion and behavior regulation (Bowlby, 1969/1982; Moss, Cyr, & Dubois-Comtois, 2004; Moss et al., 2009; Moss, Pascuzzo, & Simard, 2012; Nader & Nader, 2012). Securely attached children exhibit better adaptation than their insecure or disorganized peers (Moss et al., 2004). In general, studies show that insecure/avoidant and insecure/ambivalent children are midway on a risk continuum between the secure and disorganized preschool and school age groups (Moss et al., 2004). Insecure youth are more likely to exhibit increased hostility or rejection sensitivity, as well as more internalizing and externalizing

problems; they are less likely to demonstrate better school adjustment or more effective coping and interaction styles than securely attached youth (Bureau & Moss, 2010; Dykas, Ziv, & Cassidy, 2008; Moss et al., 2009). Children with disorganized (D) attachments—associated with environmental unpredictability, such as frightened or frightening parenting (e.g., by a grieving or traumatizing parent or one with a high level of marital discord)—appear to be at most risk for both externalizing and internalizing behavior problems (Fearon, Bakermans-Kranenburg, van IJzendoorn, Lapsley, & Roisman, 2010; Moss et al., 2012). Reviews and meta-analyses have demonstrated that attachment disorganization is a more significant predictor of both aggressive and depressive behavioral outcomes than organized insecure (avoidant and ambivalent) attachment patterns in preschool and school-age youth (Fearon et al., 2010; Moss et al., 2012; van IJzendoorn et al., 1999).

Disorganized Attachment Subtypes. Moss and colleagues (2004) assessed three D attachment subtypes: controlling–punitive (use hostile and directive behavior toward a parent that may humiliate); controlling–caregiving (direct a parent's behavior and conversation in a helpful, emotionally positive manner); and behaviorally disorganized or insecure–other (display no organized patterns of interacting with a caregiver). Although children in all three of the D subtypes had higher behavior problem scores than children in the secure group, from preschool to school age, controlling–punitive children were rated higher on externalizing problems; controlling–caregiving children were rated higher on internalizing problems; and insecure–other children were rated marginally higher on an externalizing behavior scale by teachers. Controlling–punitive children seemed to use angry, contradictory patterns of hostility and avoidance to capture and maintain dyadic attention, and to use overt power assertion through attacking or humiliating a parent to increase parental involvement (Moss et al., 2004). Controlling–caregiving children seemed to use emotional constriction to deal with painful emotional states.

Stress and Attachment. Animal and human studies have indicated that maternal behavior toward offspring results in long-term changes in the offspring's responses to stress; that is, both stress physiology and brain morphology are affected by parenting (Champagne & Meaney, 2007; Moss et al., 2012). Social stressors and negative life events (e.g., changes in living arrangements, abuse, death of a relative, parental divorce) are associated with instability of attachment patterns (Del Giudice et al., 2011). Notably, stressors increase the likelihood of children's changing from secure to insecure attachment styles. Research suggests that insecurely attached youth tend to use cognitive and behavioral avoidance strategies more often than securely attached peers do (Mikulincer & Florian, 1995). Insecure attachments have been related to avoidant coping, which in turn may increase victimization (e.g., bullying; Ozen & Atkan, 2010) and PTSD symptoms (see Nader, 2008, in press, for summaries).

Support

A large body of evidence has documented a robust relationship between different kinds and levels of social support and health and mental health outcomes (Nader, 2008; Thabet et al., 2009). Following traumatic exposure, desirable forms of social support (e.g., warmth, kindness, respect for needs related to space or proximity), including family and peer support, are associated with lower trauma symptoms (Jaycox et al., 2010; La Greca, Silverman, Lai, & Jaccard, 2010; Nader, 2012). Evidence suggests that successful trauma and grief interventions increase perceived social support as well as reduce symptoms (Salloum & Overstreet, 2012). Unresponsive or nonsupportive parenting has been implicated in a number of disorders (Caspi, Hariri, Holmes, Uher, & Moffit, 2010). A number of studies have found a significant inverse relationship between parental support and children's posttraumatic stress reactions (Thabet et al., 2009).

Parental Mental Disorders

Youth with parents who have mental disorders are at increased risk of developing a wide range of mental disorders themselves, especially if both parents have disorders (Dean et al., 2010). Although evidence suggests a shared genetic risk for schizophrenia and BD (Lichtenstein et al., 2009; see Youngstrom & Algorta, Chapter 6, and Kuniyoshi & McClellan, Chapter 12, this volume), schizophrenia is a greater risk for those whose parents have any of a range of disorders (Mortensen, Pederson, & Pederson, 2010). Dean and colleagues (2010) found that individuals with parental history of nonserious mental disorders had an elevated risk of schizophrenia and BD, whereas individuals with parental serious mental disorders had increased

risk not only of schizophrenia or BD, but also of other disorders (e.g., mood and anxiety disorders, substance misuse, personality disorders). Parental PTSD or other disorders are also a risk factor for PTSD (Yehuda et al., 2000). In a study controlling for parental depression, Brand and colleagues (2011) found that adolescent offspring of mothers with a lifetime history of PTSD reported higher levels of lifetime stress and more chronic stress related to family relationships than did adolescents whose mothers did not have PTSD.

Child-Related Risk and Resilience Factors

A child's stress reactions can be moderated at any stage of the posttrauma process by characteristics of the individual child and his or her personal history. Although the effect of any single personal risk factor is generally small, combined risk factors may outweigh the severity of a trauma (Breslau, 2009). Child-specific risk and resilience/protective factors include, for example, self-esteem, locus of control, trust, attachment status, and coping (see Nader, 2008, for a summary). As will be discussed, genetic factors also influence outcomes. The meaning of the traumatic experience will vary according to the capacity of the individual and his or her social environment to make sense of it. Breslau (2009) found that an IQ over 115 was associated with reduced assaultive violence trauma exposure and reduced risk of PTSD. Similarly, a child's emotional and coping repertoire can affect his or her capacity for emotional processing and response. Children with early conduct disturbances (externalizing problems), anxiety disorders, or violence exposure are at increased risk of PTSD. A history of childhood trauma increases the risk of PTSD with subsequent adult exposure to traumatic events (Bremner, 2006). Individuals with longstanding or chronic PTSD have poorer treatment outcomes than those with acute-onset PTSD. In contrast to those with adult-onset PTSD, who more often have classical PTSD symptoms of hyperarousal and anxiety, individuals with early-onset PTSD have more depression, substance abuse, and character pathology. A few factors are in the early stages of study.

Coping Strategies

Coping is a subset of the ways that individuals respond to stress, including both effortful and involuntary responses (Compas, 1998). Coping methods include emotion-focused responses (e.g., escape, avoidance, fight) and cognitive processing responses (e.g., problem solving, anticipatory biases, denial, intellectualization) (Lazarus & Folkman, 1987; Mello & Nader, 2012). In a number of studies, avoidant coping has been associated with negative posttrauma outcomes (Mello & Nader, 2012; Min, Farkas, Minnes, & Singer, 2007). However, the relationship between coping and outcome is not simple. Although active coping is often associated with resilience and better posttrauma outcomes for some youth groups, after some events active coping (e.g., helping efforts, memorialization) has been associated with increased symptoms (Brown et al., 2008). While help seeking may be a positive coping method (see social support), especially for children, Abdeen and colleagues (2008) found that for adolescents seeking more emotional help, there was stronger association between posttraumatic distress and somatic complaints. However, for adolescents seeking more instrumental help, there was a weaker association between posttraumatic symptoms and somatic complaints. Research suggests that the ability to employ different types of coping behaviors flexibly, in keeping with the varying demands of a situation, is advantageous (Bonanno, Pat-Horenczyk, & Noll, 2011).

COPING FLEXIBILITY

The primary–secondary control model of coping (Rothbaum, Weisz, & Snyder, 1982) proposes that, in response to stressful situations, individuals cope either by making efforts to control the situation/event (primary control coping strategies) or by adapting to situations (secondary control coping strategies) (Babb, Levine, & Arseneault, 2010). Individuals may shape their environments in order to attain a goal (primary coping). However, primary coping may be maladaptive when circumstances are uncontrollable. The use of secondary coping strategies increases with age (Babb et al., 2010; Thurber & Weisz, 1997). Evidence suggests that accurately perceiving the controllability of a situation is a key cognitive predictor of coping flexibility; that is, individuals report more strategies directed toward adjusting to, rather than changing, situations as they become uncontrollable (Babb et al., 2010). In response to vignettes about problematic interactions with peers, normal older children demonstrate greater coping flexibility than younger normal children, as well as greater flexibility than children with ADHD in either age group (Babb et al., 2010). Youth with ADHD have demonstrated a limited repertoire of coping strategies

and a greater use of antisocial strategies. Differences in coping strategy repertoire have predicted how children cope, on their own, with nontraumatic frustrating circumstances. For young children's self-regulation, Cole and colleagues (2009) found that the more anger coping strategies and sadness coping strategies a young child recognized, the more alternative solutions the child attempted. In addition, the more strategies recognized, the less the child sought support; the fewer sadness strategies recognized, the more disruptive behavior. Children receiving higher levels of emotional support when distressed recognized more strategies for regulating anger, but generated fewer anger strategies than children with less support.

Genetic Factors

By direct and intergenerational transmission, genes influence traits, psychopathology, and behaviors (Bouchard, 2004; Champagne & Mashoodh, 2009). Marked variability in responses among people exposed to the same environmental risk suggests that genetic factors may play a part in posttrauma reactions (Caspi et al., 2010). Genetic influences are among the reasons why children exposed to traumas develop behavioral and emotional difficulties, or, conversely, evidence resilience and better functioning (Kim-Cohen et al., 2006; Nader, in press).

Twin studies demonstrate that genetic factors are important in the etiology of PTSD (Koenen, 2007). Genetic influences account for about one-third of the variance in PTSD risk (Stein, Jang, Taylor, Vernon, & Livesley, 2002). That is, PTSD is approximately 30% heritable (Koenen, 2007), consistent with findings that heritability accounts for 30–40% of the variance in risk for other mood and anxiety disorders as well (Gillespie et al., 2009). Genetically, humans are 99% identical (Koenen, 2007). Of the tiny fraction of DNA sequences that vary among individuals, 90% of those—single-nucleotide polymorphisms (SNPs)—are the primary focus of study in relationship to risk of disorders. Without a trigger, such as trauma or other adversity, the likelihood of gene-related specific dysfunction is reduced (Lau & Pine, 2008). Gene × environment correlations are evident when certain genetic constitutions seek out or otherwise are likely to be exposed to (e.g., are born into; evoke from environments) certain conditions (Arseneault et al., 2011; Bouchard, 2004). Accordingly, certain genetic groups (e.g., sensation seekers) may be more likely to be exposed to danger/traumas (Cisler, Amstadter, & Nugent, 2011) or may be more likely to develop certain disorders in response to such exposure (e.g., Arseneault et al., 2011). As noted earlier, such experiences can change inherited neurochemistry and related behaviors (Champagne & Meaney, 2007).

Gene × environment × development interactions demonstrate that environmental adversity is a key element in the expression of genetic vulnerability, which may be expressed differently at different developmental periods (Cisler et al., 2011; Dahl & Gunnar, 2009). Outcomes of exposure to a variety of adverse environmental factors (e.g., traumas, child care quality, urban residence) are influenced by developmental age and by differential susceptibility to positive and negative environments (Belsky & Pleuss, 2009; Del Giudice et al., 2011). Like other variables, genetic factors probably contribute synergistically to outcomes (Cerda et al., 2010). For example, in addition to adding to or subtracting from the expression of a trait, personality-related genes work more complexly, depending to some extent on gene pairing on a chromosome or on genes located on other chromosomes (Bouchard, 2004). Nevertheless, a few genetic polymorphisms have been linked to specific types of disorders—for instance, serotonin polymorphisms to internalizing disorders, and monoamine oxidase A (MAOA) to externalizing disorders (Nader, in press). Among them are disorders associated with trauma exposure that may occur with or without PTSD.

SEROTONIN

Significant findings, for multiple species, related to the short (s) allele of the serotonin transporter promoter polymorphism (5-HTTLPR)—which, in contrast to the long (l) allele, reduces efficiency of gene transcription—have demonstrated the validity of theories of genetically driven individual differences in stress sensitivity/vulnerability (Caspi et al., 2010). The 5-HTTLPR gene s allele is associated with increased and more rapid amygdala and HPA reactivity to stress/threatening stimuli (Caspi et al., 2003, 2010; Dannlowski et al., 2007; Furman, Hamilton, Joormann, & Gotlib, 2011; Hariri et al., 2003; Mueller, Brocke, Fries, Lesch, & Kirschbaum, 2010), as well as with elevated depression and suicidality in response to trauma and/or chronic stress (Caspi et al., 2003, 2010; Roy, Hu, Janal, & Goldman, 2007). The amygdala appears to mediate physiological and behavioral reactivity, such as autonomic arousal and reallocation of attention (Whalen

& Phelps, 2009). The brain's medial PFC regions integrate amygdala-mediated arousal and down-regulate its reactivity (Caspi et al., 2010). Medial PFC regions also are involved in extinction of conditioned fear responses, which are dependent on amygdala circuitry. The 5-HTTLPR s allele has been associated with relatively decreased amygdala and medial PFC gray matter volume (Pezawas et al., 2005), and with altered connectivity between the two regions (Pacheco et al., 2009).

Earlier evidence-based theories pointed to a correlation between a personality trait—variously described as negative affectivity, negative emotionality (NE), or neuroticism (e.g., emotional reactivity, inhibition, fear, anxiety, anger)—and depression. This correlation may be attributable to a shared genetic factor (Kendler, Neale, Kessler, Heath, & Eaves, 1993; Shiner & Caspi, 2003). Similarly, cortisol level has been associated with a behavioral inhibition phenotype, predictive of anxiety and depressive disorders and including the tendency to withdraw and avoid novel situations (Fox, Henderson, Marshall, Nichols, & Ghera, 2005; Nader & Weems, 2011; Tyrka et al., 2006). Current evidence-based theory suggests that 5-HTTLPR underlies NE, and in turn that NE is a risk factor for stress-related psychiatric disorders (Caspi et al., 2010). Studies of adults (Dalton, Aubuchon, Tom, Pederson, & McFarland, 1993; Otis & Louks, 1997) and children (Weems et al., 2007) have found introversion or NE as a risk factor for PTSD.

Evidence links 5-HTTLPR to PTSD (Xie et al., 2009) and to trauma-related symptoms such as depression, posttrauma suicide attempts (Roy et al., 2007), greater acquisition of conditioned fear responses (Lonsdorf et al., 2009), greater auditory startle response (Armbruster et al., 2009), increased sympathetic reactivity when observing others' pain (Crisan et al., 2009), laboratory-assessed aggressive reactions (Verona, Joiner, Johnson, & Bender, 2006), stress-linked alcohol consumption (Covault et al., 2007), substance use (Brody et al., 2009), emotion-induced retrograde amnesia (Strange, Kroes, Roiser, Tan, & Dolan, 2008), and stress-related sleep disturbance (Brummett et al., 2007; Caspi et al., 2010). It has also been linked to biased information processing—for instance, a threat-related attentional bias and a negative information processing bias (Caspi et al., 2010). Carriers of the s allele who have high levels of child maltreatment and adversity have shown higher levels of anxiety sensitivity (Stein, Schork, & Gelernter, 2008) and biases toward perceiving and expecting negative outcomes (Williams et al., 2009). When the number of stressful life events was low, increased risk of depression did not emerge for the genotype (Caspi et al., 2003). Children with the 5-HTTLPR s allele and with poor attachment relationships to parents exhibit poor self-regulation of negative affect (Barry, Kochanska, & Philibert, 2008; Kochanska, Philibert, & Barry, 2009; Pauli-Pott, Friedl, Hinney, & Hebebrand, 2009), which in turn predicts a number of adult psychiatric disorders (Caspi et al., 2010).

In contrast to the influence of the s allele, the l allele may be protective against some of the adverse effects of environments (Barry et al., 2008). For example, significant numbers of children exposed to institutional care have had developmental delays, delayed IQs, atypical patterns of diurnal cortisol activity, and high rates of insecure attachment patterns (Bakermans-Kranenburg, Dobrava-Krol, & van IJzendoorn, 2011). Studies using interview rather than self-report methods have found that while children with s allele genotypes (i.e., ss and sl genotypes) have shown high levels of adverse effects (e.g., emotional problems), children with the ll allele genotype have shown the lowest levels of problems (Bakermans-Kranenburg et al., 2011; Kumsta et al., 2010). In contrast (analyzing the biallelic rather than the triallelic genotype), Thakur, Joober, and Brunet (2009) found a 4.8 times greater risk of chronic PTSD for individuals with the l allele, suggesting that the s allele is protective against PTSD persistence.

FKBP5 POLYMORPHISMS

In addition to PTSD and suicidality, FKBP5 SNPs have been associated with incomplete normalization of stress-induced cortisol secretion (Ising et al., 2008; Willour et al., 2009) and with response to antidepressants and recurrence of depressive episodes (Binder et al., 2004). Four SNPs in the FKBP5 locus (rs3800373, rs9296158, rs1360780, and rs9470080) have significantly interacted with childhood trauma in predicting adult symptoms of PTSD, even after researchers have controlled for depression severity, age, sex, levels of exposure to traumas other than child abuse, and genetic ancestry (Binder et al., 2008). SNP genotypes associated with the highest FKBP5 messenger RNA induction in peripheral blood mononuclear cells by cortisol were associated with greatest vulnerability to PTSD symptoms following child abuse. The four SNPs were significantly associated with greater PTSD severity in a small group exposed to two types of child abuse, but not in a larger group exposed to one type of abuse. Sarapas and colleagues (2011) found that homozygosity

for any of the four PTSD risk-related polymorphisms at FKBP5 predicted FKBP5 expression that mediated indirect effects of genotype on plasma cortisol (hypercortisolemia) and PTSD severity. FKBP5 polymorphisms are also associated with elevated peritraumatic dissociation in medically injured children (Gillespie et al., 2009; Koenen et al., 2005).

CORTICOTROPIN-RELEASING HORMONE

Polymorphisms within the CRH receptor (CRHR1) gene may influence risk for depression, PTSD, and suicidality (Binder et al., 2010; Gillespie et al., 2009; Kertes et al., 2010; Roy, Hodgkinson, DeLuca, Goldman, & Enoch, 2012), as well as culture-specific anxiety and substance use (Enoch et al., 2008; Roy et al., 2012). Persistent hyperactivity of the HPA axis following developmental stress exposure is mediated, at least in part, by a hyperactive CRHR1 system (Gillespie et al., 2009; Lupien et al., 2009). The combination of CRHBP rs7728378 and FKBP5 rs3800373 is associated with greater suicide risk than is either polymorphism individually. In contrast, highly trauma-exposed individuals with neither major homozygote have had rates equivalent to individuals not exposed to childhood trauma. CRHR1 rs9900679 (unique to African ancestry) was protective against suicide attempt.

DOPAMINERGIC SYSTEMS

The dopaminergic systems are involved in reward systems and affect modulation (Nader, in press) and relate to endogenous opiates, which are elevated during dissociative states and diminished with hyperactivity (Byrnes, 2001; Stein & Kendall, 2004). A study of comorbid CD and substance abuse (Hoenicka et al., 2007) found that the TaqIA SNP located near the dopamine receptor D2 (DRD2) gene might be related to a nonspecific vulnerability to a wide range of impulsive and reward-inducing behaviors. Notably, genetic vulnerabilities, in interaction with parenting, influence levels of aggressive behavior problems in at-risk children (Bakermans-Kranenburg, van IJzendoorn, Pijlman, Mesman, & Juffer, 2008; Moss et al., 2012). Meta-analysis confirms that dopamine-related genes (DRD2, DAT, and DRD4) serve as moderators of the association between positive and negative environmental factors with developmental outcomes in children up to age 10 (Bakermans-Kranenburg & van IJzendoorn, 2009). Like children with s allele 5-HTTLPR polymorphism, youth with less efficient dopamine-related genes function more poorly in negative environments and also benefit most from positive environments. Research has found an association between DRD2A1 and PTSD for a subset of individuals who engaged in harmful drinking (Koenen, 2007; Young et al., 2002); a link between chronic PTSD and the dopamine transporter SLC6A3 (DAT1) 3′ polymorphism (Segman et al., 2002); and an association between PTSD symptoms (primarily arousal symptoms) and a dopamine polymorphism in preschoolers (Drury, Theall, Keats, & Scheeringa, 2009).

CONCLUDING REMARKS

For children, a concern has often been lack of sensitivity to or underrecognition of trauma and its effects. Symptomatic children without diagnosable PTSD by DSM-IV standards have been as functionally impaired as children who received the diagnosis (Nader, 2008; Scheeringa, 2011). Some but not all of the problems in applying adult criteria to children have been addressed in DSM-5. Future versions of diagnostic criteria for PTSD in the DSM may additionally adjust Criteria C and D for children under age 13 and may elaborate loss of developmental skills, brain injury, and/or gene-related outcomes. Given the importance of trauma's potential interruption of development, evaluations of pre- and postadversity developmental skills—such as self-regulation, interpersonal skills, adaptive functioning, and self-image—as well as brain development and neurochemical reactivity will be appropriate additions to evaluations of other trauma symptoms. In addition to the importance of self-regulation, relational, and coping skills to children's development, skills such as a sense of humor, which may be undermined by trauma, have been linked to social competence, popularity, and adaptability (Semrud-Clikeman & Glass, 2010). Evidence also confirms the import of examining earlier PTSD symptom findings in relation to numbers of traumas experienced.

Additional study is needed in several realms to inform the next iteration of our understanding and conceptualization of PTSD. For example, although maltreatment has been well studied and is associated with multiple adverse effects (Milot, St.-Laurent, Éthier, & Provost, 2010), the most prevalent form of maltreatment (61%; Milot et al., 2010; U.S. Dept. of Health and Human Services, 2011), neglect, is less well studied than physical or sexual abuse. Also less often stud-

ied, emotional abuse has been a precursor to or accompanied by physical victimization and has been associated with increased feelings of isolation, negative self-esteem, depressive symptoms, eating disorders, mood lability, aggression, and/or increased sexual risk-taking or abuse behaviors, as well as with external locus of control (Wonderlich et al., 2007; Younge et al., 2010; Zurbriggen et al., 2010). PTSD Criterion A will need additional revision in order to represent neglect and emotional abuse clearly. Additional research will need to determine whether the omission of natural disasters from A3 and from persistent complex bereavement disorder "with traumatic bereavement" is warranted. For example, it will be important to study, especially in children, whether learning that a parent, sibling, or other significant person is still missing when people may be buried under earthquake- or tornado-demolished buildings is also related to PTSD or traumatic bereavement.

PTSD in future DSMs is likely to be informed by genetic findings as well. Specific vulnerabilities to stress have already been identified. Questions related to genetics and specific posttrauma symptoms are likely to emerge. For example, are symptoms of negative cognition more prominent with serotonin polymorphisms, and/or does trauma induce negative cognitions? Does impulsive risk taking occur more commonly with dopamine or MAOA polymorphisms, and/or is it traumatically engendered? Such information may be important to treatment as well as to understanding childhood PTSD.

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PART V

NEURODEVELOPMENTAL DISORDERS

CHAPTER 11

Autism Spectrum Disorder

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social and communication behaviors, as well as a restricted range of activities and interests. Although autism is typically described as one syndrome, it is now recognized that it is actually a spectrum of disorders representing complex developmental disabilities with considerable variability in clinical presentation. This variability has important implications for understanding the etiologies of ASD, stability of symptoms, individual differences in the age of onset, treatment response, and profiles of social-emotional development that have been observed among children with ASD. Throughout this chapter, we use the terms "autism" and "ASD" interchangeably to refer to this complex diagnosis.

HISTORICAL CONTEXT

The term "autism" was coined by Bleuler (1911/1950) to describe individuals with schizophrenia who had a loss of contact with reality. In the early 1940s, two men, Leo Kanner (1943) and Hans Asperger (1944/1991), independently described childhood disorders involving impaired social relationships, abnormal language, and restricted and repetitive interests. They believed that these children had a loss of contact with reality similar to that described by Bleuler, without the concomitant diagnosis of schizophrenia.

In his initial report, Kanner presented case studies of 11 children whom he described as having an "extreme autistic aloneness" (p. 242). He noted that these children had an "inability to relate themselves in the ordinary way to people and situations from the beginning of life" (p. 242). In addition, he wrote that the syndrome led to language deviance characterized by delayed acquisition, echolalia, occasional mutism, pronoun reversals, and literalness. Finally, Kanner described these children as having an "obsessive desire for the maintenance of sameness" (p. 245), characterized by the development of elaborate routines and rituals. Because of their good rote memory and their normal physical appearance, Kanner concluded that these children were capable of achieving normal cognitive abilities. The diagnostic label of autistic disorder was used to refer to this group of individuals until the recent publication of the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5; American Psychiatric Association [APA], 2013) when the label was changed to autism spectrum disorder.

In 1944, Asperger described a similar, but less severely impaired, group of four children that he diagnosed as having "autistic psychopathy." Similar to Kanner, Asperger described difficulties in social interaction including eye contact, affective expression, and conversational abilities. In contrast to Kanner's report, Asperger wrote about children who developed good language abilities by the time they entered school and often spoke pedantically like adults (Asperger, 1944/1991). Despite good vocabularies and grammatical abilities, these children were impaired in their conversational skills and had unusual use of the volume, tone, and flow of speech. Asperger commented on the high level of original thought displayed by these children and their tendency to become excessively preoccupied with a singular topic of interest. The diagnostic label of Asperger's disorder was used to refer to this group of individuals until the publication of DSM-5 when this subgroup was included within the autism spectrum disorder label.

Historically, it was believed that parents of children with autism were overly intellectual, were cold-hearted, and had a limited interest in other people—including their spouses and children (Bettelheim, 1967; Kanner, 1943). Bettelheim (1967) proposed that in response to rejecting parents, children with autism withdrew from social interaction and became self-sufficient. Until the mid-1970s, treatment regimens involved helping parents (usually mothers) to become less rejecting of their children. However, these initial hypotheses regarding the etiology of autism were not supported by empirical research conducted in the 1970s and 1980s showing that parents scored within the normal range on personality measures (McAdoo & DeMyer, 1978; Koegel, Schreibman, O'Neill, & Burke, 1983). Parents of children with autism and parents of children without disabilities reported similar levels of marital satisfaction and family cohesion. Furthermore, recent research indicates that children with ASD, particularly those with average cognitive skills, develop secure attachment relationships with their primary caregivers at rates that approach those found in typically developing populations (see Rutgers, Bakersman-Kranenburg, van IJzendoorn, & Berckelaer-Onnes, 2004, for a review).

Bernard Rimland (1964) and Eric Schopler (Schopler & Reichler, 1971) were among the first researchers to argue against the theory that parents were responsible for their children's autism. Rimland proposed that the disorder was due to a neurological impairment. Schopler suggested that rather than treating the parents, the role of intervention was to involve parents as cotherapists working to help their children.

DESCRIPTION OF THE DISORDER

Originally, three domains of core symptoms were recognized as characterizing autism in DSM-IV (APA, 1994): qualitative impairments in social interaction; impairments in communication; and the presence of a restricted range of interests and behaviors. However, some research has favored a view of a single underlying continuous factor of ASD symptoms, rather than a conceptualization of three separate domains (Constantino et al., 2004; Mandy & Skuse, 2008). Alternatively, several researchers have argued that restricted and repetitive behaviors can be dissociated from social and communication symptoms, based on genetic twin studies showing that these traits were only modestly correlated (Happé, Ronald, & Plomin, 2006). Practically, it is often difficult for clinicians to separate symptoms into social versus communication impairments (e.g., difficulty engaging in a reciprocal conversation could be construed as impairment in social reciprocity and/or as impairment in communication skills). As a result of this research, the core symptoms of ASD have been reconceptualized in DSM-5 (APA, 2013) into two domains: impairments in social communication, and the presence of restricted and repetitive behaviors.

Core Symptoms

Social Communication

The impairment in social communication in ASD affects multiple domains of social behavior. For example, the ability to imitate another person, share a focus of attention with another person, recognize and process faces, and engage in pretend play are all affected and have significant impact on the ability to learn about the social and nonsocial environment. It has been hypothesized that the social impairments found in ASD may reflect an underlying abnormality in the social reward neural circuitry, which influences the motivation to attend to and engage with people (see Figure 11.1). This impairment in social motivation may help explain why at early ages, young children with ASD fail to attend to and affectively respond to socially relevant stimuli (Dawson, Carver, et al., 2002; Dawson, Webb, Wijsman, et al., 2005). A rich literature exploring the nature

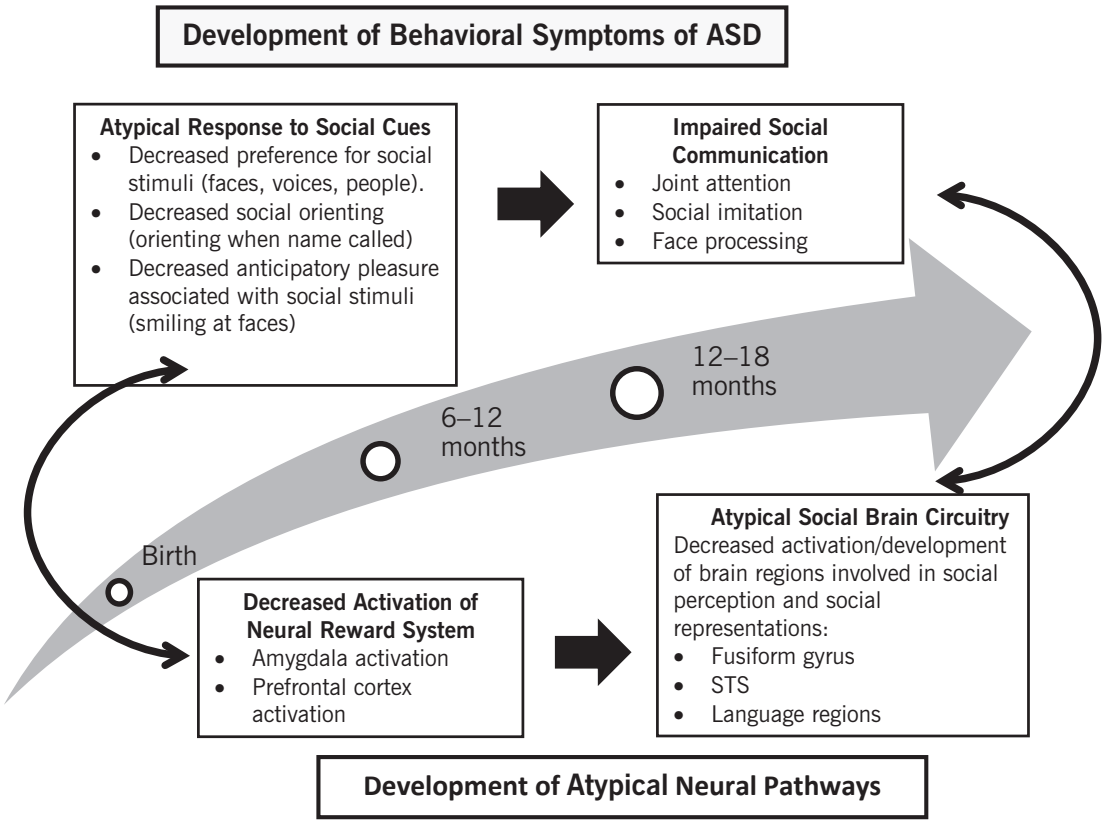

FIGURE 11.1. The emergence of autism spectrum disorder (ASD) in the first years of life.

of social impairments in ASD exists and is briefly reviewed below.

SOCIAL IMITATION

In typical development, imitation skills are present shortly after birth (Field, Woodson, Greenberg, & Cohen, 1982; Meltzoff & Moore, 1977). It has been hypothesized that early interactions involving mutual imitation facilitate infants' ability to understand the relationship between themselves and other people (Meltzoff & Gopnik, 1993; Stern, 1985). Young children with ASD have specific impairments in their ability to imitate the movements of others, including body movements and actions with objects (see Rogers & Williams, 2006, for a review). Impairments have been found in both immediate and deferred imitation (Dawson & Adams, 1984; G. Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998; Stone, Ousley, & Littleford, 1997) and have been associated with other social and language impairments displayed by children with ASD. For example, poor imitation of body movements in 20-month-old children (Charman et al., 2001) and 2-year-old children (Stone et al., 1997) with ASD has been linked to later expressive language impairments. Impaired spontaneous imitation of others has been linked to poor attention following and impaired social reciprocity skills in young children with ASD (McDuffie et al., 2007). Thus a failure to imitate may be a fundamental deficit in ASD and has been hypothesized to interfere with the development of social reciprocity, shared attention, and understanding of emotional states (Dawson, 1991;

Meltzoff & Gopnik, 1993; Rogers & Pennington, 1991; Rogers & Williams, 2006; Williams, Whiten, Suddendorf, & Perrett, 2001).

Although there is a general consensus that imitation skills are impaired in ASD, the underlying reason for these impairments has been debated (see Rogers & Williams, 2006). Theories have attributed imitation impairments to motor praxis impairments in planning, sequencing, and executing intentional motor movements (Rogers, 1998); to difficulties in understanding the intersubjective experience of others, leading to impairments in matching the movements of self and others (Hobson & Hobson, 2008; Meltzoff & Gopnik, 1993); and to inadequate procedural learning and inefficient cerebellar–basal ganglia–parietal circuitry (Mahone et al., 2006; Mostofsky, Goldberg, Landa, & Denckla, 2000). In addition, neurophysiological and brain imaging studies suggest that poor imitation may reflect absent or dysfunctional mirror neurons, which play a critical role in imitation (Bernier, Dawson, Webb, & Murias, 2007; Dapretto et al., 2006; Martineau, Cochin, Magne, & Barthelemy, 2008; Oberman & Ramachandran, 2007; Williams et al., 2006).

JOINT ATTENTION

Another mechanism by which infants gain an understanding of social information is through the use of nonverbal behaviors such as eye contact and gesture to share a focus of attention with another person. "Shared" or "joint" attention refers to the ability to "coordinate attention between interactive social partners with respect to objects or events in order to share an awareness of the objects or events" (Mundy, Sigman, Ungerer, & Sherman, 1986, p. 657). These early-developing abilities are considered important precursors to the development of spoken language (Bruner, 1975; Sugarman, 1984). Between 6 and 9 months of age, infants with typical development learn to share attention by looking between an object and a caregiver (Walden & Ogan, 1988). Later, between 9 and 12 months of age, infants learn that they can also share attention through the use of gesture (Hannan, 1987). Infants can both direct another's attention, through gestures such as pointing, and follow the gestures of others.

Impairment in the initiation of joint attention (e.g., spontaneous directing of another's attention) is considered one of the core social impairments in ASD. Indeed, it has been noted that the failure to coordinate gaze, gesture, and facial expressions as a means of sharing attention with others is among the first symptoms evident in ASD. Through both home videotape studies (Osterling & Dawson, 1994) and prospective screening studies (Baron-Cohen et al., 1996; Wetherby et al., 2004), impairments in joint attention have been documented in 12- to 24-month-old children who later received a diagnosis of ASD. A prospective study of infant siblings of children with ASD found that response to joint attention at 12 months predicted the degree of social impairment and ASD diagnosis at 33 months (Yoder, Stone, Walden, & Malesa, 2009). Later, during the preschool years, impairments in joint attention have been shown to lead to correct diagnoses in 94% of children with ASD, compared to children with intellectual disability (Mundy et al., 1986).

SOCIAL ATTENTION

Several researchers have reported that persons with ASD show decreased orienting to social stimuli. For example, in a study of home videotapes of toddlers' first birthday parties, Osterling and Dawson (1994) found that toddlers with ASD often failed to orient to social stimuli (faces, speech) in their environments. G. Dawson and colleagues (1998) found that, compared to children with Down syndrome and children with typical development who were matched on receptive language mental age, children with ASD more frequently failed to orient to both social stimuli (name calling, clapping) and nonsocial stimuli (rattle, jack-in-the-box), but this failure was much more extreme for social stimuli. Young children with ASD have been found to prefer visually examining geometric figures compared to social images (Pierce, Conant, Hazin, Stoner, & Desmond, 2011); fail to show a normal preference for speech sounds (Kuhl, Coffey-Corina, Padden, & Dawson, 2005); and orient to nonsocial contingencies rather than biological motion (Klin, Lin, Gorrindo, Ramsay, & Jones, 2009). Taken together, these results suggest that children with ASD may exhibit a basic orienting impairment, especially for social stimuli. These social attention impairments may be related to a reduced sensitivity to the reward value of social stimuli. Disruption in brain networks related to reward (e.g., the anterior cingulate cortex and orbitofrontal cortex) have been found in individuals with ASD, suggesting that social stimuli do not evoke the same significance and reward value for these individuals as they do for individuals with typical development (Dawson, Bernier, & Ring, 2012; Schmitz et al., 2008;

Scott-Van Zeeland, Dapretto, Ghahremani, Poldrack, & Bookheimer, 2010).

This failure to attend to social stimuli has been hypothesized to contribute to the imitation and joint attention impairments described previously (McDuffie et al., 2007; Swettenham et al., 1998; Toth, Dawson, Meltzoff, Greenson, & Fein, 2007). For example, Swettenham and colleagues (1998) reported that 20-month-old children with ASD spent more time shifting attention between two objects than between two people or between an object and a person. In contrast, toddlers with developmental delay and toddlers with typical development showed the opposite pattern. Toth and colleagues (2001) reported a strong correlation between reduced social orienting abilities and poor joint attention in young children with ASD. Additionally, they found that social orienting and language ability were not related, even after they controlled for the relation between joint attention and language ability. This suggests a developmental model in which social orienting impairments may lead to joint attention impairments, which then lead to delayed language development.

FACE PERCEPTION

Face recognition abilities are essential for the development of interpersonal relationships. Indeed, infants with typical development recognize their mothers' faces within the first few days of life (Bushnell, Sai, & Mullen, 1989). Lack of attention to faces is considered one of the earliest and most reliable indicators of risk for ASD (Dawson, Webb, Wijsman, et al., 2005; Wetherby et al., 2004). A lack of social motivation or attention may reduce attention to faces early in the development of individuals with ASD (Dawson, Carver, et al., 2002; Klin et al., 1999), and this may result in a failure to develop perceptual expertise of faces. This lack of an "experience-expectant" environment may result in a failure to develop the brain systems needed to process faces in a typical pattern (Dawson, Webb, Wijsman, et al., 2005). Slower habituation to faces has been demonstrated in toddlers between 18 and 30 months with ASD than in children with developmental delays, children with typical development, or infant siblings without ASD (Webb et al., 2010). Additionally, several studies have shown that individuals with ASD process faces by using abnormal strategies, including reduced attention to the core features of the face, such as the eyes and nose (Chawarska & Shic, 2009; Klin, Jones, Schultz, Volkmar, & Cohen, 2002). Face-processing abnormalities have been documented across the lifespan in older children, adolescents, and young adults with ASD (e.g., Boucher & Lewis, 1992; Hauk, Fein, Maltby, Waterhouse, & Feinstein, 1999; Tantam, Monaghan, Nicholson & Stirling, 1989; Teunisse & DeGelder, 1994).

The notion of an unusual face-processing style is supported by both electrophysiological and MRI studies of face processing in individuals with ASD. Electrophysiological results reveal abnormalities in the early stages of face processing in ASD (see Dawson, Webb, & McPartland, 2005, for a review). Young children with ASD showed an atypical faster response to objects than faces in one study (Webb, Dawson, Bernier, & Panagiotides, 2006), whereas children with typical development demonstrated the characteristically faster response to faces than objects in the right hemisphere, and children with developmental delay failed to show any differential response. In examining the response to familiar and unfamiliar faces, 18- to 47-month-old young children with ASD exhibited similar event-related potential (ERP) responses to familiar and unfamiliar faces as 12- to 30-month-old children with typical development, suggesting delayed neural development in face processing (Webb et al., 2011). Adults with ASD also showed abnormal face-processing ERP responses relative to IQ-matched typical adolescents and adults (McPartland, Dawson, Webb, Panagiotides, & Carver, 2004; O'Connor, Hamm, & Kirk, 2007). These studies suggest that in ASD, the neural system related to face processing is less efficient (slower), lacks specificity to faces, and is abnormally represented in the brain.

FUNCTIONAL AND SYMBOLIC PLAY

Play is an important precursor to language development. Typically, children progress from playing with toys functionally to playing with toys symbolically (e.g., pretending that a banana is a phone). Symbolic play gradually emerges between 12 and 22 months of age, with the majority of children achieving symbolic play by approximately 20 months of age (Riguet, Taylor, Benaroya, & Klein, 1981; Ungerer & Sigman, 1984). In a prospective medical screening study, Baron-Cohen and colleagues (1996) reported that the absence of pretend play at 18 months of age was one of the earliest symptoms of ASD. Preschool children with ASD spend more of their time unengaged and less time engaged in symbolic play, compared to children with other developmental delays (Wong & Kasari, 2012). Furthermore, play skills during the preschool years have been associ-

ated with both spoken language and cognitive ability at 8 years of age (Kasari, Gulsrud, Freeman, Paparella, & Hellemann, 2012). While children with ASD often learn to engage in symbolic play, it often lacks creativity and playfulness and appears mechanical and repetitive, without flexible, elaborate themes (Hobson, Lee, & Hobson, 2009; Wing, 1978).

COMMUNICATION ABILITIES

Given these significant impairments in early-developing social communication abilities that are considered to be precursors to language development, it is not surprising that children with ASD often have significantly delayed and deviant verbal and nonverbal communication development. Prospective studies of infants later diagnosed with ASD report that they have atypical prosody (Wetherby et al., 2004) and exhibit fewer gestures and consonants (Landa, Holman, & Garrett-Mayer, 2007), suggesting that lack of these early verbal and nonverbal communication skills may provide a key early behavioral identifier of ASD. Furthermore, longitudinal studies consistently suggest that measures of early social communication skills (imitation, joint attention, play) significantly predict verbal language outcomes in early childhood (Charman et al., 2005).

Individuals with ASD often use atypical language characterized by immediate or delayed echolalia (e.g., verbatim repetition of previously heard words or phrases) (Rydell & Mirenda, 1994); abnormal prosody (e.g., atypical rhythm, stress, intonation, and loudness) (Peppé, McCann, Gibbon, O'Hare, & Rutherford, 2007); and pronoun reversal (e.g., use of "you" instead of "I" when referring to the self) (Cantwell, Baker, Rutter, & Mawhood, 1989; Kanner, 1943). Communication impairments in ASD are most pronounced in the pragmatic, or social, aspects of language use (see Tager-Flusberg, 1999, 2001, for reviews). In a study of the speech characteristics of 4- to 7-year-old verbal children with ASD, language was characterized by inappropriate prosody and voice, including increased repetitions, loudness, high pitch, and misplaced stress (Shriberg, Paul, Black, & van Santen, 2011). The authors concluded that this pattern of errors was consistent with a view that individuals with ASD do not experience the social motivation to "tune up" the precision of their speech to match the speech of others in their environment. Problems in reciprocal conversation are often related to difficulties understanding another person's perspective (i.e., "theory of mind"; Paul, Orlovski, Marcinko, & Volkmar, 2009; Tager-Flusberg, 2000) and ignoring of conversational initiations introduced by another person (Eales, 1993; Paul et al., 2009; Tager-Flusberg, 1999, 2001).

Restrictive and Repetitive Behaviors and Interests

Restricted and repetitive behaviors (RRBs) have been conceptualized as a core feature of ASD and encompass a broad array of symptoms. These include stereotyped and repetitive motor mannerisms (e.g., hand flapping); repetitive use of objects (e.g., lining up toys); inflexible adherence to routines (e.g., insistence on driving the same route to school); preoccupations with unusual objects (e.g., electrical cords); preoccupations (e.g., with bus schedules) that are appropriate in content but overly intense; and unusual interests in or responses to sensory information in the environment (e.g., visual fascination with lights). Repetitive behaviors are not specific to ASD and are also observed in infants and young children with typical development (e.g., Evans et al., 1997; Thelen, 1979, Watt, Wetherby, Barber, & Morgan, 2008) and in other developmental and psychiatric disorders such as Tourette syndrome, fragile X syndrome, Rett's disorder, Down syndrome, Parkinson's disease, dementia, schizophrenia, and intellectual disabilities (see Leekam, Prior, & Uljarevic, 2011, for a review). However, these behaviors occur more frequently in ASD than in other disorders (Matson, Dempsy, & Fodstad, 2009).

RRBs have been identified as a potential early marker for ASD. Prospective studies of infant siblings of children with ASD found that the presence of RRBs at 12 months (e.g., spinning, rotating, and unusual visual exploration) was related to later ASD symptoms and diagnosis (Ozonoff, Heung, Byrd, Hansen, & Hertz-Picciotto, 2008; Zwaigenbaum et al., 2005). In a general populaton screening study, Watt and colleagues (2008) similarly found that children later diagnosed with ASD showed a higher frequency and duration of repetitive behaviors during the second year of life than did either children with typical development or children with non-ASD developmental delay. Specifically, they found that repetitive behavior with objects (e.g., banging, tapping, flipping, rolling) and some repetitive body movements (e.g., banging the table, rubbing the body, posturing of the hands and fingers) were more prevalent in toddlers with ASD.

Although these behaviors are often discussed as a single core feature of the disorder, research calls into

question the conceptualization of RRBs as a single entity. In a review of the research in this area, Turner (1999) suggested that the RRBs in ASD comprise two distinct categories of behaviors: lower-level behaviors that are characterized by repetitive motor movements, and higher-level or more complex behaviors that are characterized by insistence on following elaborate routines and circumscribed interests. In a longitudinal study of the emergence and stability of RRBs from 2 to 9 years of age, Richler, Huerta, Bishop, and Lord (2010) found support for the existence of these two subtypes of RRBs, which they termed "repetitive sensorimotor behaviors" (e.g., hand and body mannerisms, repetitive object use, and unusual sensory interests) and "insistence on sameness" (e.g., compulsions and rituals, resistance to change). For children with ASD, repetitive sensorimotor behaviors remained relatively high over time, indicating consistent severity, whereas insistence on sameness started low and increased over time, indicating worsening. Little research has examined the developmental trajectory into adulthood, although the studies that have been conducted indicate that RRBs persist into adolescence and adulthood (Piven, Harper, Palmer & Arndt, 1996; Rumsey, Rapoport, & Sceery, 1985).

Research on the relation between RRBs and intellectual functioning has consistently found a link between repetitive sensorimotor behaviors and comorbid intellectual disability (Campbell et al., 1990; Wing, 1988; Wing & Gould, 1979). Watt and colleagues (2008) reported that repetitive use of objects in the second year of life was associated with lower verbal and nonverbal developmental levels. Similarly, in Richler and colleagues' (2010) longitudinal study, having higher nonverbal intelligence at age 2 was associated with milder concurrent repetitive sensorimotor behaviors and predicted improvement over time. Historically, insistence on sameness was believed to be associated with less severe levels of intellectual disability (Turner, 1999), although more recent research has not supported this belief. Lam, Bodfish, and Piven (2008) found that approximately 88% of children with ASD had circumscribed interests, and that the presence of these interests was not associated with intelligence or severity of other ASD symptoms. Similarly, Richler and colleagues did not find a relation between insistence on sameness and nonverbal intelligence.

Research explaining the presence of RRBs in ASD is sparse (see Leekam et al., 2011, for a review). Some theories suggest that a lack of social attention from early childhood leads to an increased interests in objects, including an insistence on sameness. Indeed, circumscribed interests are typically nonsocial in nature. South, Ozonoff, and McMahon (2005) found that common types of circumscribed interests included vehicles, dinosaurs, particular animals, Japanese animation, space/physics, schedules, and numbers. Animal models have suggested a relation between RRBs and being reared in low-enrichment environments (Lewis, Tanimura, Lee, & Bodfish, 2007). Alternatively, RRBs have been hypothesized to serve as a self-regulatory coping strategy that helps regulate arousal levels or anxiety (Joosten, Bundy, & Einfeld, 2009). For example, some persons with ASD describe RRBs as providing a calming influence when they are aroused because of extreme positive or negative emotions. Others have suggested that RRBs are linked to the presence of specific genetic disorders such as fragile X, Williams, and Angelman syndromes (Moss, Oliver, Arron, Burbidge, & Berg, 2009). More research is clearly needed to explain the presence of RRBs as a core symptom of ASD.

DSM-5 has extended previous definitions of RRBs to include repetitive speech (echolalia) and idiosyncratic phrases, which were previously defined as impairments in communication. Also, atypical sensory interests are included in the DSM-5 under the RRB category. Little research has examined the relation between these symptoms and other types of RRBs.

DEFINITIONAL AND DIAGNOSTIC ISSUES

Although ASD is considered a neurodevelopmental disorder, there are no biological markers or medical tests for diagnosing ASD. Therefore, the diagnosis of ASD is based on behavioral symptoms and developmental history. DSM-5 (APA, 2013) has introduced a significant conceptual change in the diagnosis of ASD: It presents a complex model with a single ASD category superimposed on two primary symptom dimensions. This type of change in conceptual models of the disorder, and the related defining symptoms, has the potential to make a significant impact on the prevalence rate of ASD, and there is much interest in tracking changes in ASD diagnoses associated with these new diagnostic criteria. Furthermore, DSM-5 now acknowledges that ASD is associated with frequent comorbid developmental disabilities, psychiatric disorders, and medical complications (see Figure 11.2 for an overview). This acknowledgment of comorbidities provides a broader

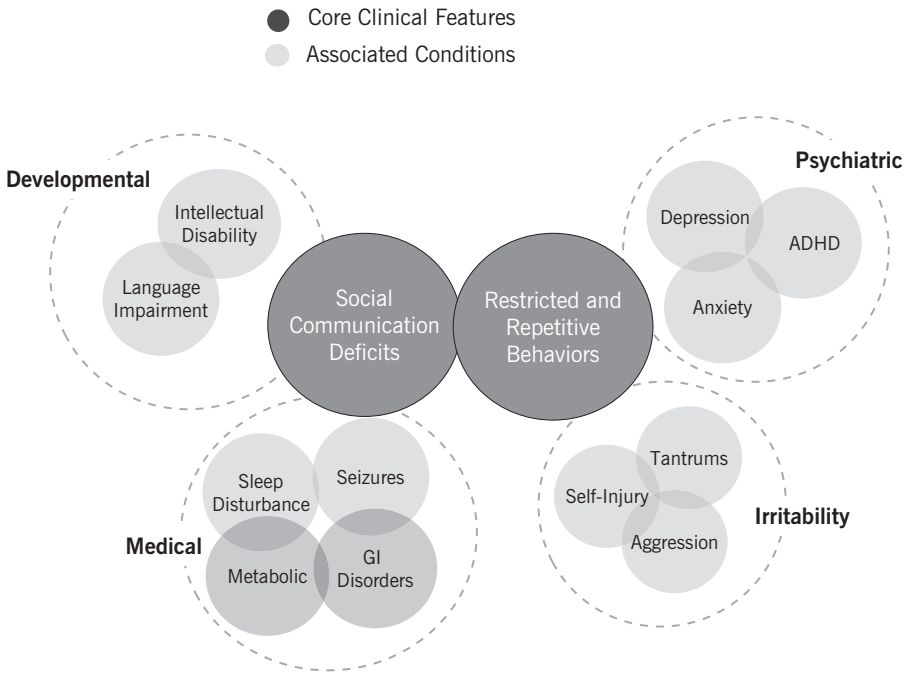

FIGURE 11.2. ASD core clinical features and associated comorbidities.

perspective on ASD, but at the same time, it complicates the diagnostic process and supports the importance of interdisciplinary evaluations.

DSM-5 Diagnosis of ASD

DSM-5 Neurodevelopmental Disorders

The DSM-5 category of neurodevelopmental disorders groups ASD with intellectual disability (intellectual developmental disorder), communication disorders, attention-deficit/hyperactivity disorder (ADHD), specific learning disorder, and motor disorders. These disorders are a group of conditions with onset early in development that have a major impact on daily functioning with regard to social, academic, and independent living behaviors. The grouping of these disorders into one cluster is explained by a suggested overlap of risks (e.g., genetic, developmental trajectories, etc.) that are not shared by disorders in other clusters (Andrews, Pine, Hobbs, Anderson, & Sunderland, 2009). The grouping of these disorders in DSM-5 is also an acknowledgment that these disorders frequently co-occur (e.g., a recognition that a comorbid diagnosis of ASD and ADHD is possible).

Autism as a Spectrum Disorder

The decision to combine the specific DSM-IV diagnoses of pervasive developmental disorders or PDDs (autistic disorder, Asperger's disorder, and PDD not otherwise specified [PDD-NOS]) into a single diagnosis of ASD has generated a great deal of controversy. Although this controversy has received a fair amount of attention in the media, researchers have long adopted the term ASD in favor of the DSM-IV term of PDD. Indeed, a MEDLINE title search of articles published between 2007 and 2012 showed that investigators used ASD over PDD by a ratio of nearly 10:1 during this period (King, Veenstra-VanderWeele, & Lord, 2013). The rationale for this change is twofold. First, trained clinicians are routinely able to differentiate the presence of ASD from other developmental disorders with consistent reliability and validity. However, the differential

diagnosis of the DSM-IV-defined subtypes of PDD has been significantly inconsistent, and it has been more closely associated with extraneous factors (such as site of diagnosis, intellectual level, and other presenting comorbidities) than with presenting ASD symptoms (Lord et al., 2012). Notably, significant variability across sites has been evident even when diagnoses were provided by expert clinicians using standardized measures (Lord et al., 2012). The controversial decision to discontinue the diagnostic label of Asperger's disorder was further supported by research showing few group differences with regard to symptom presentation and cognitive functioning in individuals diagnosed with high-functioning autism and those diagnosed with Asperger syndrome (Ozonoff, South, & Miller, 2000).

A second rationale for specifying a single disorder as opposed to a set of disorders is the acknowledgment that variability in developmental level can account for differing symptom presentation. The DSM-5 Task Force concluded that the impairments seen in daily life are best represented as a single yet multidimensional disorder, which manifests itself in unique manners across individuals due to differing cognitive strengths and weaknesses, as well as existing comorbidities (Rutter, 2011). This decision was supported by longitudinal studies reporting that while an ASD diagnosis is stable from 2 years of age onward, children often changed diagnoses across the different DSM-IV-defined subtypes (Lord et al., 2006; van Daalen et al., 2009), often because of changes in social and communication skills across development. Rather than representing true diagnostic changes, these changes are best represented as variability within a single disorder.

Although this research supports the conceptual validity of DSM-5's use of the term ASD, it does not provide information about the sensitivity and specificity of the diagnosis. Indeed, individuals with ASD, their families, and clinicians have expressed significant concern that the DSM-5 conceptualization of ASD would result in fewer individuals' meeting diagnostic criteria; the impact would be particularly strong on those with milder symptoms and intact intellectual skills who had been previously diagnosed with DSM-IV Asperger's disorder (see Wing, Gould, & Gillberg, 2011). Research examining the sensitivity and specificity of DSM-5 criteria has produced mixed results, with the interpretation of findings complicated by the fact that research was conducted on differing drafts of proposed DSM-5 criteria. Early studies using Phase 1 field trial definitions raised significant concerns suggesting that up to 39% of individuals diagnosed with a DSM-IV PDD were not diagnosed with DSM-5 ASD (Frazier et al., 2012; McPartland, Reichow, & Volkmar, 2012). In the most comprehensive study to date using the final DSM-5 criteria, Huerta, Bishop, Duncan, Hus, and Lord (2012) examined 4,453 children with a clinical DSM-IV PDD diagnosis and 690 children with a non-PDD diagnosis. The majority (91%) of children with clinical diagnoses of a DSM-IV PDD were found to meet the DSM-5 criteria in assessments with standardized diagnostic instruments (Autism Diagnostic Interview—Revised, Autism Diagnostic Observation Schedule). Despite concerns about the sensitivity of the DSM-5 criteria, adequate sensitivity was found across all DSM-IV-defined subgroups and across age, sex, and intellectual ability. Sensitivity was highest for those with previous DSM-IV diagnoses of autistic disorder (.93–.95) and lower for those with previous diagnoses of Asperger's disorder or PDD-NOS (.76–.94). Several studies have further documented the increased specificity of the DSM-5 diagnostic criteria for ASD, particularly for individuals with DSM-IV diagnoses of Asperger's disorder or PDD-NOS; the new criteria thus seem to reduce the likelihood that individuals without ASD will be inappropriately given an ASD diagnosis (Frazier et al., 2012; Huerta et al., 2012; McPartland et al., 2012).

DSM-5 Symptom Domains

As noted earlier, DSM-5 describes ASD as characterized by two primary domains: (1) persistent deficits in social communication and interactions (SCI) across multiple contexts; and (2) the presence of restricted, repetitive patterns of behavior, interests, or activities (RRBs) (see Table 11.1 for DSM-5 diagnostic criteria for ASD). This represents a significant change in the previous view of autism as a triad of symptom categories, including language and communication as the third symptom domain. This change is well supported by research supporting the existence of two independent symptom domains (see Frazier et al., 2012; Gotham et al., 2008; Mandy, Charman, & Skuse, 2012). For example, Frazier and colleagues (2012) analyzed ASD symptoms from a large sample of siblings (8,911 with ASD, 5,863 without ASD) ranging in age from 2 to 18 years, and found evidence for the DSM-5 conceptualization of ASD as both a categorical diagnosis (distinction between youth with and without ASD) and a dimensional diagnosis within two symptom areas (SCI

TABLE 11.1. DSM-5 Diagnostic Criteria for Autism Spectrum Disorder

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history (examples are illustrative, not exhaustive; see text):

1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.

Specify current severity:

Severity is based on social communication impairments and restricted, repetitive patterns of behavior.

B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text):

1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).
3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).
4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).

Specify current severity:

Severity is based on social communication impairments and restricted, repetitive patterns of behavior.

C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).

D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.

E. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

Note: Individuals with a well-established DSM-IV diagnosis of autistic disorder, Asperger's disorder, or pervasive developmental disorder not otherwise specified should be given the diagnosis of autism spectrum disorder. Individuals who have marked deficits in social communication, but whose symptoms do not otherwise meet criteria for autism spectrum disorder, should be evaluated for social (pragmatic) communication disorder.

Specify if:

With or without accompanying intellectual impairment

With or without accompanying language impairment

Associated with a known medical or genetic condition or environmental factor (**Coding note:** Use additional code to identify the associated medical or genetic condition.)

Associated with another neurodevelopmental mental, or behavioral disorders (**Coding note:** Use additional code[s] to identify the associated neurodevelopmental, mental, or behavioral disorder[s].)

With catatonia (refer to the criteria for catatonia associated with another mental disorder for definition) (**Coding note:** Use additional code 293.89 [F06.1] catatonia associated with autism spectrum disorder to indicate the presence of the comorbid catatonia.)

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and RRB). This hybrid model merges two previously competing views of ASD symptoms suggesting that ASD is a categorical disorder superimposed on quantitative symptom distributions.

SOCIAL COMMUNICATION AND INTERACTION

DSM-5 lists three symptom areas in the SCI category: (A1) "Deficits in social-emotional reciprocity"; (A2) "Deficits in nonverbal communication behaviors used for social interaction"; and (A3) "Deficits in developing maintaining, and understanding relationships" (APA, 2013, p. 50). All three symptoms are required for a diagnosis and must be persistent deficits that are present across multiple contexts. Clinically, some overlap in interpretation of these symptoms can be expected. For example, clinicians may struggle to determine whether a child who walks into the clinic and asks the receptionist her weight is demonstrating a symptom of abnormal social approach (an example of impaired social reciprocity) or is showing difficulty adjusting behaviors to suit various social contexts (an example of difficulty understanding relationships) (Huerta et al., 2012). Furthermore, it is difficult to map the DSM-5 SCI symptoms with current best-practice diagnostic instruments, such as the Autism Diagnostic Observation Schedule or the Autism Diagnostic Interview (Barton, Robins, Jashar, Brennan, & Fein, 2013; Huerta et al., 2012).

RESTRICTED, REPETITIVE BEHAVIORS

There are four symptoms listed in the RRB category: (B1) "Stereotyped or repetitive motor movements, use of objects, or speech"; (B2) "Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior"; (B3) "Highly restricted, fixated interests that are abnormal in intensity or focus"; and (B4) "Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment" (APA, 2013, p. 50). Two of these four symptoms must be present for an ASD diagnosis. Although parents, clinicians, and individuals with ASD have frequently reported atypical sensory processing abilities, this symptom has been given relatively little attention by either researchers or clinicians. The addition of atypical sensory processing as a symptom in the RRB category is new for DSM-5. Sensory processing difficulties are typically grouped into three domains: (1) sensory overresponsivity (e.g., negative responses to specific sensory stimuli, including light and sound); (2) sensory underresponsivity (e.g., nonresponsivity to various sensory stimuli, such as failure to respond to one's name): and (3) sensory seeking (e.g., engaging in actions that provide increased sensation) (Baranek, David, Poe, Stone, & Watson, 2006; Dunn, 1997; Miller, Coll, & Schoen, 2007). Approximately 56–70% of individuals with ASD are reported to exhibit sensory overresponsivity (Baranek et al., 2006; Ben-Sasson et al., 2007). Little research has examined the link between repetitive behaviors and atypical sensory behaviors. However, a recent factor analysis by Mandy, Charman, and Skuse (2012) supports the inclusion of both symptom types into a single construct.

Lifespan Disorder

DSM-5 requires that symptoms must be present in "the early developmental period" (APA, 2013, p. 50), but does not specify an age of symptom onset. This is a shift from DSM-IV, which required symptom onset by 36 months of age. Furthermore, DSM-5 allows for diagnosis in middle childhood or adulthood, acknowledging that symptoms may not manifest themselves until social demands exceed limited capacities. This caveat allows for the diagnosis of individuals previously described as having Asperger's disorder, who may not have a period of early developmental delay and whose social difficulties may not become more obvious until later in life. Additionally, DSM-5 acknowledges that symptoms may change across the lifespan, such that learned strategies may mask impairments later in life (e.g., social skills intervention may teach social reciprocity skills). A diagnosis, however, must also meet DSM-5's usual standard of impairments in current functioning that reach clinical significance in important areas. Thus it is possible that individuals with a previously well-documented diagnosis of ASD would no longer qualify for this diagnosis if their symptoms improved to the extent that a clinically meaningful impairment was no longer present (see Fein et al., 2013, for a discussion of these optimal-outcome individuals).

There have been concerns that the DSM-5 criteria may be too stringent to detect ASD in toddlers whose symptom presentation may be unclear and still emerging, particularly with regard to the presence of RRB symptoms. Huerta and colleagues (2012) did not find evidence to support this concern, noting that only 75 of 5,143 children with ASD met DSM-5 criteria for the SCI symptoms but not the RRB symptoms. How-

ever, in a sample specific to toddlers (average age = 25 months), Barton and colleagues (2013) noted that the DSM-5 criteria requiring three SCI symptoms and two RRB symptoms showed reduced sensitivity. They proposed that the criteria be relaxed for toddlers, suggesting two SCI symptoms and only one RRB symptom. More research is needed on the sensitivity and specificity of the DSM-5 criteria across the lifespan.

DSM-5 Severity Ratings

DSM-5 guidelines require a severity specifier documenting current symptom severity for SCI and RRB symptoms. For each symptom domain, severity can be recorded (APA, 2013, p. 52) as "requiring support" (Level 1), "requiring substantial support" (Level 2), or "requiring very substantial support" (Level 3). Fitting with the conceptualization that symptom domains are independent, it is possible to have very different ratings for each domain. For example, it is possible for one individual to have a Level 3 SCI score, indicating severe deficits in verbal and nonverbal social communication skills, and a Level 1 RRB score, indicating some inflexibility of behavior but not enough to interfere markedly with functioning. Because these ratings are based on current behavior, it is possible for an individual with a well-documented diagnosis of ASD to obtain a current rating below Level 1. Recognizing that symptom severity may fluctuate across context and across development, DSM-5 cautions that these ratings are not meant to determine eligibility for services. However, the practical use of these symptoms remains untested; there also remains some concern that improved ratings (e.g., a change from a Level 3 to a Level 1 specifier) may be used to determine access to services.

Comorbidity and Differential Diagnosis: Developmental Disabilities

When a clinician is considering a diagnosis of ASD, it is important to determine whether symptoms of language disorder or intellectual disability are present. At times, one of these disorders may be a more appropriate diagnosis than ASD (e.g., an 8-year-old child with an IQ score of 50 who has SCI skills consistent with those of a 4-year-old may be better conceptualized as having an intellectual disability rather than ASD). However, at other times, a comorbid diagnosis may be appropriate (e.g., a diagnosis of both ASD and intellectual disability). DSM-5 permits the use of these dual diagnoses in persons with ASD.

Communication Disorders

COMORBIDITY

Delayed language is a commonly cited initial concern for parents whose children are later diagnosed with ASD (Chawarska et al., 2007; De Giacomo & Fombonne, 1998; Siklos & Kerns, 2007). Thus, although it is not a diagnostic criterion for ASD, delayed language is a common comorbid symptom. Historically, approximately 50% of individuals with autism were found to remain mute throughout their lives (Rutter, 1978). However, with earlier diagnosis and intervention, this estimate is decreasing. One study of 9-year-old children with ASD found that while a quarter of the children were able to speak fluently using complex sentences, another quarter were still effectively nonverbal (Anderson et al., 2007). When making a DSM-5 diagnosis of ASD, clinicians are asked to specify whether this diagnosis is accompanied by a language delay.

DIFFERENTIAL DIAGNOSIS

An increasing literature has documented the existence of a group of children who do not display all of the symptoms of ASD, yet present persistent difficulties with pragmatic language impairments influencing social communication skills (Adams, 2001; Gibson, Adams, Lockton, & Green, 2013). There has been considerable controversy about whether these children should be diagnosed with ASD or a communication disorder. DSM-5 includes a new diagnosis of social (pragmatic) communication disorder (SCD) to encompass this group of children who show the SCI symptoms of ASD but do not show the RRB symptoms. Little research has been conducted on this new diagnosis, and there is significant concern that this diagnosis will be used instead of ASD for young children. However, DSM-5 highlights that children must have adequate speech and language abilities before it is possible to identify specific deficits associated with SCD. Thus DSM-5 indicates that it is rare for children younger than 4 years of age to receive an SCD diagnosis. Furthermore, DSM-5 indicates that a diagnosis of SCD should be considered only if the developmental history fails to reveal any evidence of RRBs.

A recent study by Gibson and colleagues (2013) found that children diagnosed with high-functioning ASD (i.e., average intelligence or higher) were characterized by greater degrees of pragmatic impairments, increased RRBs, and higher expressive language skills, compared to children diagnosed with a pragmatic lan-

guage impairment. Children with a pragmatic language impairment showed greater degrees of social communication difficulties and higher expressive language skills than children with a specific language impairment (SLI). Gibson and colleagues argued that this supports the existence of a diagnosis for children who do not meet diagnostic criteria for ASD or SLI, yet have significant social language difficulties. More research is needed on the validity of this diagnosis and the use of this diagnosis to capture subthreshold ASD.

Intellectual Disability

In his original description of the intellectual abilities of children with autism, Kanner (1943) wrote:

> Even though most of these children were at one time or another looked upon as feebleminded, they are all unquestionably endowed with good *cognitive potentialities* . . . The astounding vocabulary of the speaking children, the excellent rote memory for events of several years before, the phenomenal rote memory for poems and names, and the precise recollection of complex patterns and sequences, bespeak good intelligence . . . (Kanner, 1943, p. 217)

His description highlights the juxtaposition of cognitive delays and cognitive strengths that characterize this disorder. Even when individuals with ASD have a comorbid intellectual disability, there are often some strengths in cognitive abilities.

COMORBIDITY

Intellectual disability is perhaps the most common co-occurring disorder with ASD and is a strong predictor of prognosis (see Matson & Shoemaker, 2009, for a review). In his review of 36 epidemiological studies published between 1966 and 2003, Fombonne (2005) reported that the median rate of intellectual disability in individuals diagnosed with DSM-IV autistic disorder was 70.4% (range 40–100%). Across these studies, 29.3% of individuals were reported to have mild to moderate intellectual disability, and 38.5% were reported to have severe to profound intellectual disability. More recent estimates suggest that these figures may be too high and that the comorbidity rate between ASD and intellectual disability is closer to 31%, with higher rates of comorbidity being present in girls with ASD (Baird et al., 2000; Centers for Disease Control and Prevention [CDC], 2014; Chakrabarti & Fombonne, 2001). Studies have further supported the notion that intellectual disability and ASD operate independently, as most correlations were associated with communication difficulties that were largely attributed to ASD symptoms (Hoekstra, Happé, Baron-Cohen, & Ronald, 2009). The decline in rates of comorbidity between ASD and intellectual disability can be attributed to an increased diagnosis of ASD in high-functioning individuals and the effectiveness of early intervention (Chakrabarti & Fombonne, 2001; Fombonne, 2003; Matson & Shoemaker, 2009; Newschaffer, Falb, & Gurney, 2005).

The assessment of intellectual ability in ASD is often complicated by the fact that many intellectual tests rely on imitation, language, and other skills that are particularly affected by ASD; thus it is often challenging to get an accurate estimate of IQ (see Klinger, O'Kelley & Mussey, 2009, for a review). However, an assessment of intellectual functioning is considered an essential component of diagnostic assessment for ASD. IQ testing is often used as a prognostic indicator of long-term outcome for children and adolescents with ASD. Indeed, scores in children with ASD are considered to be as stable as IQ scores in children with other forms of developmental disabilities (National Research Council, 2001). However, this does not mean that IQ scores are stable across the lifespan. Mayes and Calhoun (2003) found a significant correlation between age and full-scale IQ in their sample of 164 children ages 3–15 years with autism. Average IQ scores increased from 53 for children 3 years of age to 91 for children 8 years of age and older. However, more stability in IQ scores has been reported from middle childhood to adolescence and adulthood (Beadle-Brown, Murphy, & Wing, 2006; Howlin, Goode, Hutton, & Rutter, 2004; Seltzer, Shattuck, Abbeduto, & Greenberg, 2004; Sigman & McGovern, 2005).

Traditionally, individuals with ASD were thought to have a specific profile of intellectual abilities characterized by a higher nonverbal IQ than verbal IQ (see Lincoln, Hansel, & Quirmbach, 2007, for a review), and that this profile differentiated ASD from intellectual disability. For example, individuals with ASD have frequently shown relative and absolute strengths on nonverbal visual–spatial tasks involving puzzles and arranging patterns or blocks into designs (e.g., Ghaziuddin & Mountain-Kimchi, 2004; Lincoln, Allen, & Kilman, 1995; Ozonoff, South, & Miller, 2000). However, this profile has not received uniform support in the literature. For example, Mayes and Calhoun (2003) examined intellectual profiles of 164 children with autism across a wide range of chronological age (3–15 years)

and intellectual functioning (IQ scores of 14–143). In their sample, the profile of greater nonverbal than verbal IQ was present in preschool children but gradually disappeared during the school age years. Children with IQ scores above 80 displayed an even pattern of verbal and nonverbal abilities by 6–7 years of age. Children with IQ scores below 80 maintained a greater nonverbal than verbal IQ through the preschool years and did not show similar verbal and nonverbal scores until 9–10 years of age. Thus discrepancies between verbal and nonverbal IQ scores are related to both age and IQ, and, contrary to prevailing beliefs, no single pattern is indicative of an ASD diagnosis.

DIFFERENTIAL DIAGNOSIS

Although these disorders can co-occur, a differential diagnosis is warranted when the SCI and RRB symptoms are more consistent with intellectual disability than with ASD. Children with ASD are distinct in their display of specific impairments in joint attention, motor imitation, symbolic play, and theory of mind; all of these areas are weaker than would be predicted from their receptive language skills (Maljaars, Noens, Scholte, & van Berckelaer-Onnes, 2012; Poon, Watson, Baranek, & Poe, 2012; Wong & Kasari, 2012). Thus, when social difficulties are consistent with developmental level, a diagnosis of intellectual disability without ASD should be considered. With regard to repetitive behaviors, both individuals diagnosed with ASD and those with intellectual disability exhibit motor stereotypies. However, compared to children with non-ASD intellectual disability, children with ASD showed increased hand and finger stereotypies (shaking, rapping, waving, clapping, opening-closing, and twirling the hands or fingers) and more gait stereotypies (pacing, jumping, running, skipping, spinning) in one study (Goldman, Wang, et al., 2009). Both groups showed equivalent levels of full body stereotypies (rocking, shrugging) and arm/leg stereotypies (flapping, stamping feet). Thus the types of motor stereotypies exhibited may help the clinician make a differential diagnosis between ASD and intellectual disability.

Comorbidity and Differential Diagnosis: Psychiatric Conditions

ASD is often associated with comorbid psychiatric conditions. In a population-based study, 71% of children with ASD met criteria for at least one current psychiatric disorder, 41% had two or more, and 24% had three or more diagnoses (Simonoff et al., 2008). Common comorbid psychiatric symptoms include internalizing disorders (anxiety and depression), as well as externalizing disorders such as ADHD and disruptive behavior disorders (see Mazzone, Ruta, & Reale, 2011, for a review). Whereas DSM-IV limited clinicians' ability to make several comorbid diagnoses, including ASD and obsessive–compulsive disorder (OCD) or ASD and ADHD, it is now believed that these disorders can co-occur. This is a significant change in the conceptualization of ASD.

Anxiety and Depression

COMORBIDITY

There is a growing consensus that individuals with ASD experience significant levels of anxiety and depression symptoms. The prevalence of anxiety in school-age children and adolescents with ASD varies greatly, depending on particular samples' characteristics. In a comprehensive review, White, Oswald, Ollendick, and Scahill (2009) reported that 11–84% of children with ASD experienced some degree of impairing anxiety, and that 40–50% of children met DSM-IV diagnostic criteria for an anxiety disorder. All studies have consistently demonstrated that anxiety in individuals with ASD is considerably higher than the prevalence of anxiety disorders in children and adolescents in the general population (5–10%; Merikangas et al., 2010). It is often difficult to differentiate between various anxiety subtypes in ASD, as 87% of children with comorbid anxiety and ASD have two or more anxiety disorders (Renno & Wood, 2013). Some research suggests that while anxiety occurs in children with ASD across the full range of IQ, greater levels of anxiety are seen in children and adolescents with ASD who have average or higher intelligence (Hallett et al., 2013; Strang et al., 2012), perhaps because of greater insight into their struggles with social understanding.

With regard to comorbid depression in children and adolescents with ASD, estimates range from 17 to 27% (Kim, Szatmari, Bryson, Streiner, & Wilson, 2000; Leyfer et al., 2006). Depression often occurs in high-functioning individuals during adolescence, when they have greater insight into their differences from others and a growing desire to develop friendships (Kim et al., 2000; Mayes, Calhoun, Murray, Ahuja, & Smith, 2011). In a sample of children and adolescents with

ASD who had average or higher intelligence, parent report indicated that 44% of the sample exhibited symptoms of depression, and 30% exhibited symptoms within the clinical range (Strang et al., 2012). Children with ASD do not show as much suicidal ideation as children with depression who do not have ASD. However, mothers of children with ASD reported significantly more suicidal ideation and suicide attempts than did mothers of children with typical development (Mayes et al., 2011; Mayes, Gorman, Hillwig-Garcie, & Syed, 2013). Mayes and colleagues (2013) found that suicidal ideation and attempts in children with ASD were predicted by higher levels of depression, behavior problems, and getting teased. Several studies suggest that it is important for individuals with ASD to be assessed for depressive symptoms, especially suicidal ideation (Kato et al., 2013; Mayes et al., 2011, 2013).

DIFFERENTIAL DIAGNOSIS

Despite reports of high anxiety and depression in ASD, there continues to be a controversy about the differential diagnosis of ASD and anxiety, particularly as anxiety and depression often manifest themselves within social situations (e.g., social anxiety, separation anxiety). For example, social avoidance as often seen in ASD may appear symptomatic of social anxiety disorder (social phobia) or depression, but is instead driven by a lack of social understanding or a lack of attention to social information rather than social fear or withdrawal. The unique manifestation of anxiety symptoms within ASD makes it difficult to make a differential diagnosis. For example, symptoms of obsessive–compulsive disorder (OCD, classified as an anxiety disorder until DSM-5) are common and may sometimes resemble repetitive behaviors. OCD differs from ASD in that persons with OCD are more often fixated on a single compulsion than are those with ASD (Russell, Mataix-Cols, Anson, & Murphy, 2005; Wakabayashi, Baron-Cohen, & Ashwin, 2012). Previous studies indicated the rate of comorbidity between ASD and OCD to be small, ranging between 1.5 and 29% (Lainhart, 1999; Mattila et al., 2010); more research is needed now that DSM-5 allows for the comorbid diagnoses of these disorders, however. Renno and Wood (2013) used structural equation modeling to discriminate between ASD and anxiety symptoms. They reported that children with higher anxiety severity were not more likely to have more severe ASD symptoms than were children with lower anxiety severity, and vice versa. These results suggest that anxiety is a distinct clinical diagnosis that may cause additional impairment above and beyond the ASD symptoms and warrant specific interventions. It is likely that depression is also a distinct clinical diagnosis although more research is needed.

Despite the frequency of anxiety and depression symptoms in individuals with ASD, the identification and diagnosis of these comorbid disorders may be complicated by social communication difficulties and poor emotional insight. There are as yet no scales specifically designed to evaluate psychiatric comorbidity in ASD, and current measures for populations without ASD may contain questions that measure ASD-specific symptomatology (e.g., sense of social competence) rather than depression or anxiety per se (Mazzone et al., 2012). Thus continued research, including the development of appropriate clinical diagnostic tools and tailored interventions, will be necessary to better identify and treat comorbid psychiatric symptoms in individuals affected by ASD. For example, recent interventions that have modified standard cognitive-behavioral approaches to fit the unique needs of children and adolescents with ASD have shown promising results in decreasing anxiety (Reaven, Blakely-Smith, Culhane-Shelburne, & Hepburn, 2012; Wood et al., 2009).

Attention-Deficit/Hyperactivity Disorder

It is now recognized that individuals can have comorbid diagnoses of ASD and ADHD. The frequent overlap of symptoms between the two disorders has led many diagnosticians to explore commonalities across the disorders (Mayes, Calhoun, Mayes, & Molitoris, 2012). Examples of common symptoms include (but are not limited to) inattention, hyperactivity, and impulsivity. Given the current understanding of decreased activation within the prefrontal cortex in both ASD and ADHD, this may partly explain the overlap between the two conditions (Happé, Booth, Charlton, & Hughes, 2006).

Research exploring these overlaps has expanded significantly in the past decade, with estimates of comorbid ADHD in children and adolescents with ASD ranging from 33 to 78% (Gargaro, Rinehart, Bradshaw, Tonge, & Sheppard, 2011; Goldstein & Schwebach, 2004; Sinzig, Walter, & Doepfner, 2009). For those individuals with a comorbid diagnosis of ADHD and ASD, higher rates of oppositional behavior have also been reported (Grzadzinski et al., 2011).

Comorbidity: Behavioral and Medical Complications

In addition to comorbid psychiatric disorders, ASD is associated with several related behavioral and medical symptoms. These include self-injurious behavior, sleep disturbance, seizures, eating disturbances, and gastrointestinal (GI) difficulties.

Self-Injurious Behaviors

Behaviors such as head banging, finger or hand biting, head slapping, and hair pulling have been observed in persons with ASD. When frustrated, nonverbal individuals with ASD often have no verbal means of communicating their feelings and/or needs, and as a result may engage in self-injurious behaviors as a way of expressing their frustration (Donnellan, Mirenda, Mesaros, & Fassbender, 1984; Lainhart, 1999). However, these behaviors may be more closely linked to a comorbid intellectual disability than to ASD per se (J. Dawson, Matson, & Cherry, 1998). The effect of these self-injurious behaviors is often overwhelming; higher rates of such behaviors are associated with perceived stress in families (Bishop, Richler, Cain, & Lord, 2007).

Sleep Disturbances

It is not uncommon for persons with ASD to require less sleep than other family members, and parents often report that their children awake frequently during the night. Ruth Sullivan (1992) described her son, Joseph, at 2 years of age as being extremely hyperactive. She wrote, "It was as though his idle was stuck at rocket speed. He slept an average of three to four hours a night and screamed for the rest" (p. 247). Studies have shown that 44–83% of children with ASD suffer from severe sleep problems, compared to approximately 20–30% of the general pediatric population (Allik, Larsson, & Smedje, 2006; Goldman, Surdyka, et al., 2009; Krakowiak, Goodlin-Jones, Hertz-Picciotto, Croen, & Hansen, 2008). Commonly reported sleep problems include difficulty falling and staying asleep, as well as shortened night sleep and early-morning waking. Sleep problems are more likely to be reported in children younger than 5 years of age. The research to date suggests that intellectual functioning is unrelated to sleep difficulties in ASD. Overall, children with ASD have been found to sleep less time in 24 hours than children with developmental delay and children with typical development (Goodlin-Jones, Tang, Liu, & Anders, 2008). While sleep problems improve with age, older children continue to have difficulty falling asleep and tend to sleep less at night. Treatment for sleep difficulties (e.g., supplemental melatonin) may not only improve sleep, but may also aid in treating related symptoms—including social interaction, repetitive behaviors, affective problems, oppositional and aggressive behavior, and inattention/hyperactivity symptoms (Doyen et al., 2011; Goldman et al., 2011; Malow et al., 2012; Rossignol & Frye, 2011). Although disrupted sleep is not part of the diagnostic criteria for ASD, the significant rates of sleep disorders in this population suggests that assessment and treatment of such disorders should be a routine part of clinical care for individuals with ASD.

Seizures

ASD is associated with an increased risk of epilepsy, with estimated rates ranging from 6 to 50%. This range is likely due to ascertainment differences, with one population-based study finding 5% and epilepsy clinics citing 15–30% (Clarke et al., 2005; Matsuo, Maeda, Sasaki, Ishii, & Hamasaki, 2010). There is no specific form of epilepsy that is linked to ASD. However, early-onset seizures are typically associated with poorer outcomes (Saemundsen, Ludvigsson, & Rafnsson, 2008). Seizure onset typically occurs either early in childhood or in adolescence (Parmeggiani et al., 2010). Given the high rates of comorbidity, it is recommended that electroencephalography should be conducted for individuals with ASD when there is a suspicion of seizures (Filipek et al., 2000).

Eating Disturbances and GI Difficulties

Eating disturbances are also frequently reported by parents of children with ASD, yet there is little research in this area. Eating disturbances during the early years of childhood are marked by unusual food preferences. Food preferences may be related to the texture of the food (e.g., soft foods), the particular color of the food (e.g., brown), or a specific food taste (e.g., only one brand of a specific food). Some children with ASD may develop more ritualistic behaviors around mealtimes. For example, a child may eat only a particular brand of food that is cut in a specific shape. Eating problems typically do not subside during adulthood; often adults with ASD have to be supervised to ensure that they eat a well-balanced diet. For example, Powell, Hecimovic,

and Christensen (1992) described a young man with autism who preferred foods with a soft texture: "He only eats steamed vegetables with a side dish of butterscotch pudding and half a banana for dinner" (p. 193).

In addition to food preferences, there is a high rate of GI disorders in persons with ASD, with estimates ranging from 9 to 70% (see Buie et al., 2010, for a review). Reported problems include constipation, abdominal pain, bloating, diarrhea, and nausea. The exact connection between ASD and GI disorders is not completely understood. One promising area of investigation appears to be the relation between GI symptoms and anxiety, given the high rates of co-occurrence of these symptoms in individuals with ASD. Indeed, studies have found that children with GI problems have significantly higher rates of anxiety (Mazurek et al., 2013; Nikolov et al., 2009).

DSM-5 Specifiers and Recording Procedures for ASD

As an acknowledgment of the comorbidities often associated with ASD, DSM-5 offers a specific set of recording procedures that includes specifiers for associated conditions. Diagnosticians are asked to record the presence of any identified medical/genetic condition or environmental factor that has been associated with ASD etiology as described below (e.g., ASD associated with fragile X syndrome). Similarly, diagnosticians are asked to record the presence of a comorbid neurodevelopmental, mental, or behavioral disorder (e.g., ASD with ADHD). The DSM-5 code for ASD and the DSM-5 code for the associated condition would both be recorded. Diagnosticians are also asked to specify whether or not catatonia is present. In addition to specifying the presences of an associated condition, severity is recorded as the level of support needed for each of the two symptom domains described above (e.g., "requiring very substantial support" for SCI deficits and "requiring substantial support" for RRBs). Specification for whether the individual also has a comorbid intellectual impairment should follow the severity rating. The level of language impairment should be recorded as well (e.g., "with accompanying language impairment—no intelligible speech"). This listing of associated conditioners and specifiers is somewhat cumbersome, although the resulting information is necessary to gain a full understanding of each person's ASD. Research is needed on the reliability and validity of these specifiers across clinicians and across development.

EPIDEMIOLOGY

Prevalence and Incidence

ASD is not as rare as previously believed. Historically, autism was reported to occur in 1 individual per 2,500 persons (Lotter, 1966; Wing & Gould, 1979). Studies over the past decade, however, have indicated significantly higher rates. In a population-based record review, the CDC (2014) estimated that approximately 1 in 68 children age 8 within the United States during 2010 had ASD, marking a 29% increase from the 2008 estimates and a 123% increase from the 2002 estimates. A recent national phone survey reported a 2% prevalence of parent-reported ASD among children ages 6–17 years (Blumberg et al., 2013). Much as in these U.S.-based studies, international prevalence rates have also been shown to be on the rise (Fombonne, 2009), with a recent population-based study in South Korea reporting a prevalence rate of 2.6% in 7- to 12-year-old children (Kim et al., 2011). There is ample evidence that the prevalence of the disorder is rising, but it remains unclear the extent to which the significant increase represents a true increase in numbers of children with ASD. Clearly, expanded awareness and improved detection account for some of the increase, but they do not appear to account for all of it (CDC, 2014).

Sex Differences

One of the most consistent demographic differences is in regard to sex, with the ratio of males to females with ASD being approximately 4–5:1 (CDC, 2014). Potential mechanisms include endogenous hormones (Knickmeyer et al., 2006); X chromosome inactivation (Nagarajan et al., 2008), exogenous endocrine disruptions; and polychlorinated biphenyl ethers (PCBs), which affect intrauterine growth in males but not females (Hertz-Picciotto et al., 2006). Other developmental disorders, such as ADHD and childhood asthma, also have a larger percentage of males affected (at least in childhood), suggesting that males may be more susceptible to early insults.

Affected females are more likely than males to have comorbid intellectual disability and increased behavioral symptoms (Dworzynski, Ronald, Bolton, & Happé, 2012). Among a large sample of children and adolescents with higher intelligence, symptom expression was roughly equivalent for boys and girls with the exception of fewer RRBs among females with ASD,

suggesting that differences in symptom severity may be due to the presence of comorbid intellectual disability (Mandy, Chilvers, et al., 2012).

Socioeconomic Background and Ethnicity

Most studies have been unable to disentangle the influence of race, education, and income with regard to ASD diagnosis. In European studies, where there is population-wide surveillance and universal health care, socioeconomic status (SES) is not found to be a factor in rates of ASD diagnoses (Fombonne, Bolton, Prior, Jordan, & Rutter, 1997; Larsson et al., 2005). In contrast, studies from the United States that report a relation between SES and ASD have often used passive surveillance in databases and have had an underascertainment of families with low education (Baird et al., 2006). It is believed that associations with SES may be due to the discrepant availability of resources and the ability of families with higher SES to access these resources. Thus SES may be more influential in the ability to attain a diagnosis and treatment for ASD than it is in the etiology of ASD. There is a similar story for the involvement of race/ethnicity in ASD. For instance, Hispanic children in California were less likely than non-Hispanic European American children to have an ASD diagnosis, possibly due to language barriers and lesser ability to access services. Furthermore, in a large multisite study conducted by the CDC, African Americans, Hispanics, and children in other minority racial/ethnic groups were more likely to receive a diagnosis of ASD at a later age than European American children, suggesting possible biases in clinician practices and an inability of many minority families to access services (Mandell, Ittenbach, Levy, & Pinto-Martin, 2007). Residence has been reported to be associated with ASD, such that living in an urban compared to a rural area is associated with a higher prevalence—although this too may be an artifact of greater access to diagnostic services (Hultman, Sparén, & Cnattingius, 2002; Lauritsen, Pedersen, & Mortensen, 2005).

ETIOLOGY

ASD is a group of heterogeneous disorders with multiple etiologies, including both genetic and environmental risk factors.

Genetic Factors

Elevated risk for ASD among siblings indicates that genetic factors play a role in ASD. A large-scale prospective study of infant siblings of children with ASD found that approximately 20% of these siblings developed ASD, with a nearly threefold increased risk rate for male versus female siblings (Ozonoff et al., 2011). In families with at least two children diagnosed with ASD, the odds of an additional child being diagnosed with ASD were 1 in 3, suggesting a strong genetic component.

Twin Studies

Twin studies have reported concordance rates ranging from 60–96% in monozygotic twins to 0–23% in dizygotic twins, depending on the sample and diagnostic classification (Bailey, Le Couteur, Gottesman, & Bolton, 1995; Ritvo, Freeman, Mason-Brothers, Mo, & Ritvo, 1985; Steffenburg et al., 1989). The fact that these studies showed a much higher concordance rate among monozygotic twins strongly suggested a genetic component for ASD. However, a recent population-based twin study of ASD found that environmental factors common to twins accounted for approximately 55% of the liability to ASD, while genetic heritability contributed less than 40% (Hallmayer et al., 2011). This suggests that although genetic factors may play an important role, it may be smaller than estimates from previous twin studies indicated.

The Broader Autism Phenotype

Within the past few decades, much research has been devoted to defining a broader autism phenotype. The term "broader autism phenotype" refers to the idea that relatives of persons with ASD may not have the disorder itself, but may express a "lesser variant" resulting from shared genes (Baron-Cohen & Hammer, 1997). Typically, the broader autism phenotype is defined as having difficulties in one or more of the symptom areas (social skills, communication skills, repetitive behaviors) that characterize ASD. These characteristics have been found in 4–20% of siblings who do not meet criteria for ASD (Bolton et al., 1994; Constantino, Zhang, Frazier, Abbacchi, & Law, 2010). Some parents also exhibit broader phenotype features of ASD (Bailey et al., 1995; Folstein & Rutter, 1977; Losh et al., 2009). In

a large-scale study, Pickles and colleagues (2000) reported that 178 out of 2,360 (7.5%) relatives of persons with autism fit the description of the broader autism phenotype. In comparison, only 20 out of 735 (2.5%) relatives of individuals with Down syndrome fit this description. These studies add support for the role of genetic factors in ASD.

ASD Susceptibility Genes

Recent evidence suggests that there may be multiple genetic pathways leading to the development of ASD. Previous association and linkage research had focused on identifying common variants; however, common genetic variations have been found to have only modest impacts (Abrahams & Geschwind, 2008). In fact, over 200 candidate genes have been documented for ASD research (Basu, Kollu, & Banerjee-Basu, 2009), and it is now suggested that close to 1,000 genes could contribute to risk for ASD and related conditions. Several known ASD risk genes and chromosomal loci, including SHANK2, SHANK3, NLGN4, 15q11-13, and 16p11.2, have multiple variants that differentially influence the manifestation of ASD. Current efforts are focused on subtyping in order to find potential differences due to sex, cognition, language, and presence of regression (e.g., Chapman et al., 2011; Schellenberg et al., 2006).

It has been suggested that approximately 10–20% of individuals with ASD have an identifiable genetic syndrome, observable genetic mutation, or de novo copy number variants (CNVs) (Abrahams & Geschwind, 2008). Among the cases that have a known genetic cause, the identified duplications and deletions of chromosomal regions 15q11-13 and 16p11.2 account for only approximately 1% of cases (Miles, 2011). Recent findings suggest that de novo CNVs are more common risk factors in sporadic than in familial ASD (Levy et al., 2011; Marshall et al., 2008; Sanders et al., 2011; Sebat et al., 2007). However, there is no single genetic mutation that explains a large number of ASD cases and can differentiate individuals who do not have ASD. It may be that CNVs directly lead to the development of ASD, or that they are combined with common variants in a genetic susceptibility model.

In summary, it appears that no single gene can account for the autism syndrome. Rather, there appear to be multiple rare gene mutations, either individually or together with other common or rare genetic mutations, that result in this syndrome (Folstein & Rosen-Sheidley, 2001). The identified genes and mutations are not specific to ASD and are also implicated in similar disorders and phenotypes of ASD (e.g., language difficulties). Despite the complexity and large number of ASD risk genes that have been identified, it is noteworthy that these genes appear to affect specific common pathways in the brain, which may offer possible targets for drug development (Stephenson & Fitzgerald, 2010; Webb, 2010).

Environmental Risk Factors

Given the recent finding of the strong influence of shared environment in twins who develop ASD (Hallmayer et al., 2011), it is important to examine possible environmental contributions during the first year of life.

Prenatal and Perinatal Risk Factors

A variety of prenatal and perinatal risk factors for ASD have been identified, including maternal infections, maternal medical conditions, prenatal prescription drug exposure, and birth complications (see meta-analyses by Gardener, Spiegelman, & Buka, 2009, 2011). For example, maternal fever during pregnancy has been associated with a twofold higher risk, with the strongest risk in the first and second trimesters; however, no specific associations with maternal influenza were reported (Zerbo, Iosif, Delwiche, Walker, & Hertz-Picciotto, 2011). Additionally, if mothers had at least one of several medical conditions—diabetes (type 2 or gestational), chronic hypertension, or prepregnancy obesity—this was correlated with a 60% increased risk for autism and a 150% increased risk for developmental delay (Krakowiak et al., 2012). Infections and maternal medical conditions have been hypothesized to cause a disruption of the immune response and maturational process at critical developmental periods (Hertz-Picciotto et al., 2008).

Obstetric complications at birth, including low Apgar scores, breech presentation, fetal distress, and ABO or Rh incompatibility, have also been associated with autism (Gardener et al., 2011). This may be a result of prenatal or birth hypoxia affecting central nervous system (CNS) functioning and later development. Additionally, nonelective cesarean sections have been associated with increased rates of ASD, suggesting that

a preexisting condition in prenatal development and not necessarily a complication of the surgery itself may be a risk factor (Walker, Krakowiak, Baker, Hansen, & Hertz-Picciotto, 2011).

Another proposed contribution to increased risk for ASD is prenatal exposure to medications. A large population-based study prospectively obtained data on mothers' prescription drug use; the researchers found a twofold increased risk of ASD with maternal treatment with selective serotonin reuptake inhibitors (SSRIs) during the year before delivery, and almost a threefold increase with medication use during the first trimester of pregnancy (Croen, Grether, Yoshida, Odouli, & Hendrick, 2011). This result supports previous studies citing abnormalities in serotonin and serotoninergic pathways in ASD (Murphy et al., 2006). Similarly, exposure to valproate during pregnancy to treat maternal epilepsy was associated with a nearly twofold increased risk of ASD diagnoses (Christensen et al., 2013).

SEASON OF BIRTH

Seasons of birth have been examined in relation to other disorders; however, only a limited number of such studies have been conducted for ASD. A few reports have found an excess number of births of children with ASD in March, although larger studies with improved methods did not find support for this increase (Bolton, Pickles, Harrington, Macdonald, & Rutter, 1992: Landau, Cicchetti, Klin, & Volkmar, 1999). Recently, Zerbo and colleagues (2011) reported higher risks for children conceived in the winter months, December to March. Further studies need to be conducted in order to examine the consistency of this finding and the potential mechanisms, such as variation in temperature, infectious diseases, allergens, dietary factors, vitamin deficiencies, and chemical environments.

MATERNAL AND PATERNAL AGE

Although some inconsistency in results exists, the majority of studies conducted to date indicate an association between advanced parental age and risk for ASD (see Hultman, Sandin, Levine, Lichtenstein, & Reichenberg, 2011, for a review). Men 50 years of age or older were 2.2 times more likely to have children with ASD than men younger than 30 years of age were. Given the increasing rate of births to older parents, this is an interesting finding that may contribute to the increased rates of ASD.

Environmental Toxins

Given the known teratogenic effects of environmental toxins on CNS development, attention has turned toward the possible role of these known agents in the etiology of autism. One of the main areas of focus in the ASD literature has been on mercury—specifically, the mercury-based preservative (i.e., thimerosal) that was formerly used in vaccines. To date, no consistent empirical evidence between autism and vaccines has been found (see Wilson, Mills, Ross, McGowan, & Jadad, 2003, for a review). Few studies have examined the exposure of mercury from other sources (e.g., dental amalgams, industrial emissions or water pollution, and fish or seafood). A recent well-designed study found no difference in mercury blood concentration in children with ASD compared to children with typical development, suggesting that mercury likely does not play a major role (Hertz-Picciotto et al., 2010).

A few studies have examined the impact of exposure to environmental pollutants and pesticides. A large epidemiological study found that children whose mothers lived near a freeway during pregnancy had nearly a twofold greater risk for developing ASD, suggesting a potential role of exposures to pollutants (Volk, Hertz-Picciotto, Delwiche, Lurmann, & McConnell, 2011). A few studies have examined exposure to pesticides and have suggested a potential role for these in the development of ASD as well (Eskenazi et al., 2007; Roberts et al., 2007). The potential mechanisms hypothesized are that environmental pollutants may disrupt thyroid hormones (Roberts et al., 2007), which have been implicated in intellectual disabilities, deafness, and speech problems (Porterfield, 1994), and sex steroids, which have been proposed to play a role in the sex ratio observed in ASD (Baron-Cohen, Knickmeyer, & Belmonte, 2005; Knickmeyer et al., 2006). More research is needed to confirm a link between toxins and ASD.

Gene–Environment Interactions

It is likely that genetic factors interact with environmental factors to confer risk for ASD (Newschaffer et al., 2007). It may be that gene–environment interactions occur: Infants who are genetically susceptible may be exposed to postnatal environmental risk factors

that trigger the cascade of developmental difficulties contributing to the development of ASD.

Epigenetic models of ASD have been proposed, in which a mechanism controls gene expression without directly changing DNA sequences. For instance, one possible theoretical mechanism of older paternal age related to ASD is that accumulated exposure to environmental toxins over the lifetime could result in alterations in the germ cells of older parents (Hultman et al., 2011). Alternatively, it is possible that advanced paternal age results in an increased number of de novo genetic mutations that are linked with ASD. Gene–dosage models theorize that cumulative genetic and nongenetic factors interact resulting in the emerging ASD phenotype or broader autism phenotype (Abrahams & Geschwind, 2008; Constantino & Todd, 2005). However, given that ASD is a complex condition, it is likely to involve a probabilistic model that leads to varied developmental trajectories, rather than a simple additive risk model.

Neuroanatomical Findings

Several promising findings have been reported by researchers examining possible neuroanatomical abnormalities in ASD. These findings are from studies using structural imaging techniques, brain autopsies, and animal models. In general, neuroanatomical studies support the notion that ASD is linked to a combination of brain enlargement in some areas and brain reduction in other areas (see Koenig, Tsatsanis, & Volkmar, 2001, for a review). Although these findings may seem to contradict each other, together they suggest a single theory about the underlying cause of ASD. That is, ASD may be caused by abnormal cell growth during the early stages of prenatal and postnatal brain development. In normal brain development, neurons proliferate and become interconnected, gradually decreasing in size and number once certain connections become more heavily utilized than others. It is this process of neuronal growth and pruning that seems to be abnormal in autism, leaving some areas of the brain with too many neurons and other areas with too few neurons (Minshew, 1996). Research has suggested abnormalities in several areas of the brain: the prefrontal cortex, the cerebellum, the limbic system, and the corpus callosum. Additionally, some researchers have reported an overall brain enlargement rather than localization to a specific area. Evidence for abnormalities in each of these areas is reviewed below.

Atypical Brain Growth and Volume

Using magnetic resonance imaging (MRI), studies have found that 2- to 4-year-olds with ASD have larger total cerebral volume than children with typical development and children with developmental delay (Courchesne et al., 2001; Hazlett et al., 2011; Schumann et al., 2010; Sparks et al., 2002). An atypical pattern of growth appears to be present in individuals with ASD: small to normal head size at birth, followed by an accelerated growth that occurs during the first year of life (Chawarska et al., 2011; Courchesne, Campbell, & Solso, 2010; Courchesne & Pierce, 2005; Dawson et al., 2007; Elder, Dawson, Toth, Fein, & Munson, 2008). Abnormal brain growth appears to be due to enlargement of both white and gray matter (Hazlett et al., 2011; Schumann et al., 2010). A postmortem study found increased number of neurons in the prefrontal cortex, with particularly high rates in the dorsolateral versus medial region (Courchesne et al., 2011). A large-scale study found abnormal overgrowth of the brain in ASD, but by adolescence and young adulthood, there may be abnormal decline and possible degeneration (Courchesne et al., 2010). Courchesne and colleagues (2010) theorize that overgrowth and excessive neuron numbers and aberrant patterns of connectivity in early development could trigger a "corrective" phase in later development, involving processes that attempt to prune the excess aberrant axon connections, synapses, and neurons to improve neural circuit function. All of these findings are supported by the theory that ASD is linked to abnormal neuronal migration and pruning during brain development.

Cerebellum

Interest in the possible role of the cerebellum in ASD came from evidence that many individuals with ASD are clumsy and uncoordinated (Gillberg, 1999), have difficulties with sequencing language, and exhibit difficulties in shifting attention—all of which are known to be partially mediated by the cerebellum. In addition, the inability to shift attention may lead to deficits in joint attention, theory of mind, and possibly RRBs and difficulties with transitions, all of which are implicated in ASD (Carper & Courchesne, 2000; DiCicco-Bloom et al., 2006; Iarocci & McDonald, 2006). Support for abnormalities in the cerebellum of persons with autism comes from MRI, magnetic resonance spec-

troscopy (MRS), and autopsy studies. Research using MRS suggests that decreased concentrations of a neural substrate that indicates decreased functioning in the cerebellum is found in children with ASD (Chugani, Sundram, Behen, Lee, & Moore, 1999; DeVito et al., 2007). In addition, functional MRI studies found that high-functioning adolescents with ASD had reduced cerebellum activity during attention and motor task. Courchesne and colleagues have consistently found cerebellar enlargement in individuals with ASD in MRI studies (Carper & Courchesne, 2000; Courchesne, Redcay, Morgan, & Kennedy, 2005). Interestingly, one of these studies found that the volume of the cerebellum was inversely related to the volume of the frontal lobes, with larger frontal lobe volume associated with smaller cerebellar volume (Carper & Courchesne, 2000). The authors suggest a possible shared genetic or environmental pathology involving the cerebellum and frontal lobe; alternatively, these areas may be interconnected such that abnormalities in the early-developing cerebellum may cause abnormalities in the frontal lobes later in development.

Consistent with some MRI studies, postmortem autism studies have revealed Purkinje and granule cell loss in the neocerebellum of individuals with autism—an area that receives auditory and visual information (Bauman & Kemper, 1985, 1996; Carper & Courchesne, 2000; Palmen, van Engeland, Hof, & Schmitz, 2004; Ritvo et al., 1986; Whitney, Kemper, Rosene, Bauman, & Blatt, 2009). Additionally, a brain tissue study (Fatemi, Stary, Halt, & Realmuto, 2001) revealed decreased amounts of two proteins (Reelin and Bcl-2) in the cerebellum. Interestingly, these proteins have been implicated in cell migration and pruning, suggesting a possible biochemical marker for the structural abnormalities observed in autism.

Prefrontal Cortex

MRI studies reveal that the frontal lobes, particularly the prefrontal cortex, show abnormal development in ASD (Carper & Courchesne, 2005; Carper, Moses, Tigue, & Courchesne, 2002). The same MRS study that found decreased concentrations of a neural substrate indicating decreased function in the cerebellum also found similar decreased numbers of glutaminergic neurons in the frontal lobes, suggesting general frontal lobe dysfunction in persons with ASD (DeVito et al., 2007). Functional MRI studies have found cortical thinning in areas identified as the mirror neuron system (Dapretto et al., 2006; Hadjikihani, Joseph, Snyder, & Tager-Flusberg, 2006). A positron emission tomography (PET) scan study found that individuals with ASD showed decreased activation in the medial prefrontal cortex compared to individuals with typical development during a theory-of-mind task (Happé et al., 1996). These studies suggest that dysfunction in the frontal lobes may be related to the deficits in social cognition, theory of mind, and mirror neuron functioning observed in individuals with ASD. In addition, the authors suggest that frontal lobe abnormalities may explain difficulties often observed in working memory, problem solving, and attention.

Limbic System

Autopsy studies have revealed reduced neuronal cell size in limbic structures (Bauman & Kemper, 1988, 2005; Schumann & Amaral, 2006). Amygdala enlargement relative to total cerebral volume has been found in children with more severe symptoms (Schumann et al., 2004; Schumann, Barnes, Lord, & Courchesne, 2009; Sparks et al, 2002) and enlarged amygdala at 3 years of age predicted a more severe course from 3 to 6 years of age (Munson et al., 2006). Individuals with ASD have also been found to have decreased functioning in the orbitofrontal cortex, amygdala, and superior temporal sulcus in response to fearful faces. Possible hypotheses for amygdala abnormalities include that there are fewer neurons generated in early development, or that an excessive number are generated; the latter is consistent with the finding of an enlarged amygdala.

Corpus Callosum

Several studies have found evidence of reduced corpus callosum size in adults and children with ASD (Boger-Megiddo et al., 2006; Egaas, Courchesne, & Saitoh, 1995; Hardan, Minshew, & Keshavan, 2000; Manes et al, 1999; Piven, Bailey, Ranson, & Arndt, 1997; Vidal et al., 2006). Anatomical support for disordered cortical connectivity includes the observation of increased white matter in ASD, with frontal lobe white matter showing the greatest increase (Herbert et al., 2004). These findings suggest that there may be a link between autism and impaired communication between brain hemispheres (Penn, 2006) as well as between neural systems (Belmonte et al., 2004; Courchesne & Pierce, 2005; Just, Cherkassaky, Keller, & Minshew, 2004; Rippon, Brock, Brown, & Boucher, 2007).

Other Brain Regions

In addition to the areas just discussed, abnormalities in other regions of the brain have been tentatively associated with aspects of ASD. For instance, the parietal lobe may be linked with deficits in imitation and possible mirror neuron system dysfunction (Oberman & Ramachandran, 2007; Schumann & Amaral, 2006); the basal ganglia may be associated with the repetitive and stereotyped behaviors observed in ASD (Moldin, Rubenstein, & Hyman, 2005). Other areas studied include the thalamus and hypothalamus (Moldin et al., 2005) and the temporal lobes (Schumann et al., 2010), including the fusiform face area (Schultz, 2005).

Brain Connectivity

Structural and functional studies have found abnormal brain connectivity in ASD. Diffusion tensor imaging (DTI) allows for examination of white matter tracts in the brain. Use of this technology reveals abnormal structural connectivity (Ameis et al., 2011; Cheng et al., 2010; Shukla, Keehn, & Muller, 2011). Aberrant development of white matter tracts has been found in infant siblings who later developed ASD (Wolff et al., 2012). These white matter abnormalities were present at 6 months of age and preceded the onset of behavioral symptoms of ASD, suggesting a relation between atypical brain connectivity and later symptom development.

Pathways with disruptions include structures that process biological motion and eye gaze, face identity, emotional expressions and significance, novel stimuli, and visual learning; that decode emotional content in auditory stimuli; and that are involved with self-regulation and information processing (Ameis et al. 2011; Cheon et al., 2011; Jou et al., 2011). Functional studies have found reduced functional integration between the amygdala and secondary visual areas; however, the study also found increased connectivity between the right inferior frontal gyrus and frontal cortex, suggesting that ASD may be a disorder of both under- and overconnectivity in the brain (Rudie et al., 2012).

Summary

There is overwhelming evidence that autism is linked to abnormalities in brain development, leading some regions of the brain to be overdeveloped and others to be underdeveloped. In general, studies of the cerebral cortex have supported a theory of early brain overgrowth, followed by a plateau in rate of growth and possible degeneration in later life. Studies suggest that there may be abnormal connections between subcortical and cortical pathways in persons with autism (Koenig et al., 2001). More research is needed to identify the specific pathways that are impaired and the specific prenatal and postnatal neuronal migration systems that are involved, as well as to determine whether there is abnormal cell proliferation or cell loss. It is unlikely that a single neuropathological cause or brain region will be implicated for all types of ASD, given the wide heterogeneity. Thus future studies will need to be conducted to examine the neurodevelopmental patterns across the varied phenotype.

Cortical Electroencephalographic Findings

Studies using electroencephalography (EEG) and ERPs allow for the examination of brain functioning, alterations in resting and active states, and potential under- and overconnectivity of the brain in individuals with ASD. ERP and EEG studies suggest that individuals with ASD may have subtle impairments in the integrative stages of visual processing and attentional allocation (Bertone, Mottron, Jelenic, & Faubert, 2005; Hoeksma, Kemner, Verbaten, & van Engeland, 2004; Milne, Pascalis, Buckley, & Makeig, 2008; Vandenbroucke, Scholte, van Engeland, Lamme, & Kemner, 2008). Disruptions in lower-level processes could have "downstream" consequences for higher-level cognitive and social processes, such as reduced attention to social stimuli. For instance, multiple studies have reported abnormalities in an early ERP component sensitive to faces, the N170, for individuals with ASD as well as in parents of children with ASD (Dawson, Webb, Wijsman, et al., 2005; McPartland et al., 2004; Webb et al., 2006). In addition, ERP studies have found faster responses to objects than faces, and a tendency for individuals with ASD displaying a more neurotypical ERP response to have less severe ASD symptoms (McPartland et al., 2004; O'Connor et al, 2007; Webb et al, 2006, 2010). Eye gaze ERP studies have found that direct gaze elicits a larger response than averted gaze in children with ASD (Grice et al., 2005; Kylliainen, Braeutigam, Hietanen, Swithenby, & Bailey, 2006). This is an intriguing finding, given that individuals with ASD often have atypical eye contact and avoid direct gaze (Baranek, 1999; Charman et al., 2001; Klin et al., 2002; Osterling, Dawson, & Munson, 2002).

Given that imitation is one of the core deficits observed in ASD, recent attention has turned toward the mirror neuron system. The EEG mu rhythm is believed to reflect activity of this system involved in execution–observation matching. Research analyzing the EEG mu rhythm in individuals with ASD suggests that the expected mu attenuation only occurs when individuals are executing an action, however, not while they are observing the same action (Bernier et al., 2007; Oberman et al., 2005; Oberman, Ramachandran, & Pineda, 2008). These findings have matched deficits found in behavioral performance of imitation.

Abnormalities in spontaneous EEG rhythms, such as elevated power in the theta range and decreased power in the alpha range, have been found in individuals with ASD (Coben, Clarke, Hudspeth, & Barry, 2008; Daoust, Limoges, Bolduc, Mottron, & Godbout, 2004; Murias, Webb, Greenson, & Dawson, 2007). In addition, reduced coherence (synchronization between neural populations) was found in these studies, suggesting impairments in communication between neural systems. A study assessing functional cortical connectivity found increased coherence in the group with ASD, especially for the theta range within the left frontal and temporal regions; reduced coherence was found for the alpha range in the frontal region and other scalp regions (Murias et al., 2007). This suggests potential underconnectivity of the frontal lobe with the rest of the cortex, while there may be overconnectivity in local regions. This is also consistent with neuroanatomical findings of reduced callosal volume, suggesting that cortical connectivity may be impaired in longer connections in favor of increased local connections. Studies of infant siblings of children with ASD who are at high risk also show early differences in EEG activity, as discussed below.

DEVELOPMENTAL COURSE AND PROGNOSIS

Early Predictors, Onset, and Emergence of ASD Symptoms

By 2 years of age, ASD affects all areas of development, including social attention, social skills, communication skills, and play skills. When writing about her 2-year-old daughter with autism, Catherine Maurice (1993) described the pervasiveness of her daughter's atypical development:

> It wasn't just that she didn't understand language. She didn't seem to be aware of her surroundings. She wasn't figuring out how her world worked, learning about keys that fit into doors, lamps that turned off because you pressed a switch, milk that lived in the refrigerator. . . . If she was focusing on anything, it was on minute particles of dust or hair that she now picked up from the rug, to study with intense concentration. Worse she didn't seem to be picking up anyone's feelings. (pp. 32–33)

This description highlights the link between atypical early attention and the unfolding of the SCI symptoms that characterize ASD. A goal of recent research has been to explain this symptom onset process, identifying atypical cognitive and neurophysiological precursors to the behavioral symptoms of ASD.

Onset of Behavioral Symptoms

A number of prospective studies are currently following younger siblings of children with ASD and infants screened during well-child primary care visits, to determine whether reliable early behavioral and neural indicators exist for ASD during the first and second years of life. In addition to providing information about early indicators of ASD, these longitudinal studies provide vital data about the developmental trajectory of ASD. By studying infants who do and do not go on to develop ASD, this research has the potential to determine the genetic and environmental effects of the development of ASD, as well as possible protective factors (Dawson, 2008; Elsabbagh & Johnson, 2007; Rogers, 2009). Identifying other characteristics of ASD in infancy can also inform the course of symptom expression and severity over time.

Infants at risk for autism generally do not exhibit clear symptoms at 6 months, and there is evidence that children later diagnosed with ASD have social function comparable to that of children with typical development in the first months of life (Landa & Garrett-Mayer, 2006; Ozonoff et al., 2010; Zwaigenbaum et al., 2005). As presented in Table 11.2, early signs often manifested at the end of the first year of life include the core symptoms of ASD described earlier (impaired joint attention, imitation, face processing, etc.). Additional early signs often include other behaviors that are considered outside the core symptoms of ASD, such as temperamental and motor characteristics. Specifically, prospective studies of high-risk infants and primary care screening studies

TABLE 11.2. Early Signs of ASD

Developmental domain	Typically develops	Children with ASD[a]
Social		
Looking at faces	Birth	Less[a, b] at 8-12 months
Following person's gaze	6–9 months	Less[a, b] at 18 months
Turning when name called	6–9 months	Less[a, b] at 8–12 months
Interest in social games	6–9 months	Less[2] at 9 and 12 months
Reduced positive emotion	6–9 months	Less[2] at 12 months
Showing objects to others	9–12 months	Less[a] at 12 months
Symbolic play	14 months	Absent[a] at 18 months
Communication		
Directed vocalizations	6–9 months	Less[a, b] at 12 months
Pointing at interesting objects	9–12 months	Less[a, b] at 12 and 18 months
Pointing to request	9–12 months	Not delayed[a] at 18 months
Other behaviors		
Atypical behaviors (e.g., sensory and repetitive behaviors)	NA	Observed[2] at 12–24 months
Increased attention to objects	NA	Observed[2] at 12 months
Difficulty disengaging attention	NA	Observed[2] at 12 months
Intense reactions to distress	NA	Observed[2] at 12–24 months

Note. NA, not applicable. "Less" indicates that this behavior was observed significantly less often in children with ASD than in children with typical development at this chronological age.

[a]Based on Baranek (1999), Baron-Cohen et al. (1996), Osterling and Dawson (1994) comparing children who later received a diagnosis of autism and children with typical development.

[b]Based on Bryson et al. (2007), Clifford and Dissanayake (2008), Landa and Garrett-Mayer (2006), Nadig et al. (2007), Ozonoff et al. (2008), Ozonoff et al. (2010), Rozga et al. (2011), Wetherby et al. (2004), Yirmiya et al. (2006), Yoder et al. (2009), and Zwaigenbaum et al. (2005) examining infant siblings of children with ASD who also developed ASD and prospective well-child primary care studies.

of infants who later develop ASD indicate the following early signs of ASD: delayed verbal and nonverbal communication; reduced social engagement, smiling, and eye contact; as well as reduced responding to their own names beginning at 12 months of age (Landa & Garrett-Mayer, 2006; Nadig et al., 2007; Ozonoff et al., 2010; Presmanes, Walden, Stone, & Yoder, 2007; Wetherby et al., 2004; Yirmiya et al., 2006; Yoder et al., 2009; Zwaigenbaum et al., 2005). Furthermore, infants who later develop ASD have higher rates of atypical behaviors with objects (e.g., spinning and unusual visual regard); repetitive motor mannerisms, including arm waving; and sensory hyperresponsiveness, evidenced by covering ears (Loh et al., 2007; Ozonoff et al., 2008; Wetherby et al., 2004). Some infants also start to show delays in fine or gross motor development, with increasing difficulties in the second year of life (Landa & Garrett-Mayer, 2006). Increased attention to objects at 12 months has been found to be related to a later diagnosis of ASD in multiple prospective infant sibling studies (Bryson et al., 2007; Wetherby et al., 2004; Zwaigenbaum et al., 2005). Other attentional problems include difficulty in disengaging from one visual stimulus and attending to another at 12 months of age (Zwaigenbaum et al., 2005). Temperamental differences are also identified as a risk factor, including more intense distress and more time spent fixating on objects, and exhibiting less behavioral approach and more difficulties with emotional regulation by 24 months.

Neuropsychological Risk Markers

Neurophysiological risk measures are also being investigated in prospective studies to search for early markers for ASD. Several studies have found atypicalities in visual processing of both social and nonsocial stimuli in high-risk infants as a group (Elsabbagh & Johnson, 2007; McCleery, Allman, Carver, & Dobkins, 2007; Noland, Steven Reznick, Stone, Walden, & Sheridan, 2010). An electrophysiological study found that high-risk siblings processed objects faster than faces, compared to low-risk siblings (McCleery, Akshoomoff, Dobkins, & Carver, 2009); another found a later latency in response to direct gaze in an electrophysiological component for 10-month-old high-risk siblings (Elsabbagh et al., 2009). Interestingly, many of these studies have found similarities in processing social stimuli, but enhanced performance in processing nonsocial stimuli, suggesting that a potential risk factor may have more to do with increased attention to objects rather than people during the first year of life. Abnormal brain growth in the first year of life has also been found in infants who later develop ASD (Courchesne, Carper, & Akshoomoff, 2003; Elder et al., 2008). Additionally, abnormal development of white matter tracts was reported in 6-month-olds who later received a diagnosis of ASD (Wolff et al., 2012). Reduced hemispheric specialty for face processing and speech processing has been found in infants at risk for ASD, suggesting this as a potential endophenotype (McCleery et al., 2009; Seery et al., 2010). Multiple research groups are currently examining similar neurophysiological measures, with the hope of uncovering biomarkers that may be present even before behavioral differences emerge during the second year of life.

Early Developmental Trajectories

Thus current evidence suggests that behavioral ASD symptoms and risk signs begin to arise during the second year of life, with autism emerging between 6 and 24 months (Ozonoff et al., 2008). Importantly, no single behavior or deficit has been found to be predictive of ASD. Rather, there seems to be a constellation of social, attentional, and motor behaviors that are risk markers for ASD (Zwaigenbaum et al., 2005). Several different theories explaining the developmental trajectory of ASD symptoms across the first years of life have been proposed, with the majority of theories identifying concerns related to early attention allocation. Dawson and colleagues (Dawson, 2008; Dawson, Bernier, & Ring, 2012; Dawson, Webb, Wijsman, et al., 2005) have proposed a social motivation/attention hypothesis, characterizing ASD as a disorder of early-emerging impairments in social attention believed to be related to a reduced sensitivity to the reward value of social stimuli (see Figure 11.1). This decreased attention to other people's faces and voices suggests a lack of typical pleasure or reward value from interacting with others, associated with a decreased activation of the neural reward system (amygdala, prefrontal cortex). There is a mutual relation between the behavioral and neural systems, such that impairments in one system lead to further atypical development in the other system. Dawson and colleagues (2008) describe ASD as an unfolding process whereby infants show increased preference or attention toward objects and miss the important information occurring in the social environment. As a result, the next phase of SCI skills (i.e., joint attention, social imitation, and face processing) fails to develop. Thus autism emerges across the first 2 years of life through a complex association among atypical attention, atypical brain development, and subsequent symptom onset. Dawson (2008) highlights the importance of early behavioral intervention in altering this atypical developmental trajectory that results from early lack of attention to social cues.

Klin and colleagues have also highlighted the role of impaired social attention, suggesting that difficulty regulating attention in complex social scenes may be an early marker of ASD (e.g., Jones, Carr, & Klin, 2008). For example, Shic, Macari, and Chawarska (2014) reported that 6-month-old infants showed less attention to faces when the persons were speaking than when they were silent. This difference in attention allocation could be due to impaired social attention or due to difficulty with audiovisual integration. More research is needed to identify whether these attention impairments are specific to social information processing or are more general in nature (see Klinger, Klinger, & Pohlig, 2006). Elsabbagh and colleagues (2013) examined attention allocation via a nonsocial paradigm and reported that between 7 and 14 months of age, infants who were later diagnosed with ASD showed atypical patterns of visual orienting; by 14 months, they were exhibiting "sticky" attention, in which they had difficulty disengaging their attention. Across all of these studies, the emerging pattern of findings suggests that atypical early attention can have a detrimental impact on subsequent learning and neural development. Infants with

typical development attend to faces and voices as a way to learn about social interaction. Without this early attentional focus, infants with ASD may miss out on important information in their environment—information that leads to language development and social understanding.

Subtypes of Developmental Onset

Three subtypes of developmental trajectories have been identified, in which children display a developmental plateau, progress at a slower rate, or show a regression in previously acquired skills (Ozonoff et al., 2008). This provides further evidence that ASD represents a complex and heterogeneous set of disorders with potentially different genetic etiologies. The fact that some infants who display more aberrant behaviors and more serious delays before 12 months of age go on to have more severe ASD symptoms and intellectual disability suggests that these infants may have de novo mutations or other chromosomal abnormalities (Tager-Flusberg, 2010).

REGRESSION

The phenomenon of a developmental decline or regression is estimated to occur in 24% of children with ASD prior to 36 months (Parr et al., 2011). Parental reports of regression during the second year of life are well documented (Lord, Shulman, & DiLavore, 2004; Werner & Dawson, 2005). Werner and Dawson (2005) compared videotapes of two groups of infants with autism (those with parental reports of a regressive course and those with early onset), as well as a comparison group of infants with typical development. Infants with regression had similar joint attention behaviors and *more frequent* use of words or babbling, compared with infants at 12 months with typical development, while these behaviors were significantly reduced in the early-onset group. By 24 months, both groups of children with ASD had fewer social and communication behaviors than comparison children.

Role of Early Intervention in Altering Atypical Developmental Course

The large variability in ASD has offered clues about risk and protective factors, as well as insight into possible different genetic etiologies. To a considerable extent, the outcomes of ASD can be accounted for by the nature and severity of the effects of genetic and environmental risk factors on early biological development. It is now known that early social development and experience is another important factor, particularly the degree to which early influences alter early interactions between the child and the environment.

Models of typical development of social and language brain circuitry and development stress the importance of early parent–child interactions in the development of the social brain and language systems (Dawson, Webb, & McPartland, 2005; Kuhl, 2007). Early intervention allows for a greater chance to alter the abnormal developmental trajectory and possibly reduce or prevent the full syndrome of ASD (Dawson, 2008). Early intervention that focuses on facilitating early social attention, engagement, and reciprocity between young children with ASD and their social partners can enhance normal social and linguistic input to the developing brain. A recent study showed that 2 years of early intensive behavioral intervention resulted in significant improvements in IQ, language, social behavior, and adaptive behavior, as well as normalized brain responses to social stimuli, in young children with ASD (Dawson, Jones, et al., 2012; Dawson et al., 2010). Predictive factors that offer better outcomes for children with ASD (and thus suggest potential protective markers for ASD) include higher level of social engagement, higher intellectual ability, and increased prelinguistic and linguistic ability. Although it is optimal to begin intervention as early as possible, it is believed that neuroplasticity occurs throughout the lifespan, and that continued interventions and services through adulthood will result in the best possible outcomes.

Adult Outcomes

The estimated prevalence of ASD among 8-year-olds increased 123% between 2002 and 2010 (CDC, 2014). The original 2002 cohort from the Autism and Developmental Disabilities Monitoring Network is making the transition from school to adult services, and data from this cohort suggest that a 123% increase in demand for adult services for individuals with ASD can be expected. There is an emerging literature describing the quality of life in young adults with ASD. Overwhelmingly, this literature suggests that young adults with ASD have few social (Liptak, Kennedy, & Dosa, 2011; Orsmond et al., 2004), educational, or employment (Shattuck et al., 2012; Taylor & Seltzer, 2011) opportunities after leaving high school. Furthermore, the

evidence suggests that young adults need substantial support to become involved in daily activities.

Employment Outcomes

Young adults with ASD experience chronically low rates of postschool employment—rates that are significantly below those for young adults with other developmental disabilities (Shattuck et al., 2012). Adults with high-functioning ASD are underemployed, switch jobs frequently, have difficulty adjusting to new job settings, make less money than their counterparts, and are much less likely to be employed than peers with typical development (Hendricks, 2010). One recent study found that only 12% of young adults with ASD were employed (Taylor & Seltzer, 2011). Shattuck and colleagues (2012) reported that 2 years after completing high school, 52% of young adults with ASD were not participating in either vocational or educational activities (N = 500). Furthermore, young adults with ASD but without intellectual disability are three times more likely to have no daytime activities than are young adults with both ASD and intellectual disability (Taylor & Seltzer, 2011).

Behavioral and Cognitive Outcomes

Several recent studies have examined developmental trajectories across young adulthood and provide a mixed picture of declines, plateaus, and improvements during this developmental period. For example, Taylor and Seltzer (2010) conducted a 10-year longitudinal study across the transition to adulthood; they found that while ASD symptom severity and maladaptive behavior decreased through adolescence, these improvements largely plateaued after individuals left high school (N = 242, mean age of 26 at follow-up), perhaps due to a lack of consistent adult services.

Very few studies have examined middle-adulthood functioning in adults diagnosed as having autism in childhood (see Gillespie-Lynch et al., 2012, for a review). Howlin and colleagues (2004) reported that 58% of their sample of 68 adults (average age of 29 years) experienced "poor" or "very poor" outcomes. In contrast, Farley and colleagues (2009) conducted a 20-year follow-up study examining outcomes of 41 individuals with high-functioning ASD (mean age of 32 years) and reported that 17% of their sample experienced "poor" or "very poor" outcomes. Howlin, Savage, Moss, Tempier, and Rutter (2014) conducted a 40-year follow up of middle-aged adults diagnosed with ASD without comorbid intellectual disability as children. Overall, IQ was stable across time, suggesting that childhood IQ is a predictor of adult cognitive ability. Language skills improved from childhood to adulthood. However, a small subgroup showed declines across development, particularly those with epilepsy. More research is needed on predictors of successful adult outcome with regard to employment, education attainment, and independent living.

CONCLUSIONS

The past decade has witnessed substantial progress in our understanding and treatment of individuals with ASD across the lifespan. In particular, important strides have been made in our understanding of the genetic and environmental risk factors associated with ASD, the early behavioral symptoms of ASD, and the unfolding of these symptoms across development. Furthermore, we have a greater understanding that ASD is a spectrum disorder with significant variations in SCI skills and RRBs. DSM-5 now acknowledges the complexity of this diagnosis with regard to symptom variability across the lifespan, as well as the presence of comorbid disorders and problems (including significant attention, anxiety, and depression symptoms). Through early diagnosis and intervention, significant improvements in intellectual functioning, social skills, and language abilities have been documented, with some individuals showing "optimal outcome" (Fein et al., 2013). Despite this progress, overall outcomes for adults remain poor with regard to quality of life in employment, educational, and independent living skills. Research examining the developmental trajectory of ASD from infancy through older adulthood is essential both to our understanding of the disorder and to the identification of appropriate intervention goals that facilitate positive outcome. Finally, as we understand more about the early screening, diagnosis, and treatment of ASD, it will be a challenge to translate these scientific findings into social policy. Considerable funding and effort are required to implement large-scale early detection efforts and intensive behavioral intervention programs. However, cost–benefit analyses clearly document that early intervention services reduce the lifetime cost of supporting individuals with ASD (Jacobson & Mulick, 2000). Thus research on strategies to translate scientific findings into meaning-

ful and sustainable community-based efforts will be an increasing focus of the future.

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CHAPTER 12

Early-Onset Schizophrenia

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Schizophrenia is a debilitating neuropsychiatric disorder characterized by disruptions in cognition, perception and social relatedness. The World Health Organization (2008) has ranked schizophrenia as one of the leading causes of disability worldwide. Schizophrenia rarely first presents in childhood, but it increases in prevalence through adolescence. "Early-onset schizophrenia" (EOS) is defined as schizophrenia with onset prior to age 18 years; "childhood-onset schizophrenia" (COS) refers to this disorder with onset prior to age 13 years. Although EOS is considered to be continuous with adult-onset schizophrenia, it presents with unique developmental and social challenges (McClellan, Stock, & AACAP Committee on Quality Issues, 2013).

This chapter reviews the history and description of EOS, including issues specific to COS when relevant literature is available. We address clinical characteristics, comorbidities, epidemiology and diagnostic issues, with a focus on identifying core characteristics of the disorder and on providing a foundation for differentiating EOS from other psychiatric conditions. Furthermore, we explore the genetic and neurobiological literature to understand and orient current and future relevant research.

BRIEF HISTORICAL CONTEXT

Descriptions of madness and insanity date back to antiquity. In the early 20th century, Emil Kraepelin (1909) characterized two forms of insanity: manic–depressive illness and dementia praecox. Dementia praecox, or "dementia of the young," was specified to separate it from other dementias such as that associated with syphilis. Bleuler (1911) redefined the diagnosis of dementia praecox as schizophrenia ("splitting of the mind"), due to the observation that the illness was not associated with dementia—but rather with the loss of associated thought processes, and the disruption of thought, emotions, and behavior. Schneider (1959) proposed that "first-rank symptoms" were specific to schizophrenia (auditory hallucinations, thought broadcasting, delusions of control, delusional perception). Although it is now recognized that these psychotic symptoms may also present as part of other syndromes (e.g., psychotic mania), there is merit in understanding how the conceptual understanding of schizophrenia has evolved.

The original descriptions of schizophrenia identified a pattern of onset during adolescence and young adulthood, with rare cases in younger children. These cases were similar to the adult form of the disorder, and distinct from autism and other pervasive developmental disorders (Werry, 1979). However, the concept of childhood schizophrenia, influenced by the work of Bender, Kanner, and others, evolved to include syndromes defined by neurodevelopmental lags in the maturation of language, perception, and motility (Fish & Kendler, 2005). This definition, which was adopted in the second edition of the *Diagnostic and Statistical Manual of*

Mental Disorders (DSM-II), did not require hallucinations or delusions as necessary criteria, and included infantile autism. As a result, the literature on COS prior to the publication of DSM-III (American Psychiatric Association [APA], 1980) overlaps with that of autism and other pervasive developmental disorders.

Seminal studies by Kolvin (1971) and Rutter (1972) refined our understanding of the various childhood psychoses and the continuity between child and adult schizophrenia (Kolvin, 1971; Rutter, 1972). Based on this research, the DSM-III diagnosis of schizophrenia required the same criteria for youth and adults. Subsequent research has generally demonstrated that EOS appears to be continuous with the adult-onset illness in regard to symptoms, course of illness, outcome, and some shared neurobiological features.

DESCRIPTION OF THE DISORDER

Schizophrenia is a syndrome defined by a set of core symptoms and is classified into subtypes demonstrating differences in functionality and severity. An accurate diagnostic assessment in youth requires a developmental understanding of symptom presentation, and a recognition of the overall characteristic pattern of illness, rather than the simple application of diagnostic criteria as a checklist.

Diagnostic Criteria

The diagnosis of schizophrenia in children and adolescents continues to be made with the same criteria as in adults; the most recent version of these criteria (see Table 12.1) appears in DSM-5 (APA, 2013). DSM-5 requires that two or more core symptoms—that is, hallucinations, delusions, disorganized speech, disorganized or catatonic behavior, and/or negative symptoms—must be present for at least 1 month (less if successfully treated). One of the required symptoms must be delusions, hallucinations, or disorganized speech. Active, prodromal, or residual symptoms of the disorder must be present for at least 6 months and associated with a significant decline in social or educational/occupational functioning. In children and adolescents, this may include the failure to achieve age-appropriate levels of interpersonal or academic development. Schizoaffective disorder (Table 12.2) and psychotic mood disorders are ruled out as follows: Either there are no concurrent mood episodes; or, if such episodes are present, their total duration is "a minority" of the total duration of active-phase symptoms. If the patient has a history of autism spectrum disorder or a childhood communication disorder, prominent hallucinations or delusions must be present for at least 1 month (less if successfully treated).

The DSM-5 criteria (Tables 12.1 and 12.2) mirror those of DSM-IV-TR (APA, 2000), with a few substantive changes. Delusions, hallucinations, or disorganized speech are required to make the diagnosis. Commenting and conversing hallucinations and bizarre delusions are no longer accorded special diagnostic status. The subtypes of schizophrenia (e.g., disorganized, paranoid, undifferentiated) have been eliminated, given their lack of diagnostic stability, as well as their limited utility as markers for either treatment or biological research.

A proposed "attenuated psychosis syndrome"—defined by the emergence of distressing and disabling hallucinations/perceptual abnormalities, delusions/delusional ideas, or disorganized speech/communication in the context of relatively intact reality testing—has been recommended for further study by the DSM-5 committee and is listed in Section III of the manual. Although research studies have defined criteria that predict the development of psychosis in high-risk individuals, it is not clear at this time whether the attenuated or prodromal syndrome can be accurately diagnosed in community settings.

Symptomatology

Core features of schizophrenia include positive and negative symptoms, as well as disorganized thinking and behavior. Positive symptoms include hallucinations and delusions. Hallucinations in schizophrenia can be present in any sensory modality, including olfactory or tactile. Auditory hallucinations are the most common and are often experienced as voices that are separate from a person's thoughts (McClellan et al., 2013). Auditory hallucinations may involve multiple voices, conversing with each other, or provide commentary on the person's thoughts or actions. Delusions are defined as fixed false beliefs that are unrealistic in the context of one's life experience and culture. Delusions may be persecutory (e.g., one is being followed by the CIA), referent (e.g., one is receiving special messages from the television), grandiose (e.g., one has special powers), somatic (e.g., one is suffering from a terminal illness, despite medical evidence), or religious (e.g., one is a

TABLE 12.1. DSM-5 Diagnostic Criteria for Schizophrenia

A. Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated). At least one of these must be (1), (2), or (3):

1. Delusions.
2. Hallucinations.
3. Disorganized speech (e.g., frequent derailment or incoherence).
4. Grossly disorganized or catatonic behavior.
5. Negative symptoms (i.e., diminished emotional expression or avolition).

B. For a significant portion of the time since the onset of the disturbance, level of functioning in one or more major areas, such as work, interpersonal relations, or self-care, is markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, there is failure to achieve expected level of interpersonal, academic, or occupational functioning).

C. Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or by two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

D. Schizoaffective disorder and depressive or bipolar disorder with psychotic features have been ruled out because either 1) no major depressive or manic episodes have occurred concurrently with the active-phase symptoms, or 2) if mood episodes have occurred during active-phase symptoms, they have been present for a minority of the total duration of the active and residual periods of the illness.

E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

F. If there is a history of autism spectrum disorder or a communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations, in addition to the other required symptoms of schizophrenia, are also present for at least 1 month (or less if successfully treated).

Specify if:

The following course specifiers are only to be used after a 1-year duration of the disorder and if they are not in contradiction to the diagnostic course criteria.

First episode, currently in acute episode: First manifestation of the disorder meeting the defining diagnostic symptom and time criteria. An *acute episode* is a time period in which the symptom criteria are fulfilled.

First episode, currently in partial remission: *Partial remission* is a period of time during which an improvement after a previous episode is maintained and in which the defining criteria of the disorder are only partially fulfilled.

First episode, currently in full remission: *Full remission* is a period of time after a previous episode during which no disorders specific symptoms are present.

Multiple episodes, currently in acute episode: Multiple episodes may be determined after a minimum of two episodes (i.e., after a first episode, a remission and a minimum of one relapse).

Multiple episodes, currently in partial remission

Multiple episodes, currently in full remission

Continuous: Symptoms fulfilling the diagnostic symptom criteria of the disorder are remaining for the majority of the illness course, with subthreshold symptom periods being very brief relative to the overall course.

Unspecified

Specify if:

With catatonia (refer to the criteria for catatonia associated with another mental disorder for definition).

Coding note: Use additional code 293.89 (F06.1) catatonia associated with schizophrenia to indicate the presence of the comorbid catatonia.

Specify current severity:

Severity is rated by a quantitative assessment of the primary symptoms of psychosis, including delusions, hallucinations, disorganized speech, abnormal psychomotor behavior, and negative symptoms. Each of these symptoms may be rated for its current severity (most severe in the last 7 days) on a 5-point scale ranging from 0 (not present) to 4 (present and severe). (See Clinician-Rated Dimensions of Psychosis Symptom Severity in the chapter "Assessment Measures.")

Note: Diagnosis of schizophrenia can be made without using this severity specifier.

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TABLE 12.2. DSM-5 Diagnostic Criteria for Schizoaffective Disorder

A. An uninterrupted period of illness during which there is a major mood episode (major depressive or manic) concurrent with Criterion A of schizophrenia.

Note: The major depressive episode must include Criterion A1: Depressed mood.

B. Delusions or hallucinations for 2 or more weeks in the absence of a major mood episode (depressive or manic) during the lifetime duration of the illness.

C. Symptoms that meet criteria for a major mood episode are present for the majority of the total duration of the active and residual portions of the illness.

D. The disturbance is not attributable to the effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

Specify whether:

295.70 (F25.0) Bipolar type: This subtype applies if a manic episode is part of the presentation. Major depressive episodes may also occur.

295.70 (F25.1) Depressive type: This subtype applies if only major depressive episodes are part of the presentation.

Specify if:

With catatonia (refer to the criteria for catatonia associated with another mental disorder for definition).

Coding note: Use additional code 293.89 (F06.1) catatonia associated with schizoaffective disorder to indicate the presence of the comorbid catatonia.

Specify if:

The following course specifiers are only to be used after a 1-year duration of the disorder and if they are not in contradiction to the diagnostic course criteria.

First episode, currently in acute episode: First manifestation of the disorder meeting the defining diagnostic symptom and time criteria. An *acute episode* is a time period in which the symptom criteria are fulfilled.

First episode, currently in partial remission: *Partial remission* is a time period during which an improvement after a previous episode is maintained and in which the defining criteria of the disorder are only partially fulfilled.

First episode, currently in full remission: *Full remission* is a period of time after a previous episode during which no disorder-specific symptoms are present.

Multiple episodes, currently in acute episode: Multiple episodes may be determined after a minimum of two episodes (i.e., after a first episode, a remission and a minimum of one relapse).

Multiple episodes, currently in partial remission

Multiple episodes, currently in full remission

Continuous: Symptoms fulfilling the diagnostic symptom criteria of the disorder are remaining for the majority of the illness course, with subthreshold symptom periods being very brief relative to the overall course.

Unspecified

Specify current severity:

Severity is rated by a quantitative assessment of the primary symptoms of psychosis, including delusions, hallucinations, disorganized speech, abnormal psychomotor behavior, and negative symptoms. Each of these symptoms may be rated for its current severity (most severe in the last 7 days) on a 5-point scale ranging from 0 (not present) to 4 (present and severe). (See Clinician-Rated Dimensions of Psychosis Symptom Severity in the chapter "Assessment Measures.")

Note: Diagnosis of schizoaffective disorder can be made without using this severity specifier.

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religious prophet). Delusions may also involve thought withdrawal or insertion, or delusions of being controlled by an outside force.

Negative symptoms refer to deficits in functioning and behavior, such as avolition, alogia, affective flattening, anhedonia, and social withdrawal. Avolition is defined as difficulties with initiating and maintaining motivation in order to complete tasks necessary for successful functioning. Alogia typically manifests itself as poverty in the content and amount of speech. Persons with schizophrenia typically demonstrate a limited range of facial expression (affective flattening). Affected individuals may also suffer from a general lack of interest in enjoyable activities (anhedonia). Negative symptoms may be difficult to differentiate from comorbid depression and side effects of antipsychotic medications.

In addition to positive and negative symptoms, individuals with schizophrenia often display disorganized thinking and behavior. Persons with schizophrenia typically have difficulty attending to stimuli in their environment, and may change topics suddenly or provide oblique responses to questions. Their speech is often characterized by loosening of associations (i.e., frequent, sudden, and apparently unrelated changes in the subject of conversation), as well as tangential or incoherent utterances. Affected individuals may appear to be responding to internal stimuli, and may also demonstrate behavior that is bizarre or unrelated to their environment. Some severely impaired individuals present with catatonia. Catatonic behavior involves a general lack of response to one's environment and includes symptoms of motor immobility, mutism, posturing or stereotyped behavior, excessive motor behavior, echolalia, or echopraxia.

Because youth are diagnosed with schizophrenia according to the same criteria as those used for adults, they should present with the same core symptomatology. There are, however, some developmental differences in the pattern and qualitative presentation of symptoms in juveniles. EOS most often presents with hallucinations, thought disorder, and flattened affect; systematic delusions and catatonia are observed less frequently (McClellan et al., 2013). Across different early-onset psychotic illnesses, negative symptoms appear to be the most specifically associated with EOS (McClellan, McCurry, Speltz, & Jones, 2002). Youth with COS often describe both auditory and visual hallucinations (David et al., 2011). Thought disorder in EOS is generally characterized by loose associations, illogical thinking, and impaired discourse skills (Caplan, Guthrie, Fish, Tanguay, & David-Lando, 1989).

Moreover, developmental issues specific to children must be recognized and accounted for when adult definitions of psychopathology are applied to children. Differences in language and cognition may affect the range and quality of symptom presentation. The complexity and content of delusional beliefs or hallucinatory experiences are influenced by one's knowledge base, experience, and cognitive abilities. For example, it is uncommon for children with schizophrenia to present with typical adult delusions, such as believing that the FBI is spying on them, since such topics are not relevant to their lives. Delusions in children typically reflect their surrounding experiences, such as fixed bizarre beliefs regarding fictional characters.

Failing to recognize developmental differences between children and adults can lead to the misinterpretation of symptom reports and misdiagnosis. Children often report psychotic-like symptoms, yet most will not have a true psychotic illness (McClellan, 2011). Childhood false beliefs are more likely to represent wishful thinking or active imagination than delusions. Immature or delayed cognitive and language skills can appear disorganized, and disruptive behaviors often seem illogical or bizarre. None of these commonplace childhood problems by themselves represent psychosis. The diagnosis of schizophrenia should be based on overt evidence of psychotic symptoms, including findings on mental status exam (McClellan et al., 2013).

Social/Occupational Dysfunction

To diagnose schizophrenia, the development of psychotic symptoms must be accompanied with a decline in the level of social, occupational/educational, and self-care functioning. In children and adolescents, this may include the failure to achieve age-appropriate levels of interpersonal, academic, or occupational development. This decline in functioning should be pervasive, rather than limited to one or two specific situations (e.g., school refusal because of persecutory beliefs). Although functioning may improve with treatment, deficits are often chronic and functioning may not return to premorbid levels (McClellan et al., 2013).

Course of Illness

In both youth and adults, schizophrenia is characterized by four phases: prodromal, acute, recovery, and

residual. To qualify for a diagnosis of schizophrenia, the disturbances must be present for a period of at least 6 months. This period must include an active phase of illness (i.e., psychotic symptoms) with or without a prodromal or residual phase. This acute phase, when most affected individuals are first diagnosed, is characterized by significant positive symptoms. During this phase, patients may be grossly disorganized, confused, and potentially dangerous to themselves or others.

Recovery from acute psychotic episodes generally takes several months or longer, depending on response to treatment. In youth, recovery is often incomplete. Longer duration of untreated psychosis and greater severity of negative symptoms at the time of diagnosis predict greater functional impairment over time (Brown & Pluck, 2000; Clarke et al., 2006). Individuals who recover from an acute phase generally have persistent functional deficits, residual disordered thinking, and negative symptoms. Most youth with EOS demonstrate some degree of chronic impairment across their lifespan (Bunk, Eggers, & Klapal, 1999; Eggers, 1978, 2005; Eggers & Bunk, 1997; Hollis, 2000; Jarbin, Ott, & Von Knorring, 2003; Maziade, Bouchard, et al., 1996; Maziade, Gingras, et al., 1996; McClellan, Werry, & Ham, 1993; Ropcke & Eggers, 2005; Werry, McClellan, & Chard, 1991).

Prior to the onset of positive symptoms, individuals generally display prodromal symptoms coupled with a decline in function that presages the illness. Abnormalities during the prodromal period include social isolation, academic difficulties, odd or idiosyncratic preoccupations, and mood symptoms. This phase can last from days to weeks, or for a more chronic course of years. COS tends to have a more chronic onset than EOS, with signs in early childhood (Fish & Kendler, 2005), while the presentation in adolescence can have either an acute or more insidious onset (Kolvin, 1971; McClellan & McCurry, 1998; McClellan et al., 1993; Werry et al., 1991). In addition, the majority of youth with EOS have histories of premorbid problems, including cognitive delays, learning problems, behavioral difficulties, and social withdrawal or oddities (Paya et al., 2013).

Premorbid functioning, cognitive ability, early treatment response, and adequacy of therapeutic resources influence short-term outcome (Remschmidt, Martin, Schulz, Gutenbrunner, & Fleischhaker, 1991; Vyas, Hadjulis, Vourdas, Byrne, & Frangou, 2007). Poor long-term outcome is predicted by family history of nonaffective psychosis, low premorbid functioning, insidious onset, earlier age of onset, low intellectual functioning, and severe symptoms during acute phases (Clemmensen, Vernal, & Steinhausen, 2012; Eggers, 1989; Jarbin et al., 2003; Maziade, Bouchard, et al., 1996; Ropcke & Eggers, 2005; Werry & McClellan, 1992) When followed into adulthood, children with EOS demonstrated greater social deficits, had lower levels of employment, and were less likely to live independently, relative to those with other childhood-onset psychotic disorders (Hollis, 2000; Jarbin et al., 2003).

DIFFERENTIAL DIAGNOSIS: OTHER SYNDROMES WITH PSYCHOTIC SYMPTOMS

The appropriate clinical management of schizophrenia relies upon the ability to diagnose the condition accurately. Therefore, it is important to recognize other syndromes and conditions that present with psychotic symptoms. Table 12.3 presents the differential diagnosis of EOS, which includes both psychotic and nonpsychotic disorders that can present with reports of psychosis. Appropriate diagnostic evaluation requires strategies to evaluate for comorbid/confounding medical and psychiatric disorders, and to assess detailed symptom phenomenology, prodromal symptoms, family history, and social stressors (see McClellan et al., 2013, for a detailed discussion of assessment methods for EOS). The most important alternative diagnoses to consider when one is assessing a child for schizophrenia are reviewed below.

Medical Conditions

Numerous medical conditions can result in symptoms of psychosis. Recognition and correction of these conditions can result not only in the remission of psychotic symptoms, but also in the treatment of a potentially life-threatening illness. For example, psychosis caused by an underlying medical condition is often associated with delirium, a condition associated with significantly increased morbidity and mortality. Delirium presents with an acute change in cognitive functioning, associated with significant impairments in attention, orientation, and fluctuating mental status findings (Blazer & van Nieuwenhuizen, 2012). Individuals suffering from delirium may present with acute psychosis, including vivid auditory and visual hallucinations. This complex diagnosis with numerous potential etiologies (Table

TABLE 12.3. Disorders That Can Present with Psychosis or Psychotic-Like Symptoms

Psychiatric disorders
Psychotic disorder due to another medical condition
Bipolar disorders
Major depressive episode with psychotic features
Schizoaffective disorder
Posttraumatic stress disorder
Obsessive–compulsive disorder
Autism spectrum disorder
Conduct disorder
Psychosocial factors
Abuse
Traumatic stress
Chaotic family environment
Medical conditions
Substance intoxication (both legal and illegal drugs)
Delirium
Brain tumor
Head injury
Seizure disorder
Meningitis
Porphyria
Wilson's disease
Cerebrovascular accident
AIDS
Electrolyte imbalance
Blood glucose imbalance
Endocrine imbalance

12.3) requires treatment that may include judicious psychopharmacological treatment with antipsychotic medication for symptom management until the underlying cause can be determined and eliminated (DeMaso et al., 2009). Thus a thorough medical and neurological examination at the time of first presentation of psychosis is indicated, especially in cases with acute onset or rapid progression of symptoms associated with severe disorientation and confusion.

Substance Intoxication

Both legal and illegal drugs can result in the acute onset of psychosis (Bukstein et al., 2005). In these cases, the goal is to identify and eliminate the offending agent, while using brief psychopharmacological treatment for symptom management as needed. Prescription drugs associated with psychosis, especially when taken inappropriately, include corticosteroids, anesthetics, anticholinergics, antihistamines, amphetamines, and dextromethorphan. Drugs of abuse that can result in psychosis include dextromethorphan, LSD, hallucinogenic mushrooms, psilocybin, peyote, cannabis, stimulants, salvia, and inhalants. Some drugs, such as methamphetamine, are reported to cause more chronic impairment beyond the period of detoxification. Prolonged impairment may represent independent drug effects or the triggering/exacerbation of schizophrenia in a vulnerable individual. Regardless, the development of psychosis in the context of substance abuse requires ongoing assessment and treatment, with a focus on both resolution of symptoms and abstinence from illicit agents.

Schizoaffective Disorder

By definition, schizoaffective disorder (Table 12.2) requires the presence of psychotic symptoms plus prominent mood episodes (meeting full criteria for mania or depression) that are present for "the majority" of the duration of the illness. DSM-5 emphasizes the requirement of a full mood episode. This is an important distinction because mood symptoms such as dysphoria, irritability, or grandiosity are common in individuals with schizophrenia, and the reliability of the diagnosis of schizoaffective disorder in clinical settings has been poor (Buckley, Miller, Lehrer, & Castle, 2009).

Youth with schizoaffective disorder demonstrate the same severity of psychotic symptoms and functional impairment as those with schizophrenia (Frazier et al., 2007). The stability of early-onset schizoaffective disorder as a diagnosis appears to vary over time, and this disorder can be difficult to distinguish from schizophrenia (Fraguas et al., 2008; McClellan & McCurry, 1999).

Affective Psychosis

Psychotic mood disorders (especially bipolar disorders) can present with a variety of affective and psychotic symptoms (McClellan, Kowatch, Findling, & AACAP Work Group on Quality Issues, 2007). In children and adolescents with schizophrenia, negative symptoms may be mistaken for depression, especially since it is common for patients to experience dysphoria with their illness. Alternatively, mania in teenagers often presents with florid psychosis, including hallucinations, delusions, and thought disorder (McClellan et al.,

2007). Psychotic depression may present with mood-congruent or mood-incongruent psychotic features, either hallucinations or delusions (Birmaher et al., 2007)

This overlap in symptoms increases the likelihood of misdiagnosis at the time of onset (Ruggero, Carlson, Kotov, & Bromet, 2010). Longitudinal reassessment is needed to ensure accuracy of diagnosis.

Autism Spectrum Disorder

Autism spectrum disorder is distinguished from schizophrenia (1) by the absence or transitory nature of psychotic symptoms; and (2) by the predominance of the characteristic abnormal language patterns, aberrant social relatedness, and ritualistic or repetitive repertoires of behavior (APA, 2013). The earlier age of onset and the absence of a normal period of development are also indicative of autism, whereas the premorbid abnormalities in EOS tend to be less pervasive and severe (Kolvin, 1971; Rutter, 1972).

Youth with schizophrenia often have premorbid and/or comorbid problems with aloofness, idiosyncratic interests, and communication oddities, which may be mistakenly characterized as autism spectrum disorder (Rapoport, Chavez, Greenstein, Addington, & Gogtay, 2009). These symptoms are likely to be nonspecific markers of disrupted brain development, and may also reflect shared biological processes that are disrupted in both syndromes (Sporn et al., 2004). Once significant psychotic symptoms develop, the diagnosis of schizophrenia takes precedence.

Differentiating True Psychotic Symptoms from Other Phenomena

Reports of psychotic-like experiences are common in children. Fanciful thinking, overactive imaginations, and attempts to describe internal mental processes may be misinterpreted by clinicians (and researchers) as psychosis. This is particularly problematic if checklist approaches to diagnosis are used without clinical judgment, and if adult diagnostic criteria are applied carte blanche without developmental considerations. Potential symptom reports needed to be assessed in the context of clinical presentation, mental status exam, contributing psychosocial factors, and developmental status.

Most children reporting apparent psychotic symptoms do not have a true psychotic illness (Kelleher et al., 2012). Such children typically report symptoms suggestive of hallucinations and delusions without observable evidence of psychosis, such as thought disorganization and bizarre behavior. Youth reporting atypical psychotic symptoms are more likely to be diagnosed with emotional and behavioral disorders (Hlastala & McClellan, 2005; Kelleher et al., 2012), and to have histories of trauma (Freeman & Fowler, 2009) and posttraumatic stress disorder (Hlastala & McClellan, 2005).

Psychotic-like symptom reports can be differentiated from true psychosis via the clinical presentation, mental status examination, and the context within which symptoms are reported (McClellan, 2011). Atypical reports of psychotic symptoms are often characterized by the following: (1) Symptom reports are inconsistent, and there is no other documented evidence of a psychotic process (e.g., thought disorder, bizarre/disorganized behavior); (2) the qualitative nature of the reports is not typical of psychotic symptoms (e.g., greatly detailed descriptions or reports more suggestive of fantasy or imagination); and/or (3) the reported symptoms only occur in specific situations (e.g., only hearing voices after an aggressive outburst) (Hlastala & McClellan, 2005).

COMORBIDITIES

Children and adolescents with EOS often suffer from a number of comorbid conditions and problems (McClellan et al., 2013). Comorbid conditions can significantly contribute to the morbidity and mortality of the disorder; they can also create diagnostic confusion, given overlapping symptom domains (e.g. distinguishing negative symptoms from depression). Below, we highlight the most clinically relevant comorbidities that need to be assessed in patients with EOS.

Depression

In adults with schizophrenia, comorbid depression is relatively common (23–57%), although measurement and definitional issues substantially influence reported rates of comorbidity (Buckley et al., 2009; Conus et al., 2010; Hausmann & Fleischhacker, 2002). Substantial rates of depression are also reported in individuals with EOS, including those with COS (Eggers & Bunk, 2009; Frazier et al., 2007; Ross, Heinlein, & Tregellas, 2006).

Depression in individuals with schizophrenia may represent an independent disorder, may be secondary to the functional and social impacts of psychosis or treat-

ment, or may be an inherent part of the schizophrenia. The ABC Schizophrenia Study suggests that the prodromal stages of schizophrenia and unipolar depression are quite similar until the onset of active psychotic symptoms (Hafner, Maurer, & an der Heiden, 2013). Cornblatt and colleagues (2003) note that depression and social isolation are core characteristics of the prodromal period of schizophrenia in adolescents.

Comorbid depression in adults with schizophrenia is associated with improved insight but worse prognosis; higher rates of relapse; early and longer hospitalizations; increased symptoms, environmental burdens, and personal suffering; decreased responses to psychopharmacological treatment; and decreases in cognitive, social, and vocational/academic functioning (Buckley et al., 2009; Conley, Ascher-Svanum, Zhu, Faries, & Kinon, 2007; Sim, Chua, Chan, Mahendran, & Chong, 2006; Sim, Mahendran, Siris, Heckers, & Chong, 2004; Tsai & Rosenheck, 2013). Furthermore, depression in individuals with schizophrenia is associated with increased risk (three- to sevenfold) of attempted and completed suicide (Hawton, Sutton, Haw, Sinclair, & Deeks, 2005; Hor & Taylor, 2010; Palmer, Pankratz, & Bostwick, 2005; Siris, 2001).

Distinguishing between depression and negative symptoms is challenging, given the overlap in related phenomena, such as apathy, avolition, and flat affect. Schizophrenia and schizoaffective disorder differ only in the relative proportion of concurrent mood episodes—the assessment of which usually depends on historical recall, and which can change over the duration of the illness. Symptoms of schizophrenia and of mood disorders with psychotic features often overlap at the initial presentation and may require long-term assessment to differentiate (McClellan & McCurry, 1999; Ruggero et al., 2010).

Regardless as to whether depression symptoms are independent or constitute a core component of schizophrenia, these symptoms must be adequately assessed and addressed in treatment. This includes ongoing assessment for suicide, given the risk in this population.

Anxiety and Related Disorders

Comorbid anxiety with schizophrenia is associated with increased core symptoms, dysfunction, and suicidality. A meta-analysis of the adult literature found that 38.3% of patients with schizophrenia suffered from a comorbid DSM-IV anxiety disorder (Achim et al., 2011). Mean pooled prevalence rates were 12.1% for obsessive–compulsive disorder (OCD), 14.9% for social phobia, 10.9% for generalized anxiety disorder, 9.8% for panic disorder, and 12.4% for posttraumatic stress disorder—all higher than rates typically reported for the general population. Comorbid anxiety disorders are also reported in youth with EOS (Frazier et al., 2007; McClellan & McCurry, 1999).

Distinguishing specific anxiety symptoms from characteristics of schizophrenia can be a challenge. For example, paranoia and thought disorder often induce panic and fearfulness. The core symptoms of schizophrenia should be addressed first before treatment focuses on comorbid anxiety.

An additional diagnostic dilemma is akathisia, a side effect of associated with the antidopaminergic activity of antipsychotic medication (Sethi, 2001). Akathisia is characterized by an uncomfortable internal restlessness associated with pacing and the need for physical movement. The failure to address akathisia often results in treatment noncompliance.

Persons with schizophrenia often suffer from obsessive–compulsive symptoms (Achim et al., 2011; Buckley et al., 2009). In adults, comorbid OCD and schizophrenia are associated with poorer cognitive, social, and vocational functioning (de Haan, Sterk, Wouters, & Linszen, 2013; Schirmbeck & Zink, 2013); increases in global, positive, and negative symptoms (Cunill, Castells, & Simeon, 2009); and increases in suicidality (Sevincok, Akoglu, & Kokcu, 2007). However, the relationship between, and effective treatment options for, comorbid OCD and schizophrenia remain unclear (Lysaker & Whitney, 2009). Increases in OCD symptoms are reported to be associated with the antiserotonergic activity of some second-generation antipsychotics (Schirmbeck & Zink, 2013).

Substance Use Disorders

Comorbid substance use disorders occur in a substantial portion of individuals with schizophrenia (Buckley et al., 2009; Regier et al., 1990), including in those with EOS (Hsiao & McClellan, 2007). Furthermore, in population-based studies, cannabis use in teenagers is associated with a higher risk of eventually developing psychosis (Moore et al., 2007). Comorbid substance misuse predicts treatment noncompliance and poorer outcomes (Kerfoot et al., 2011), and was associated with increased aggression and more suicidal behaviors (Hor & Taylor, 2010; Shoval et al., 2007). Comorbid substance use is currently thought of as a co-occurring

disorder, as evidence supporting a distinct subtype is lacking (Buckley et al., 2009; Tsai & Rosenheck, 2013). The increased risk of suicide underscores the importance of early detection and treatment (Hor & Taylor, 2010; Hunt et al., 2006).

Intellectual Deficits

An estimated 10–20% of individuals with EOS have IQs in the borderline range of intellectual functioning or lower (McClellan et al., 2013). Neuropsychological studies suggest that children and adolescents with schizophrenia have impairments in attention, memory, and executive functions, as well as global intellectual deficits (Hooper et al., 2010). However, there are no specific neuropsychological profiles diagnostic for schizophrenia.

Suicidality

Perhaps the most concerning comorbidity of schizophrenia is that of suicidality. The rate of completed suicide over the lifetime of individuals with schizophrenia, including those with EOS, is approximately 5% (McClellan et al., 2013). Ten percent of all suicides occur in individuals with schizophrenia (Arsenault-Lapierre, Kim, & Turecki, 2004; Suominen, Isometsa, & Lonnqvist, 2002). The morbidity of the illness, the associated social isolation, the accompanying cognitive impairments, and comorbid conditions all contribute significantly to prolonged dysfunction and suffering and to the risk for suicide.

EPIDEMIOLOGY

The prevalence of schizophrenia is approximately 1% in the general population, with an overall male–female ratio of approximately 1.4:1 (McGrath, 2006). Onset prior to age 13 years appears to be rare, but the prevalence then increases throughout adolescence (McClellan et al., 2013). Although there are reported cases of schizophrenia in children younger than 6 years of age, the diagnostic validity of the illness in preschoolers has not been established (McClellan et al., 2013).

Population-based registries in Denmark suggest that the diagnosed incidence of EOS has increased over the last four decades. Rates there have increased from 1.80 per 100,000 for youth ages 0–18 years (5.02 per 100,000 for those ages 12–18 years) during the period 1971–1993, to 5.15 per 100,000 for youth ages 0–18 years (15.73 per 100,000 for those ages 12–18 years) during the period 1994–2010 (Okkels, Vernal, Jensen, McGrath, & Nielsen, 2013). From the first period to the second, the relative proportion of females to males diagnosed with EOS also increased. It is not clear whether the increased rates are due to differences in diagnostic criteria, community practices, or true changes in the incidence of the disorder.

NEURODEVELOPMENT AND ETIOLOGY

Schizophrenia is a complex disorder with apparent vast etiological heterogeneity. To date, no single set of common causes has been identified. Neurobiological research suggests that EOS and adult-onset schizophrenia may share underlying neurobiological mechanisms, although early-onset forms may reflect more severe disruptions of neurodevelopment (Rapoport & Gogtay, 2011).

Genetic Factors

Family, twin, and adoption studies all support a strong genetic component for schizophrenia. The lifetime risk of developing the illness is 5–20 times higher in first-degree relatives of affected persons than in the general population. The rate of concordance among monozygotic twins is approximately 40–60%, whereas the rate of concordance in dizygotic twins and other siblings is 5–15% (Cardno & Gottesman, 2000).

Until recently, most research on the genetics of schizophrenia hypothesized that the illness is the sum result of different susceptibility genes, with each genetic risk variant only contributing a small degree of risk. This “common-disease, common-variant” model posits that some combination of common risk variants and/or exposures to environmental risk factors ultimately leads to the illness. Some postulate that thousands of risk alleles with very small individual effects contribute to the illness (International Schizophrenia Consortium et al., 2009).

Research based on the common-disease, common-variant model has identified scores of candidate genomic loci and candidate genes. Genome-wide association studies, using large collaborative international cohorts, have published findings implicating different genomic regions and genes, including the major histocompatibility complex (6p21.1), MIR137, and ZNF804a (Irish

Schizophrenia Genomics Consortium & Wellcome Trust Case Control Consortium 2, 2012; Psychiatric GWAS Consortium Coordinating Committee et al., 2009; Ripke et al., 2011). For EOS, positive associations have been reported for candidate genes implicated by the adult literature, including dysbindin (Gornick et al., 2005), neuregulin (Addington et al., 2007), DAOA/G30 (Addington et al., 2004), GAD1 (Addington et al., 2005), and Prodh2/DGCR6 (Liu et al., 2002).

However, the search for common risk alleles in schizophrenia has been hampered by small/diminishing effect sizes, variable findings, lack of replication, and the difficulty in establishing definitive causality for any given candidate gene or haplotype (McClellan & King, 2010b). A targeted study of the 14 most promising candidate genes in 1,870 individuals with schizophrenia and 2,002 controls found no evidence of association for any of the previously reported risk alleles (Sanders et al., 2008). More generally, across all of medicine, putative common risk variants do not explain the vast majority of genetic liability for complex disease (Manolio et al., 2009).

Alternatively, strong evidence suggests that rare genetic mutations, many of which are de novo or have arisen in recent generations, are important for complex human diseases, including neuropsychiatric conditions such as schizophrenia (McClellan & King, 2010a). Persons with schizophrenia are significantly more likely than unaffected persons to harbor rare gene-affecting copy number variants (CNVs)—that is, genomic duplications and deletions (Guilmatre et al., 2009; International Schizophrenia Consortium, 2008; Kirov et al., 2009; Need et al., 2009; Stefansson et al., 2008; Walsh et al., 2008; Xu et al., 2008). The effect is greater for those who present with onset before age 18. De novo CNVs are more common in patients with sporadic schizophrenia than in healthy individuals (Kirov et al., 2012; Walsh et al., 2008), whereas rare inherited CNVs are significantly more common among individuals with familial schizophrenia (Xu et al., 2009). Genes affected by rare CNVs function disproportionately in cellular signaling and neurodevelopmental processes, including neuregulin and glutamate pathways (Xu et al., 2008).

Most of the rare deleterious copy number mutations detected in affected persons are unique; others recur independently at genomic hotspots, including chromosomes 1q21.1, 3q29, 15q11.2, 15q13.3, 16p11.2, 16p12.1, 16p13.11, 17p12, and 22q11.2 (Bassett, Scherer, & Brzustowicz, 2010; Cardno & Gottesman, 2000; International Schizophrenia Consortium et al., 2009; Itsara et al., 2009; Mulle et al., 2010). Recent studies demonstrate the association of schizophrenia with genomic duplications in the neuropeptide receptor VIPR2 (Levinson et al., 2011; Vacic et al., 2011), and with rare missense mutations in genes important to neurodevelopmental pathways, including GRM1, MAP1A, GRIN2B, CACNA1F, NLGN2, and DGCR (Frank et al., 2011; Myers et al., 2011; Sun et al., 2011; Xu et al., 2011).

In research using exome-sequencing technologies, de novo point mutations and small insertions and deletions (indels) have been identified in persons with schizophrenia (Girard et al., 2011; Xu et al., 2011, 2012). Affected individuals harbor more damaging de novo mutations than their healthy siblings (Gulsuner et al., 2013). The genes altered by these events are highly coexpressed in fetal prefrontal cortex, and operate in pathways critical to brain development, including neuronal migration and synaptic integrity. These findings implicate disruptions in fetal prefrontal cortical neurodevelopment as critical to the illness (Gulsuner et al., 2013).

The importance of rare deleterious mutations for human disease reflects evolutionary forces that shape the human genome (McClellan & King, 2010a). All humans carry dozens of de novo point mutations, small insertions and deletions, and larger CNVs. The rate of de novo mutations increases with paternal age (Stefansson et al., 2008), which helps explain the increased risk of schizophrenia and autism with advancing age of fathers. The steady influx of new mutations can account for the persistence of complex neuropsychiatric disorders, despite their significant impact on reproductive fitness.

Collectively, these findings suggest that schizophrenia is characterized by vast genetic heterogeneity (McClellan & King, 2010a). So far, no single gene or genomic locus explains more than ~1% of schizophrenia. Schizophrenia appears to be caused by multiple different mutations in multiple different genes and genomic loci. At the same time, the same mutation, or different mutations in the same gene, may lead to different neuropsychiatric phenotypes in different individuals, including autism, bipolar disorders, or intellectual disability (McClellan & King, 2010b). Potential contributions from somatic mutations, epigenetic mechanisms, gene–gene and/or gene–environment interactions, and environmental exposures further add to causal complexity. Given the vast number of genes and genomic regulatory mechanisms related to brain development,

and the number of mutational mechanisms that can disrupt these processes, it is possible that most affected people have a unique genetic cause.

Neuroanatomical Abnormalities and Neuroimaging

Individuals with schizophrenia, including those with EOS, have higher rates of minor physical anomalies (Gourion et al., 2004; Hata et al., 2003; Ismail, Cantor-Graae, & McNeil, 2001)), deficits in smooth-pursuit eye movements (Frazier et al., 1996; Jacobsen et al., 1997; Jacobsen & Rapoport, 1998; Karp et al., 2001; Zahn et al., 1997), and structural anomalies on brain imaging (Gogtay, Vyas, Testa, Wood, & Pantelis, 2011). Each of these findings provides evidence of disrupted neurodevelopment.

Multiple regional brain volumetric reductions have been described in schizophrenia at first diagnosis, regardless of age (Gogtay et al., 2011; Gur, 2011; Rapoport, Giedd, & Gogtay, 2012). Enlarged volumes of lateral ventricles and gray matter reductions in hippocampus, thalamus, and frontal lobe volumes have been consistently reported. White matter changes have also been reported, but the affected tracts vary among studies (Fitzsimmons, Kubicki, & Shenton, 2013; Rapoport et al., 2012; Samartzis, Dima, Fusar-Poli, & Kyriakopoulos, in press). The illness appears to be characterized by a loss of brain connectivity (Fitzsimmons et al., 2013; Rapoport et al., 2012).

The National Institute of Mental Health COS study has demonstrated significant gray matter volumetric reductions in its cohort. Longitudinal studies have shown a more rapid progressive loss of gray matter in patients with COS—3–4% per year, as compared to 1–2% in controls. The loss occurs in a parietal-to-frontal pattern during adolescence (Gogtay et al., 2011). Follow-up studies show that cortical thinning in COS may plateau in early adulthood, when it becomes similar to the regional pattern in adults with schizophrenia (Greenstein et al., 2006; Sporn et al., 2003). These changes appear specific to COS, including medication-naïve patients (Narr, Bilder, et al., 2005; Narr, Toga, et al., 2005); they are not found in studies of patients with transient psychosis (Gogtay et al., 2004) or in studies of adults (Greenstein et al., 2006; Sporn et al., 2003). In a 5-year longitudinal study, brain structure abnormalities do not appear to be progressive in the chronic stage of schizophrenia, but progression in subcortical regions may be associated with poor outcome (Nesvag et al., 2012).

Volumetric reductions in gray matter found in COS are theorized to be due to the disruption of specific neurodevelopmental processes that occur during adolescence. One such hypothesized process is the pruning of synaptic projections. Pruning in the developing brain proceeds from subcortical to cortical regions, following a pattern in which more complex processes mature only after less complex maturation has been completed (Gogtay et al., 2004; Toga, Thompson, & Sowell, 2006). Excessive pruning may lead to the disruption of functional connectivity in patients with COS (Alexander-Bloch et al., 2013).

Youth with COS were found to have slower growth rates of white matter, relative to controls, during adolescence (Gogtay et al., 2008). Nonpsychotic siblings of the patients with COS were also found to have early slowing in white matter growth that normalized with age (Gogtay, Hua, et al., 2012). The investigators suggested that white matter growth might be an age-specific endophenotype for schizophrenia, although further study is needed to confirm these findings.

The relationship between cortical volumetric reductions and clinical status is not well established (Kerns & Lauriello, 2012; Rapoport et al., 2012). Gray matter changes have been associated with ratings of psychotic symptoms and global function (Gogtay, Weisinger, et al., 2012). Volumetric reductions have been variably associated with either more (Cannon et al., 2002; Gur et al., 2000) or less severe (Gur et al., 1998; Vidal et al., 2006) symptoms. In COS, impaired cognitive functioning was not associated with increased rates of frontal cortical thinning (Gochman et al., 2004), whereas greater cortical thickness predicted patient remission (Greenstein, Wolfe, Gochman, Rapoport, & Gogtay, 2008).

Neuroimaging techniques can also be used to examine the impact of treatment on brain morphology. Antipsychotic medications appear to improve hippocampal gray matter losses in a longitudinal study of individuals at risk for psychosis (Walter et al., 2012). However, recent evidence also suggests that the use of antipsychotic medications is correlated with gray matter loss (Haijma et al., 2013; Ho, Andreasen, Ziebell, Pierson, & Magnotta, 2011). Cognitive therapy has been correlated with the attenuation of abnormal brain responses (Kumari et al., 2011) and improvement in white matter abnormalities characteristic of schizophrenia (Penades et al., 2013).

Environmental Factors

Genes and the environment interact to influence both the development and progression of schizophrenia (Rapoport et al., 2012). Environmental exposures may

act via direct neurological damage, gene–environment interactions, epigenetic effects, and/or de novo mutations to mediate disease risk. To date, the best-replicated risk factors include advancing paternal age (Malaspina et al., 2002) and *in utero* exposure to maternal famine (St. Clair et al., 2005; Susser et al., 1996), both of which may confer risk by increasing the rate of de novo germline mutations or somatic mutations in developing brain (McClellan, Susser, & King, 2006). Other risk exposures associated with schizophrenia are prenatal risk factors, including maternal infections and obstetrical complications, marijuana use, and migrant status (Messias, Chen, & Eaton, 2007).

Psychosocial Factors

Expressed Emotion in Families

Psychological or social factors, by themselves, do not appear to cause schizophrenia. However, psychosocial factors may interact with biological risk factors to mediate the timing of onset, course, and severity of the disorder. Although interactions with family members influence the disorder, historically many families of youth with schizophrenia were unfairly indicted as causing psychosis. Family support is essential for assistance in managing stressful situations and promoting appropriate social interaction, both of which are important for reducing symptoms.

Since family interactions influence the course and morbidity of illness, shaping family interactions are important treatment strategies. High levels of criticism, emotional overinvolvement, and hostility in families—which have been collectively described as high "expressed emotion" (EE)—have been associated with worse outcomes in adults with schizophrenia (Wearden, Tarrier, Barrowclough, Zastowny, & Rahill, 2000). High EE is a strong predictor of future relapse in hospitalized patients (Butzlaff & Hooley, 1998). Positive remarks from caregivers are associated with decreased negative symptoms and improved social functioning (O'Brien et al., 2006). Higher scores on warmth scales are associated with decreased relapse rate (Breitborde, Lopez, Wickens, Jenkins, & Karno, 2007) and improved social functioning (Bertrando et al., 1992). It is important to recognize that high EE may be a response of caregivers to a family member severely affected with mental illness, rather than a causal factor (Hooley & Campbell, 2002).

A few studies have examined cultural differences on EE in families of adults with schizophrenia. A study of Mexican American families found a curvilinear association between emotional overinvolvement and relapse (Breitborde et al., 2007). In this study, midlevel emotional overinvolvement and high-level warmth were associated with improved outcome— possibly reflecting the importance of family involvement tempered with a sense of independence. Conversely, a study of African American families did not find high EE to be a predictor of relapse. High levels of critical and intrusive behavior were associated with improved outcome over a 2-year follow-up period (Rosenfarb, Bellack, & Aziz, 2006). These findings suggest that cultural context influences how the patient perceives the family's behavior.

Peer Relationships

As part of normal development, children make the transition from family-centered to peer-centered relationships. During adolescence, success in same-age relationships is a core developmental goal. Youth with schizophrenia are especially vulnerable to difficulties in interpersonal relationships. Even before the onset of the illness, most affected youth experience a prodromal period characterized by relationship difficulties and withdrawal (Cannon et al., 2001). Greater deficits in peer relations and social relatedness predict a poorer outcome. Therefore, intervention strategies are needed to address these issues.

Cultural and Diversity Issues

Cultural influences shape views and perspectives, and need to be considered in interpretations of mental health symptoms and diagnosis. Societal beliefs should be considered in the context of interpreting psychotic symptoms or the impact of the diagnosis and treatment on family functioning. Religion often can have a large impact on an individual's belief system. Differentiating a psychotic thought process from culturally and religiously reinforced beliefs can be a challenge. Potential symptoms should be examined in the context of the individual's belief system. For example, a belief in God is often congruent with individual beliefs, but removing one's right hand "because God told me to" violates most societal norms. By definition, delusions and hallucinations should be incongruent with the beliefs and values of the individual's environment and culture.

The prevalence rates of schizophrenia are similar across different cultures (McGrath, 2006). Interestingly, first- and second-generation immigrants have

an increased risk of schizophrenia, with those coming from developing countries being at greater risk (Cantor-Graae & Selten, 2005). Cultural influences may also occur within a region, such as the noted increased risk associated with urban environments (Spauwen, Krabbendam, Lieb, Wittchen, & van Os, 2004). These findings suggest that increased stress—whether arising from illness, from population density, or from family or societal roles—may result in an increased risk of schizophrenia and disease symptoms. It is also possible that diagnostic practices are influenced by differences in the backgrounds of clinicians and patients.

CURRENT ISSUES AND FUTURE DIRECTIONS

Current research into schizophrenia focuses on increasing our understanding of the etiology and disease process. Recent research suggests vast genetic heterogeneity, which has enormous implications for biological and treatment research. Psychiatric and developmental disorders are perhaps best conceptualized as final common pathways stemming from disruptions in critical neurobiological pathways. Key pathways important to any disorder are likely to involve many genes and multiple processes. Any disruption along these paths may lead to illness. Although most affected individuals appear to have different genetic causes, a substantial number may still exhibit disruptions in the same or related neurobiological processes.

As investigations into genetic and environmental factors continue, elucidation of neurobiological pathways and mechanisms underlying the disorder will evolve. This will eventually allow the classification of syndromes based on underlying etiologies, rather than solely on clinical symptom criteria (Insel et al., 2010). Characterizing critical pathways will contribute enormously to our understanding of disease factors that influence functionality and disability. This knowledge will ultimately enhance the development of improved treatment strategies, both psychopharmacological and psychosocial.

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CHAPTER 13

Intellectual Disability

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Throughout history, intellectual disabilities have existed. However, the conceptualizations of what is now called intellectual disability (ID) and what it should be called have evolved considerably—most notably since the 1970s. In order to understand the current phenomenon of ID, it is important to discuss briefly its historical evolution.

BRIEF HISTORICAL OVERVIEW

The study, treatment, and education of those with ID largely originated in the 1800s, when Samuel Gridley Howe and his colleagues believed that it was in the best interest to replace individuals' family homes with training schools or institutions (Richards, 2004). The establishment of training schools led the way to a number of advances in the field, such as standardized testing and multidisciplinary service delivery. Indeed, in 1876, the training directors of such schools met to form a group that is now called the American Association on Intellectual and Developmental Disabilities (AAIDD) (Richards, 2004). AAIDD not only advocates for people with ID, but also publishes three journals devoted to research on intellectual and developmental disabilities, and has been at the forefront of assessment of adaptive behavior.

The history of ID has been plagued by a number of injustices. Most notable was the eugenics movement in the early 1900s. Reports of the purported benefits of sterilization appeared within psychological journals in the 1920s and 1930s, and sterilization laws were passed in states such as Indiana, California, and Virginia (Hothersall, 2003). Additionally, by the mid-1900s, many training schools were viewed more as large-scale, inhumane institutions that significantly isolated those with ID, rather than as centers where optimal care was provided.

However, with significant shifts in policy, research, and advocacy, the field of ID has made important social advances. In addition to refinement of classification and definitions of ID, opportunities for individuals with ID in education, employment, and society have increased considerably since 1970. These improvements have led to significant changes in how ID is conceptualized by researchers, service providers, policymakers, and the public in general. Great gains have been made in identifying the etiology of a number of genetic disorders causing ID, and advances in interventions and education have had a significant impact on the outcome of many individuals with ID. The 21st century has seen growing movements in the United States toward fuller inclusion of those with ID, ranging from education to employment (Fesko, Hall, Quinlan, & Jockell, 2012).

We have also seen increased quality of life (Schalock & Verdugo Alonso, 2002) and well-being. As our understanding of ID deepens, so does the appreciation for the wide variation in presentation in regard to etiology, supports needed, and life outcomes.

This chapter covers a range of issues related to the definition of ID, its presentation, etiology, and other issues of unique significance to the field of ID, including obstacles in assessment and dual diagnosis. Throughout the chapter we emphasize common factors associated with ID, while recognizing the enormous diversity among individuals with ID.

WHAT IS INTELLECTUAL DISABILITY?

Core Features

Often when people think of ID, genetic syndromes such as Down syndrome come to mind. In their coverage of people with disabilities, the mass media and others tend to use images of individuals with distinctive, observable features. However, the phenomenon of ID is much more complex and heterogeneous than this. Individuals with ID present with a wide range of abilities, behaviors, and roles within communities and society. Children with ID are often integrated into general education classrooms. Many adolescents and young adults with ID are actively participating in events on college campuses and in their communities (Izzo & Shuman, 2013). This can include participation in athletics within Special Olympics, community-based book clubs (Fish, Rabidoux, Ober, & Graff, 2006), and other special-interest clubs and activities. Adults with ID are often a part of the work force, and some (a small minority) are raising families of their own. Others have complex medical, emotional, and/or physical conditions, which may lessen their ability to be more fully included in activities in schools, employment, or the community.

Contributing to further heterogeneity within ID are the multiple factors attributed to the etiology of ID, which are discussed in more detail later in this chapter. Whereas some cases of ID are due to genetic disorders, such as Down syndrome, many others can be attributed to a multitude of pre-, peri-, and postnatal factors. During the past decade, advances in genetic research have enabled a number of genome-wide discoveries, such that recommended genetic tests (e.g., microarray) are able to identify a cause for ID in 15–20% of cases (Mefford, Batshaw, & Hoffman, 2012); nevertheless, a definitive etiological explanation remains elusive for most.

Despite this high level of heterogeneity, there are three core features that indicate the presence of ID. The first is a deficit in intellectual functioning. Within current practice, an intelligence test is administered to an individual in order to obtain an intelligence quotient (IQ). Deficits are then defined by IQ scores below specified cutoffs. However, deficits in intellectual functioning alone are not sufficient to diagnose ID. Equally important is how the individual is able to *function* within the world in which he or she lives. This second core feature is commonly referred to as "adaptive behavior." There are varying options and different standardized instruments used to assess adaptive behavior. These include the Adaptive Behavior Assessment System—Second Edition (ABAS-II; Harrison & Oakland, 2003); the Scales of Independent Behavior—Revised (SIB-R; Bruininks, Woodcock, Weatherman, & Hill, 1996); the Vineland Adaptive Behavior Scales, Second Edition (Vineland-II; Sparrow, Cicchetti, & Balla, 2005) and numerous others.

Broadly defined, adaptive behavior comprises three factors: practical, conceptual, and social skills (Tassé et al., 2012). *Practical skills* include activities of daily living (personal care), occupational skills, use of money, safety, health care, travel/transportation, use of schedules/routines, and use of the telephone. *Conceptual skills* encompass knowledge of language, reading, writing, time, and number concepts. *Social skills* include interpersonal skills, social responsibility, self-esteem, following rules and obeying laws, avoiding gullibility or victimization, and social problem solving (Tassé et al., 2012). Adaptive behavior is usually defined in terms of cultural or societal expectations and is meant to be evaluated in relation to functioning in an environment with one's peers and without supports (Borthwick-Duffy, 2007). The additional requirement of adaptive behavior deficits for a diagnosis of ID is both important and necessary, as it speaks to the impairment aspect of the diagnosis.

The final necessary component of an ID diagnosis is that the cognitive and adaptive behavior deficits must have originated during the developmental period (American Psychiatric Association [APA], 2013). Although the exact age at which the developmental period ends has varied according to different definitions and time, it is generally thought to be somewhere between 18 and 22. Therefore, an adult (operationally defined as an individual older than 18–22 years) who experiences

an initial onset of significant cognitive and adaptive behavior deficits due to significant brain injury, debilitating mental illness, or infection will *not* qualify for a diagnosis of ID, even though his or her deficits may be similar to those of people with ID.

Presentation

Thus deficits in cognitive and adaptive functioning, together with an onset during the developmental period, are essential features of ID. However, the associated strengths and weaknesses of individuals with ID, and therefore the supports they need, vary widely. Historically, factors such as IQ, level of adaptive behavior, or supports needed have been used to distinguish among individuals with varying degrees of ID. The exact definition and criteria are discussed in more detail in "Definitional and Diagnostic Issues," below. Regardless, general behavioral and cognitive features are associated with the different levels of ID, which are generally referred to as "mild," "moderate," "severe," and "profound." Individuals with mild ID have the highest IQs (e.g., approximately 70 ± 5 to 55) and mildest adaptive behavior deficits; they constitute the largest group, accounting for about 80–90% of those with ID (Schalock et. al., 2010). Often members of this group have no clear identifiable cause for their disability, are not physically distinguishable from the general public, and have a wide range of behavioral presentations and outcomes (Schalock et al., 2010). Frequently, children with mild ID are not identified as having a disability until the school years. Children with mild ID require some level of support in the school setting, as they can have difficulty retaining information and may require direct instruction techniques in order to learn to read or to command other subjects. However, with appropriate support, such children can often participate within the general education classroom in some capacity and take part in extracurricular activities. As adults, individuals with mild ID may be able to live independently with appropriate support, hold jobs, marry, and even raise families (Brown, Renwick, & Raphael, 1999).

Moderate ID is the second most common level of ID. Individuals with moderate ID have more significant deficits in adaptive behavior and intellectual ability. Due to the impact of their disability, these individuals are more likely to be identified during the preschool years. Individuals with moderate levels of deficit are more likely to have an identifiable biological cause (e.g., genetic disorder, cerebral palsy, premature birth) of their disability. Children with moderate ID require more significant modifications to their curriculum, and often present with more significant language and communication deficits than those with mild ID. Many individuals with moderate ID will require continued supports into adulthood.

Those with severe to profound ID are most likely to have an organic cause for their disability. One study of those with severe ID found that 50% of the individuals had a genetic or congenital disorder to which the severe ID was attributed (Arvio & Sillanpää, 2003). The researchers found that another 19% of these cases could be attributed to some sort of encephalopathy, asphyxia, physical trauma, or infection perinatally or early in development. Due to these factors, individuals with severe and profound ID tend to be identified either prior to or shortly after birth. Individuals with severe to profound ID are also more likely to have physical disabilities, as well as significant health care needs. As such, they typically require a high level of support, which must be sustained throughout adulthood. Individuals with severe ID usually have some basic speech and/or communication ability, whereas those with profound ID are usually unable to speak. Seizure disorders become more common with severity of ID, and up to 40% of individuals with profound ID also have seizure disorders (Bowley & Kerr, 2000).

DEFINITIONAL AND DIAGNOSTIC ISSUES

The terminology used to describe ID has changed considerably over the past 50 years, evolving from "mental deficiency" in the first edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-I; APA, 1952), to "mental retardation" in DSM-II through DSM-IV-TR, and finally to "intellectual disability" most recently in DSM-5 (APA, 2013). Historically, other terms were used (Noll & Trent, 2004), such as "idiot" (for a person with severe ID), "imbecile" (for a person with moderate ID), and "moron" (for a person with mild ID). Whereas these terms had technical meanings initially, they illustrate how terminology drifts with time to assume extremely derogatory connotations. More recently, the term "retardate" has taken on extreme pejorative connotations. Despite these changes in terminology, the essential elements of ID—namely, deficits in intellectual functioning, limitations in adapting to environmental demands, and onset during the developmental period—have

not changed substantially with time (Schalock et al., 2010). However, the devil is in the details. How these essential elements are defined, named, and measured have significant impacts on public policy and social services, and in some cases (i.e., capital court cases), they can be matters of life or death.

The potential of older terms to have negative consequences has been recognized by both the federal government and the DSM-5 (APA, 2013) Work Group. One recent example is President Barack Obama's signing of Rosa's Law in 2010 (Public Law No. 111-256; Congressional Research Service, 2010), which amended all federal acts, enactments, and regulations to change prior references to "mental retardation" to references to ID. It further declared "that the changes by this Act are made without any intent to: (1) change the coverage, eligibility, rights, responsibilities, or definitions referred to in the amended provisions; or (2) compel states to change terminology in state laws for individuals covered by a provision amended by this Act" (Congressional Research Service, 2010).

Careful consideration and discussion surrounded the terms finally adopted in DSM-5, "intellectual disability (intellectual developmental disorder)." The word *disorder* has been the source of some concern because it is typically paired with psychiatric conditions. The APA (2013) has been careful to note in its opening description of ID: "The term *intellectual disability* is the equivalent term for the ICD-11 diagnosis of *intellectual developmental disorders.* Although the term *intellectual disability* is used throughout this manual, both terms are used in the title [of this section of the manual] to clarify relationships with other classification systems" (p. 33). DSM-5 goes on to clarify that ID is the common term used in research journals, as well as by medical and educational personnel, other professionals, and the lay public. Indeed, two representatives of AAIDD stated their concerns about the proposed use of "intellectual developmental *disorder*" in a letter to APA's president (Gomez & Nygren, 2012):

> The use of the term "intellectual developmental disorder" is not consistent with the AAIDD position, contemporary practice, and will most foreseeably lead to direct harm to individuals in educational, service, and judicial settings. The term intellectual disability (ID) is the most commonly used term—nationally and internationally—to refer to the condition previously named mental retardation. The term intellectual disability is preferred because it: (a) is consistent with national and international moves to adopt this terminology as a replacement for "mental retardation," (b) better reflects the changed construct of disability promoted by both the World Health Organization's International Classification of Functioning and AAIDD; (c) better aligns with current professional practices that focus on functional behaviors and contextual factors; (d) provides a logical basis for understanding supports provision due to its basis in a social-ecological framework; and (e) is less offensive to people with disabilities (i.e., "disability" is preferred to "disorder"). (p. 2)

The DSM-5 Work Group heeded this correspondence, while still being mindful of worldwide practices, by using the name "intellectual disability (intellectual developmental disorder)." Clearly, decisions regarding terminology are more than mere matters of aesthetics; they have important implications for government entities, researchers, and insurance companies.

Definition

As illustrated above, the precise definition of ID is complicated. Moreover, the two professional groups that produce manuals on definition and classification—the APA and the AAIDD (formerly the American Association on Mental Retardation)—do not define it in quite the same ways.

The definition put forth in the most recent edition of the AAIDD's manual (Schalock et al., 2010) states that "intellectual disability is characterized by significant limitations in both intellectual functioning and in adaptive behavior as expressed in conceptual, social, and practical adaptive skills. This disability originates before age 18" (p. 6). The AAIDD defines "significant limitation in cognitive functioning" as "an IQ score that is approximately two standard deviations below the mean, considering the standard error of measurement for the specific instruments used and the instrument's strengths and limitations" (p. 31). AAIDD guidelines state that when clinicians are establishing significant limitations in adaptive behavior for diagnosing ID, standard measures normed on the general population should be used. (Examples of such measures, as noted above, include the ABAS-II, the SIB-R, and the Vineland-II.) The guidelines define "significant limitations" on standardized measures as performance that is "approximately two standard deviations below the mean on either (a) one of the following three types of adaptive behavior: conceptual, social, or practical or (b) an overall score on a standardized measure of concep-

tual, social, and practical skills" (p. 43). Furthermore, the AAIDD manual puts forth assumptions that it states "are essential to the application of this definition" (p 11). The assumptions emphasize that limitations in an individual's functioning should be measured against *what would be expected* in typical inclusive community environments. They also stress that any assessment should take into account cultural diversity and the individual's communication ability, as well as any complicating sensory, motor, or behavioral factors. One key tenet of the AAIDD definition is that describing an individual's limitations should lead to the development of a profile of supports needed by the individual. This insistence on acknowledging supports is intended to emphasize the need for society to recognize that it has obligations to all of its citizens.

The core of the DSM-5 definition is largely consistent with that of AAIDD: It emphasizes deficits in cognitive and adaptive functioning with onset during the developmental period. It defines ID as a disorder "with onset during the developmental period that includes both intellectual and adaptive functioning deficits in conceptual, social, and practical domains" (APA, 2013, p. 33). Deficits in intellectual functioning are described as those that affect "reasoning, problem solving, planning, abstract thinking, judgment, academic learning, and learning from experience"; these deficits are to be "confirmed by both clinical assessment and individualized, standardized intelligence testing" (p. 33). In contrast to previous versions, the criteria are not as explicit with score cutoffs, stating, "Individuals with ID have scores of approximately two standard deviations or more below the population mean. . . . On tests with a standard deviation of 15 and a mean of 100, this involves a score of 65–75 (70 ± 5)" (p. 37). Deficits in adaptive functioning are those that "result in a failure to meet developmental and sociocultural standards for personal independence and social responsibility" (p. 33). In terms of societal supports, the definition states, "Without ongoing support, the adaptive deficits limit functioning in one or more activities of daily life" (p. 33). Of note in this version is the emphasis placed on clinical judgment. Throughout the DSM-5 definition, significant weight is placed on clinical judgment in the interpretation of score results, and balancing conclusions of standardized assessments with observed and reported functioning and decision making in real-life situations. This version also refers to the "developmental period" as being critical for onset, but does not list an explicit age for this critical window.

Classification Systems

Although deficits in cognitive and adaptive functioning are two core features of ID, the types of impairments and associated strengths and weakness of individuals with ID vary widely. It is for this reason that researchers and clinicians have tended to rely on classification systems to group individuals further for such purposes as conducting research, providing services/reimbursement, developing services and supports, and communicating among professionals. The approach to classification has varied over time and among the various organizations involved.

AAIDD's Conceptual Framework

In its 2010 manual (Schalock et al., 2010), the AAIDD proposes a multidimensional classification system based on a "Conceptual Framework of Human Functioning." This conceptualization takes into account multiple dimensions and emphasizes individualized supports. This model highlights that the presentation in ID involves a complex interaction among the dimensions of intellectual functioning, adaptive behavior, health, participation, context, and individualized supports. Other current and previous approaches to classification have relied on the single dimension of intellectual functioning, or the two-dimensional view (i.e., adaptive functioning and intellectual functioning). AAIDD's framework expands classification beyond just intellectual and adaptive functioning; it also considers physical and mental health, the individual's involvement in his or her environment and the context within which all factors operate. As depicted in the "Conceptual Framework," all of these dimensions interact with individualized supports to result in optimal functioning.

Severity

Historically, DSM has included severity specifiers in its definition of ID. Although the various axes in the overall multiaxial system used from DSM-III to DSM-IV-TR covered associated psychological disorders, medical conditions, psychosocial and environmental problems, and a judgment of overall level of functioning, the severity grid was meant to describe the degree of impairment associated with ID in particular. In DSM-IV-TR (APA, 2000), severity classification was based solely on IQ. Those with IQ scores from 55–55 to

approximately 70 were to be classified as having "mild mental retardation"; those with scores of 35–40 to 50–55, "moderate mental retardation"; those with scores of 20–25 to 35–40, "severe mental retardation"; and those with IQs below 20 or 25, "profound mental retardation" (APA, 2000, p. 42). In DSM-5, by contrast, levels of severity are defined on the basis of adaptive functioning and not IQ scores. The rationale is that "it is adaptive functioning that determines the level of supports required" (p. 33). Rather than providing specific score cutoffs on standardized measures of adaptive behavior, DSM-5 includes a table that delineates the characteristics of those at the various severity levels, broken down according to conceptual, social, and practical domains. Each of these descriptions also includes typical supports that would be needed by individuals at the various levels of functioning. The characteristics are presented in Table 13.1.

Implications

Although to some readers this may seem to be a somewhat esoteric theoretical discussion, the implications of precise definitions and criteria cutoffs have implications with significant consequences. For example, changing the criteria to "approximately 70 or 75" may seem to be squabbling over a few IQ points. However, MacMillan, Gresham, and Siperstein (1993) wrote that "Small shifts in the upper limit have substantial consequences for the percentage of the population eligible to be diagnosed with mental retardation. . . . *Twice as many people are eligible* when the cutoff is 'IQ 75 and below' as when it is 'IQ 70 and below' " (p. 327; original emphasis). This has significant implications for the distribution of financial resources, available interventions, and funds for indicated interventions and supports.

Nowhere are the implications of definitions illustrated more poignantly than in the case of *Atkins v. Virginia*. In 2002, the U.S. Supreme Court concluded that executing death row inmates with "mental retardation" is a violation of the Eighth Amendment, which bans cruel and unusual punishment. This landmark ruling was intended to end the execution of those with ID. However, Greenspan (2009) has noted that a major problem with the ruling is that the group of people to whom it would apply is not well defined. For example, some states set the IQ criterion rigidly at 70, while others are more flexible, and some do not define boundaries at all. It is important to note that most *Atkins* cases are incredibly close calls: There is often evidence for and against the presence of an ID, such that if the individual has ID, it is in the mild range (Olley, 2009). This determination can literally be a matter of life and death.

SITUATIONAL AND CONTEXTUAL FACTORS

There are a number of factors adding to the complexity of ID; these include identification, evaluation, and the assignment of diagnosis. The Individuals with Disabilities Education Improvement Act of 2004 (IDEA; Public Law No. 108-446) requires all states to have a "comprehensive child find system," so that children from birth to 21 years of age who are in need of early intervention or special education services can be located, identified, and referred to early intervention or special education programs. As noted above, children with more significant deficits tend to be identified prior to entering school; nevertheless, a large proportion of individuals (especially those with mild ID) still are not identified until they reach the school system.

Within the schools, students whose teachers are concerned that they may have ID are sent to an assessment team, which is considered a prereferral intervention team. Implementing prereferral intervention teams is an approach to school-based consultation. Such a team may implement interventions that address a child's difficulties within the school system, such as academically, behaviorally, socially, or with activities of daily living (Meyers, Valentino, Meyers, Boretti, & Brent, 1996). If these interventions are not successful and the impairment persists, further assessments are conducted. These evaluations are typically interdisciplinary in nature, and they can often address standardized testing of cognition, adaptive behavior, social-emotional functioning, language, fine and gross motor skills, and general health.

Educational versus Psychological Classifications

One issue for the ID field concerns the inconsistencies in labeling between the educational and psychological systems. Often educational classification and nomenclature do not directly align with the diagnostic definitions proposed by either the APA or the AAIDD. As such, a child may have an IQ in the mildly delayed range and impaired adaptive behavior, but the child may still be educationally classified as having a "learning disability." One study found that of 35 children whose IQs were below 75, only 6 (17%) of these children were classified

educationally as having ID (MacMillan, Gresham, Siperstein, & Bocian, 1996). Recently, Larson and Lakin (2010) found a significant shift in the primary special education diagnostic categories for students ages 6–21. They found that across the United States, the number of students who were classified as having ID decreased by 121,900, whereas the number classified with a "developmental delay" increased by 77,100, and the number classified with autism increased by 227,500. There was no significant change to DSM criteria during this interval, which could otherwise have accounted for this change; yet schools appeared to be using the label "developmental delay" more frequently for children ages 6–9 years. This use of terminology contrasts with standing diagnostic practices and now also with DSM-5 (APA, 2013), which reserves the term "developmental delay" for children below 5 years.

A further issue is the increased use of autism spectrum disorder (ASD) as an educational label, due to changes in state special education criteria for an ASD categorization. Broadly speaking, a diagnosis of ASD requires significant impairment in social communication and the presence of restrictive interests and repetitive behavior. However, when assessing and diagnosing a child as a part of the special education process, school districts are not required to use DSM criteria. A child's educational diagnosis is determined by the educational team, which is made up of parents, teachers, and others (who may include school psychologists or special education teachers), but is not required to have a licensed psychologist.

Adult Diagnosis

The timing of the diagnosis of ID is another important aspect of defining and assessing ID. We have already indicated that the majority of children with ID are identified in the school years, and that diagnostic criteria require the onset of disability to occur during the developmental period. However, as noted above, often children are classified under various academic categorizations (e.g., developmental delay, learning disability, cognitive disability), regardless of IQ and adaptive behavior scores in the range of mild ID. Furthermore, some children may receive school-based services for difficulties associated with ID, but may never receive a formal diagnosis. Formal diagnostic assessment may not have been sought, as school personnel and family members may have felt that these children/adolescents were receiving all necessary services. However, there are implications as these individuals move into adulthood and make transitions into different community and work environments. There are some feasible scenarios in which an adult would seek a first-time diagnosis of ID. This may occur when it is suspected that the adult's functioning is impaired and eligibility for financial assistance is being examined, or when the adult is accused of committing a crime and ID may be a mitigating factor (Reschly, 2009). Keys to resolving this question include a number of diagnostic issues, such as (1) collecting previous records, (2) determining the most appropriate manner to assess current functioning, and (3) establishing how to determine with certainty that onset occurred within the developmental period.

DEVELOPMENTAL COURSE AND PROGNOSIS

As noted earlier, ID begins in childhood and is generally thought to persist into adulthood. However, several important factors should be taken into account when conclusions are being drawn about the developmental course of ID.

Stability of Intelligence Assessments

In examining the diagnosis of ID and its course, it is important to have a clear understanding of the stability of intelligence scores. It is widely accepted that for the majority of the population, the results of tests of infant development do not predict later IQ with any precision (Sattler, 2008). Historically, reports of consistency between infant developmental tests and school-age intelligence test results range from near zero to small positive correlations (Humphreys & Davey, 1988). Young children have a great deal of plasticity, and their development progresses at variable rates. Change in intellectual development is more rapid during the preschool years than during the school years. Humphreys and Davey (1988) hypothesized that this may be due to the rapid increase in preschool children's repertoire of knowledge; new additions to the repertoire may not be correlated with the previous knowledge base. Humphreys and Davey did find that as children enter schools, the relationship strengthens: They found that by the time a child is 4 years old, the correlations with IQ at 15 years is .60, and when the child is tested at age 9, it is .80.

Historically, researchers have found that patterns of stability vary for children at different functioning levels. Bernheimer and Keogh (1988) noted that "predic-

TABLE 13.1. DSM-5 Severity Levels for Intellectual Disability (Intellectual Developmental Disorder)

Severity level	Conceptual domain	Social domain	Practical domain
Mild	For preschool children, there may be no obvious conceptual differences. For school-age children and adults, there are difficulties in learning academic skills involving reading, writing, arithmetic, time, or money, with support needed in one or more areas to meet age-related expectations. In adults, abstract thinking, executive function (i.e., planning, strategizing, priority setting, and cognitive flexibility), and short-term memory, as well as functional use of academic skills (e.g., reading, money management), are impaired. There is a somewhat concrete approach to problems and solutions compared with age-mates.	Compared with typically developing age-mates, the individual is immature in social interactions. For example, there may be difficulty in accurately perceiving peers' social cues. Communication, conversation, and language are more concrete or immature than expected for age. There may be difficulties regulating emotion and behavior in age-appropriate fashion; these difficulties are noticed by peers in social situations. There is limited understanding of risk in social situations; social judgment is immature for age, and the person is at risk of being manipulated by others (gullibility).	The individual may function age-appropriately in personal care. Individuals need some support with complex daily living tasks in comparison to peers. In adulthood, supports typically involve grocery shopping, transportation, home and child-care organizing, nutritious food preparation, and banking and money management. Recreational skills resemble those of age-mates, although judgment related to well-being and organization around recreation requires support. In adulthood, competitive employment is often seen in jobs that do not emphasize conceptual skills. Individuals generally need support to make health care decisions and legal decision, and to learn to perform a skilled vocation competently. Support is typically needed to raise a family.
Moderate	All through development, the individual's conceptual skills lag markedly behind those of peers. For preschoolers, language and pre-academic skills develop slowly. For school-age children, progress in reading, writing, mathematics, and understanding of time and money occurs slowly across the school years and is markedly limited compared with that of peers. For adults, academic skill development is typically at an elementary level, and support is required for all use of academic skills in work and personal life. Ongoing assistance on a daily basis is needed to complete conceptual tasks of day-to-day life, and others may	The individual shows marked differences from peers in social and communicative behavior across development. Spoken language is typically a primary tool for social communication but is much less complex than that of peers. Capacity for relationships is evident in ties to family and friends, and the individual may have successful friendships across life and sometimes romantic relations in adulthood. However, individuals may not perceive or interpret social cues accurately. Social judgment and decision-making abilities are limited, and caretakers must assist the person with life decisions. Friendships with typically developing peers are often affected by	The individual can care for personal needs involving eating, dressing, elimination, and hygiene as an adult, although an extended period of teaching and time is needed for the individual to become independent in these areas, and reminders may be needed. Similarly, participation in all household tasks can be achieved by adulthood, although an extended period of teaching is needed, and ongoing supports will typically occur for adult-level performance. Independent employment in jobs that require limited conceptual and communication skills can be achieved, but considerable support from co-workers, supervisors, and others is needed to manage social expectations, job complexities, and ancillary responsibilities such as scheduling, transportation,

	take over these responsibilities fully for the individual.	communication or social limitations. Significant social and communicative support is needed in work settings for success.	health benefits, and money management. A variety of recreational skills can be developed. These typically require additional supports and learning opportunities over an extended period of time. Maladaptive behavior is present in a significant minority and causes social problems.
Severe	Attainment of conceptual skills is limited. The individual generally has little understanding of written language or of concepts involving numbers, quantity, time, and money. Caretakers provide extensive supports for problem solving throughout life.	Spoken language is quite limited in terms of vocabulary and grammar. Speech may be single words or phrases and may be supplemented through augmentative means. Speech and communication are focused on the here and now within everyday events. Language is used for social communication more than for explication. Individuals understand simple speech and gestural communication. Relationships with family members and familiar others are a source of pleasure and help.	The individual requires support for all activities of daily living, including meals, dressing, bathing, and elimination. The individual requires supervision at all times. The individual cannot make responsible decisions regarding well-being of self or others. In adulthood, participation in tasks at home, recreation, and work requires ongoing support and assistance. Skill acquisition in all domains involves long-term teaching and ongoing support. Maladaptive behavior, including self-injury, is present in a significant minority.
Profound	Conceptual skills generally involve the physical world rather than symbolic processes. The individual may use objects in goal-directed fashion for self-care, work, and recreation. Certain visuospatial skills, such as matching and sorting based on physical characteristics, may be acquired. However, co-occurring motor and sensory impairments may prevent functional use of objects.	The individual has very limited understanding of symbolic communication in speech or gesture. He or she may understand some simple instructions or gestures. The individual expresses his or her own desires and emotions largely through nonverbal, nonsymbolic communication. The individual enjoys relationships with well-known family members, caretakers, and familiar others, and initiates and responds to social interactions through gestural and emotional cues. Co-occurring sensory and physical impairments may prevent many social activities.	The individual is dependent on others for all aspects of daily physical care, health, and safety, although he or she may be able to participate in some of these activities as well. Individuals without severe physical impairments may assist with some daily work tasks at home, like carrying dishes to the table. Simple actions with objects may be the basis of participation in some vocational activities with high levels of ongoing support. Recreational activities may involve, for example, enjoyment in listening to music, watching movies, going out for walks, or participating in water activities, all with the support of others. Co-occurring physical and sensory impairments are frequent barriers to participation (beyond watching) in home, recreational, and vocational activities. Maladaptive behavior is present in a significant minority.

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tive validity of developmental tests is related to level of performance early on, with less reliable prediction for the children within the higher developmental quotient range" (p. 541). Conversely, those with more severe or profound deficits in cognitive functioning tend to have more stable scores. In one study, infants with low composite scores (50 or lower) on developmental tests were likely to have low IQs in childhood and adult years (Maisto & German, 1986).

There are two important considerations for diagnosing ID in the context of IQ stability. First, because some infants will gain skills more rapidly after early testing, it is important not to give a diagnosis of ID based on a single test score in infancy (Sattler, 2008). As noted above, clinicians use the term "developmental delay" to describe young children with delays in cognition and adaptive skills, rather than diagnosing ID. This reflects the understanding that in some children, it is possible that the delay is one that will not persist over time or be a lifelong disability (Brown, 2007). Sattler (2008) has reiterated this, noting that "Generally, IQs obtained *before* 5 years of age have to be interpreted with caution. When a child is 5-years-old or older, however, his or her IQ tends to remain relatively stable" (p. 171). DSM-5 has also addressed this, adding the diagnostic category of "global developmental delay" for children under age 5 "when the clinical severity level cannot be reliably assessed during early childhood" (APA, 2013, p. 41).

Second, it is important to note that most study results demonstrating stability and change in cognitive level are based on aggregated data for groups of children. Examination of patterns of individual children within groups, however, suggests that individual children may show consistent patterns of increases or decreases in cognitive level (Keogh, Bernheimer, & Guthrie, 1997). For example, Stavrou (1990) reported stability coefficients of .77 and .74 for Wechsler Intelligence Scale for Children—Revised (WISC-R) Full Scale IQs over three time points for children identified as having learning disabilities or mild mental retardation. At the same time, he noted that the scores for 37% of the children with learning disabilities and 15% of the children with mild mental retardation changed by at least 9 IQ points from the first to the third test. Truscott, Narrett, and Smith (1994) also found significant stability coefficients for WISC-R IQs in a group of children with learning disabilities over 3- and 6-year test–retest periods (r = .77 and .81, respectively). However, some of the individual children had scores decreasing over 30 IQ points.

There have been a number of longitudinal and follow-up studies of children with ID, exploring a range of outcome variables. A proportion of these projects have focused on specific subgroups with well-defined diagnostic profiles, such as Down syndrome (Carr, 1994, 2000, 2012), Williams syndrome (Einfeld, Tonge, & Rees, 2001), and fragile X syndrome (Mazzocco, 2000). Some studies have focused on cognitive and adaptive skills. For example, Carr (1994, 2012) conducted a longitudinal study of a cohort of individuals with Down syndrome born in 1964. They were followed from approximately 6 weeks of age for intervals up to the age of 45 years. In early childhood, IQs declined from 73 at 6 weeks to 44 at 4 years old and 40 at 11 years on the Merrill–Palmer. This decline from early childhood is consistent with previous studies of Down syndrome (see Dykens, Hodapp, & Finucane, 2000, for a review). However, the pattern changes in adulthood. In Carr's sample, the male sample as a whole with Down syndrome did not have significant decreases in their IQs between the ages of 21 and 45, but the scores in the women's group declined by an average of 10 points. This decline appeared to be largely attributable to two women who were significantly affected by Alzheimer's disease. At the conclusion of the evaluation, eight women were known or strongly suspected of having Alzheimer's disease. Self-help (adaptive skills) for the entire group increased to a peak at 30 years, and declined slightly afterward. Similar declines in cognitive assessments during the school years have been noted in longitudinal studies of fragile X syndrome (see Mazzocco, 2000).

Others have examined the stability of emotional and behavioral problems in specific samples. Einfeld and colleagues (2001) followed individuals with Williams syndrome for 5 years (from ages 9 to 14 years), tracking the course of their emotional and behavioral problems. They found that the emotional and behavior problems of those with Williams syndrome remained relatively stable over the course of the 5 years.

Others have examined mixed groups of individuals with ID. One such project, Project Research on the Early Abilities of Children with Handicaps (REACH), began over 20 years ago (Bernheimer & Keogh, 1988). This longitudinal study followed a sample of 44 children with identified delays at the age of 3 years, assessing them at 6, 9, 12, 18, and 22 years of age (Bernheimer, Keogh, & Guthrie, 2006; Keogh, Bernheimer, & Guthrie, 2004). The Project REACH researchers found that, by and large, those identified as having non-

specific delays had long-term handicaps into childhood and adolescence. In their long-term follow-up, they found that a child's developmental status (IQ, language, adaptive skills) at age 6–7 years was more predictive of developmental status at age 22 (correlation of .76) than was developmental status at age 3 years (correlation of .59), but that both were significantly related to developmental outcome at age 22.

There are strengths and weaknesses to approaching outcomes by looking at specific genetic conditions on the one hand, and by looking at all individuals with ID on the other. As we discuss below, those with specific genetic profiles (e.g., Down syndrome) have specific predispositions and are at risk for a number of conditions that may have adverse impacts on their outcomes (e.g., congenital heart defects, increased risk of Alzheimer's disease); they may have other characteristics that may act as protective factors (e.g., facial characteristics). Conversely, studies that include individuals with all types of ID, regardless of etiology, inherently have a diverse group in which many confounding factors may have effects on outcomes. That being said, if researchers only include individuals with ID of clearly understood etiology in their studies, a large proportion of those with ID will be excluded—and thus the research will only speak to outcomes for a portion of those with ID.

Early Intervention

There is a consensus in the field that the developmental trajectory of those with ID can be altered if intervention occurs within the first 5 years of life (e.g., Bryant & Maxwell, 1997; Guralnick, 1997; Haskins, 1989; Ramey & Ramey, 1998). Children with ID who participate in sustained, high-quality early intervention before the age of 5 seem to have better long-term outcomes than children who do not receive intervention or begin receiving intervention at a later age (e.g., Guralnick, 2005). For example, children who participated in the model early intervention programs of the Abecedarian Project (Ramey, Campbell, & Bryant, 1987), the Milwaukee Project (Garber, 1988), and Project CARE (Wasik, Ramey, Bryant, & Sparling, 1990), which all started before the age of 3, exhibited resoundingly better long-term outcomes than children who did not (Ramey, Ramey, & Lanzi, 2007). In addition, one meta-analysis of 31 studies designed to improve cognitive, social-emotional, or life skills of children less than 66 months of age reported that early intervention produced developmental progress in infants and toddlers with biologically based developmental disabilities (Shonkoff & Hauser-Cram, 1987). Furthermore, there is some work suggesting that children with ID who do *not* participate in early intervention show cognitive declines (e.g., Guralnick, 1998).

Although there are different schools of thought regarding exactly how early intervention should be implemented (e.g., Bruner, 1990; Cooper, Herron, & Heward, 1987), Ramey and colleagues (2007) explain that there does seem to be agreement regarding a few critical features of early intervention: intensity, direct engagement with the child, multiple types of supports and services, and long-term follow-up. With respect to intensity, young children with ID seem to do better over the long term when they participate in interventions that last for more hours per day, more days per week, and more weeks per year. In one demonstration early intervention project, children who were coded as having a "high" rate of participation demonstrated a 9-fold reduction in rates of mental retardation, whereas those coded as having "low" participation showed a 1.3-fold reduction rate. Additionally, interventions that work specifically with the children tend to have better results than those that do not. For example, in the Project CARE study, children who were able to participate in center-based programming as well as home visits had better outcomes than children who were only enrolled in home visits. Early intervention programs that provide multiple types of supports and services, such as parent education, transportation assistance, and social work services, are also hypothesized to have more positive effects on children than those that do not provide such supports. Finally, it appears critical that these interventions and supports do not stop when a particular early intervention program is discontinued. Most model early intervention programs that have conducted long-term follow-up studies and report long-term benefits have some continuing services.

EPIDEMIOLOGY

Prevalence

The prevalence of ID has been the focus of several investigations across many decades. Recent systematic reports and meta-analyses seem to have reached a consensus that ID is present in about 1% of the global population (e.g., Harris, 2006; B. H. King, Toth, Hodapp, & Dykens, 2009; Maulik, Mascarenhas, Mathers, Dua,

& Saxena, 2011). These reports pull together a large body of prevalence studies that define ID according to diagnostic criteria established by the APA, the AAIDD, and the *International Classification of Functioning, Disability and Health* (ICF; World Health Organization, 2013).

Within the broad category of ID, the different severity levels seem to be present at different frequencies. It is generally accepted that "mild" cases occur more frequently than those classified as "moderate" or "severe" (e.g., Chapman, Scott, & Stanton-Chapman, 2008). For example, one investigation reported proportional rates of 85%, 10%, 4%, and 2% in cases identified as mild, moderate, severe, and profound, respectively, among all of those identified with ID (B. H. King et al., 2009). In other words, about 85% of all those with ID have mild disability, whereas about 2% have profound disability.

Interestingly, not all epidemiologists agree with the 1% overall prevalence figure for ID. In fact, this figure is much lower than older prevalence rates and smaller than those suggested by a few current epidemiological ID investigations (e.g., Stromme & Hagberg, 2000). A recent meta-analysis indicated that ID prevalence rates can range anywhere from 1 per 1,000 to 12.6 per 1,000 (Maulik et al., 2011), depending on a range of measurement and sociodemographic issues.

There are a number of potential influences on this fluctuation. Most people hypothesize that prevalence figures change for the following reasons: IQ measurement problems, different ID definitions, varying study designs, and different populations being investigated. Measurement of IQ is argued to be problematic in this population for at least two reasons. First, there is a belief that the IQ of the larger population is increasing (Flynn, 1987), due to the "Flynn effect." The Flynn effect is a documented phenomenon in which mean scores on intelligence tests increase substantially over years. Flynn recommended a contentious idea of lowering test scores to account for this effect (Flynn & Windaman, 2008). More specifically, he advocated administering a reasoning test and adopting the use of a simple formula when using the U.S.-normed WISC, Wechsler Adult Intelligence Scale (WAIS), or Stanford–Binet:

$$\text{Test score} - (\text{Interval between when the test was normed and when the subject was tested} \times 0.3) = \text{IQ}$$

In addition, the study designs themselves vary substantially. Data are gathered in a multitude of ways in these studies. The primary sources of prevalence data are random household surveys, hospital data/administrative registries, schools, and use of key informants. Prevalence rates tend to be highest for household and hospital data/administrative data (Maulik et al., 2011), in which the diagnosis of ID is rarely confirmed with standardized assessments. It will be important for future work to understand better why these differences emerge from varying designs and to reach a consensus regarding the ideal way to sample ID occurrence.

The specific population under investigation is another factor that may influence prevalence of ID. In particular, the age of the target population and the country of investigation seem to make a difference. About two-thirds of all ID prevalence studies utilize data from children and adolescents, and it appears that the prevalence figures are highest in child and adolescent populations (Maulik et al., 2011). The higher prevalence among younger populations is hypothesized to be due to the significant role the educational system plays in case identification (Leonard & Wen, 2002), as well as the higher morbidity rate for populations with ID (i.e., older people with ID die sooner, on average, than those in the general population).

Sociodemographic Factors

There is an increasing belief that variability in ID prevalence and expression *may* be due to sociodemographic factors, such as maternal age, maternal and paternal education, and maternal marital status (Chapman et al., 2008). Some argue that a large percentage of the biomedical causes of ID can be linked to sociodemographic factors (Accardo & Capute, 1998). Additionally, about half of all prevalence studies have reported that the causal factors are unknown, suggesting that antenatal, perinatal, and postnatal causes account for only some of the variance, and that the larger environment (or environmental deficiencies) might explain some of the differences (Maulik et al., 2011). More specifically, sex, socioeconomic status, and culture may account for much of the variability in the number of individuals diagnosed with ID.

Sex

ID tends to occur at higher rates among males than females. For example, one study found that males were 1.6 times more likely to be classified with ID than females (Drews, Yeargin-Allsopp, Decouflé, & Murphy, 1995). The higher prevalence of males with ID remains

constant across all levels of ID impairment (Hodapp & Dykens, 2005).

A few explanations have been proposed for these sex differences. Perhaps most important is that many cases of ID are due to X-linked heritability (Tariverdian & Vogel, 2000). One way to think about the differential impact is to realize that because males only have one X chromosome, they are more susceptible to X-linked traits; conversely, females have two X chromosomes, and therefore must have both chromosomes affected in order to show characteristic impairments. For example, fragile X syndrome is carried on the X chromosome and is believed to occur in 1 of 4,000 males (Turner, Webb, Wake, & Robinson, 1996). Also, it has been hypothesized that the male central nervous system is more vulnerable to trauma than the female nervous system (McLaren & Bryson, 1987). For example, Lary and Paulozzi (2001) reported the overall prevalence of major defects at birth for males to be 3.9% and for females to be 2.8%. Similarly, maternal smoking seems to have a greater impact on male than on female fetal growth (Zaren, Lindmark, & Bakketeig, 2000), and the impact of extreme birth weight on IQ seems stronger in males than in females (Matte, Bresnahan, Begg, & Susser, 2001).

Socioeconomic Status

Communities of low income are usually reported to have a higher prevalence of ID. Some studies have reported that maternal education at delivery is related to ID without the presence of neurological conditions (Chapman, Scott, & Mason, 2002; Chapman et al., 2008), particularly among women who are African American (Decouflé & Boyle, 1995). Additionally, participation in school free-lunch programs increases the likelihood of receiving a label of "mental retardation" (Chapman et al., 2008), as does living in a single-parent home (Fujiura & Yamaki, 2000). This trend of higher ID prevalence for lower socioeconomic status even holds constant when high-income and low-income countries are compared (Maulik et al., 2011).

Systems-related issues are speculated to account for this economic disparity. Individuals living in low-income environments are more likely to be exposed to illness, injury, chronic health conditions, protein energy malnutrition, dietary micronutrient deficiencies, and environmental toxins that could have adverse impacts on intellectual development (Bergen, 2008; Fujiura, Yamaki, & Czechowicz, 1998). Research also suggests that children from homes classified as low-income may be more likely to be immersed in low-stimulation environments or chaotic environments (e.g., Hart & Risley, 1995). These risk factors may contribute to the higher ID prevalence in low-income samples.

Culture

There is an increasing body of literature suggesting that factors more likely to affect particular cultures influence the prevalence of ID in specific ethnic groups. However, this research is wrought with notable methodological limitations, and contradictory studies exist (Emerson, 2012). Recent data suggest that the association between culture and socioeconomic status is strong, and that the increased likelihood that particular cultural groups experience poverty may better account for ID prevalence differences (Emerson, 2007).

Nonetheless, current data do suggest that individuals from nonwhite ethnicities are more likely to receive an ID diagnosis than those who are white. For example, in one study conducted in the United States, individuals who were black were more likely to have a diagnosis of ID than those who were white or Latino (Fujiura & Yamaki, 1997). In this same study, there were almost identical rates of ID among Latinos and white Americans. Another study in Australia found that ID was proportionately higher among Aboriginals than among other population groups (Glasson, Sullivan, Hussain, & Bittles, 2005). A more recent study reported that minority ethnic status of individuals living in English state-funded schools was associated with lower rates of ID identification (Emerson, 2012).

Individuals who are low-income *and* black appear to be at significantly elevated risks for ID (Drews et al., 1995; Fujiura & Yamaki, 1997). Black Americans exhibit a heightened risk for both mild and severe ID (Croen, Grether, & Selvin, 2001). One report documented a 50% increase in ID of unknown etiology in black Americans, compared to other ethnic groups (Croen et al., 2001). Of particular concern is the overrepresentation of black Americans and other minorities served under the ID label in the special education system (e.g., Patton, 1998; Zhang & Katsiyannis, 2002).

Why exactly some cultural groups may have an overrepresentation of those with ID is less clear. Some theorize that behaviors that may increase the risk of developing an ID are shaped and influenced by social and cultural forces. At the most basic level, it seems understandable that a host of maternal conditions dur-

ing pregnancy, such as hypertension, response to inflammation, and the body's response to stress, might increase the prevalence of ID in offspring (Christian, 2012). An emerging body of literature suggests that racial disparities account for the higher rates of preterm infants (Christian, 2012), and that stress-induced inflammatory responses are higher in black than in white women during both pregnancy and nonpregnancy (Christian, Glaser, Porter, & Iams, 2013). Additionally, growing up in a racially segregated and disadvantaged community seems to have a more dramatic impact on IQ than individual and familial factors do (Breslau et al., 2001). Likewise, some argue that individuals from nonwhite backgrounds may not be assessed in culturally sensitive ways (Reschly & Jipson, 1976), and that these assessments may under- or overestimate the true prevalence of ID in various groups (Roeleveld, 1997).

THEORY

Historically, many different theoretical models have been used to explain the development of ID. The most commonly referenced current models include ones that are interactional. Each includes a set of assumptions about how individuals with ID learn. The theories are not necessarily mutually exclusive of one another, and some theories may better explain some presentations of ID than others.

Generally speaking, these theories tend to range along a gene-to-environment continuum. At one end of the continuum are theories maintaining that at least some forms of ID are more biologically based, and that genes themselves play a large role in shaping the outcome of individuals with ID. At the other end of the continuum are theories contending that the environment plays a larger role in shaping development.

Among theories that genes play a more central developmental role is the idea that "general genetic factors" may predispose an individual to develop ID (Percy, 2007). In fact, there are cases of ID that arise from single-gene conditions, and chromosomal aberrations find common variants of one or more genes that affect the clinical expression of a disability (Percy, 2007). As noted earlier, for example, a sizable percentage of ID cases are X-linked, meaning that the condition is carried on the X chromosome. Those who emphasize the biological model contend that the genes children are born with predispose them not only to particular biological and cognitive conditions, but also to particular temperaments that ultimately shape the types of activities and behaviors they engage in with social partners. Treatments in this biological orientation tend to focus on drugs, biofeedback, dietary control, exercise, and/or mitigating environmental factors that can worsen the physiological impact of the disorder (Kauffman, 2005).

In contrast to the strong role that some believe genes play, other theories posit that the interface of the individual with the world plays a more central role, including the prenatal environment, toxins, germs, and trauma. Some of these determinants include prenatal factors such as protein calorie malnutrition, folic acid deficiency, vitamin A deficiency and excess, iodine deficiency, iron deficiency, lead, mercury, alcohol, prenatal maternal smoking, maternal obesity, maternal diabetes, abnormal thyroid function, and maternal phenylketonuria (PKU) (Percy, 2007). Others emphasize the impact of the postnatal environment, including trauma and parenting practices. Individuals who subscribe to this view also believe that environmental factors influence the ways in which a clearly identifiable cause of ID is expressed (Horowitz & Haritos, 1998).

There are significant differences in views of just how the environment ultimately influences development. These theories tend to place different emphases on cognition, culture, and social factors. The most influential theories are described below.

Piaget's Theory

One influential learning theory is Jean Piaget's theory of intellectual development. According to Piaget, individuals progress through a series of fixed "stages" that build upon one another and are based on an individual's cognitive ability to respond and modify existing schemes or thoughts. Several researchers contend that individuals with ID proceed through Piagetian stages just as individuals who are typically developing, though they do this at later chronological ages or at a different pace (e.g., Zigler, 1969). According to this theory, to successful treatment of an individual with ID would involve working to help the individual advance to the next Piagetian stage. Several interventions have attempted to do this and have reported favorable outcomes (e.g., Williams, 2007).

Vygotsky's Theory

Another influential theory is that of Lev Vygotsky (see Rodina, 2006). Vygotsky's social constructionist the-

ory proposes that increasingly sophisticated cognition emerges as the result of the way an adult—or a more skilled "instructor"—mediates learning through social interactions. The instructor sets up problem-solving opportunities that are within an individual's "zone of proximal development," or reach of understanding. Vygotsky made specific statements regarding how this overarching developmental theory applies to those with ID in his theory of *dysontogenesis*—that is, theory of "deficient development compared to normal individual development" (Rodina, 2006). Vygotsky believed that as a result of a "primary disorder," a child is often excluded from the sociocultural environment, causing "secondary disability" (Rodina, 2006). Vygotsky believed that secondary disability can be prevented and even eliminated by teaching the child through his or her zone of proximal development. This theory acknowledges the profound role that the environment and culture can play in shaping development (Rodina, 2006) and encourages a strengths-based approach to intervention. Current work does suggest that there can be value in systematically measuring the zone of proximal development in individuals with ID (e.g. Rutland & Campbell, 2007) and then targeting intervention around this.

Ecological Systems Theory

Ecological systems theory, first proposed by Urie Bronfenbrenner, contends that an individual's development is shaped by a complex interaction of processes in five different environmental systems: the microsystem, the mesosystem, the exosystem, the macrosystem, and the chronosystem. This theory asserts that there is a bidirectional impact of the factors in each system. The theory acknowledges that the biological characteristics of an individual with a disability influence all these "spheres," and that they ultimately influence outside factors and determine how the outside factors influence the individual (Bronfenbrenner & Ceci, 1994). Thus, in this theory, just because an individual has a particular general genetic factor that predisposes him or her to ID, this does not mean that the individual will think, behave, and develop in a manner dictated by these genes. Because each environmental system is believed ultimately to have an impact on development, effective intervention must be comprehensively applied to each system. Though it is certainly beneficial to intervene in a particular system, true lasting success, according to this theory, will mean tapping into each dynamic system as an individual ages.

Applied Behavior Analysis

Another commonly referenced theory for those with ID is applied behavior analysis (ABA). ABA is a "process of systematically applying interventions based upon the principles of learning theory to improve socially significant behaviors to a meaningful degree" (Baer, Wolf, & Risley, 1968). Unlike those endorsing the previously mentioned theories, proponents of ABA believe that learning is explained almost exclusively by observable, external environmental events. There are not specific stages through which individuals progress, but rather specific ways that individuals are believed to learn in their environment. ABA has been widely adopted in the field of ID and has been used to teach a range of adaptive, academic, social, and language skills. Of the environmental theories discussed here, ABA has had by far the most practitioners and likewise the most profound impact on the field.

Family Systems Theory

Family systems theory is yet another commonly referenced theory in the field of ID. The theory was first proposed by Murray Bowen and, as the name indicates, asserts that the family system plays a profound role in shaping an individual's development. More specifically, the theory asserts that an individual's family is composed of interrelated elements (family members) and structures (interrelationships among family members) (Morgaine, 2001). An individual's development is influenced by the manner with which these elements and structures predictably interact and are influenced by external events. A family member's ID affects the structures within the family system in particular ways, and this ultimately shapes an individual's development. For example, research suggests that families of those with ID and developmental disabilities experience a higher rate of divorce than those without disabilities (Hodapp & Krasner, 1995). Thus the presentation of ID and treatment of ID will necessitate involvement of the whole family.

The referenced biological and environmental theories provide a unique and valuable contribution when it comes to understanding the presentation and course of ID. It is important to recognize that no *one* theory explains how all individuals with ID learn. As others have advocated, it is most likely necessary to adopt an integrated model of IDs (Kauffman, 2005). In such a

model, one recognizes that multiple theories can be used to hypothesize how an individual with ID will learn. This model also acknowledges that the theories are complementary; aspects of these theories that seem to be in direct contrast to one another are in fact valid in different presentations and cases of ID. When one is adopting such a model, it is important not to be too eclectic or too contradictory, and to allow empirical data ultimately to guide one's decision regarding which theoretical aspects to adopt (Kauffman, 2005).

Family Stress

Although many families of children with ID adapt positively to their children's disability (e.g., Hodapp & Dykens, 2012), the literature suggests that families of children with ID tend to experience more stress on average than families of children who are typically developing (Hanson & Hanline, 1990). In one such investigation, mothers of children with Down syndrome, hearing impairment, and neurological impairment completed parental stress measures at various stages of the children's development (Hanson & Hanline, 1990). The study ascertained that mothers of children with intellectual and developmental disabilities reported higher stress than parents of children who were typically developing.

Parental stress seems to be higher in families of children with ID because of the unique stressors associated with ID. Guralnick (2000) reported three unique stressors. First, the family system seems to be taxed by the need for caregivers to seek out information regarding the child with the disability. Additionally, there appears to be an increased risk of interpersonal and family distress arising from situations directly linked to having a child with a disability, such as disagreement regarding the diagnostic process (e.g., the decision to seek the evaluation, what is shared during the process, or how to respond to evaluation recommendations). Finally, there is also often stress on family resources, such as money needed to pay for the child's therapy. These three stressors are believed to undermine feelings of parental confidence and control. It is also important to recognize that individual characteristics of the child (existence of maladaptive behaviors, child's health status, child's personality, child's facial characteristics, timing of problems, and even the predictability of expectedness) seem to directly affect the functioning of the parents and family system (Hodapp & Dykens, 2009).

It is critical to appreciate the role of these stressors because they seem to have a major impact on the child's overall development and the health of the family system. In particular, the quality of parent–child transactions, family-orchestrated child experiences, and the very health and safety provided by the family are hypothesized to be influenced by these stressors (Guralnick, 2000). If these family patterns of interaction are hindered, the child's overall development and the proper functioning of the family will likewise be hindered (Guralnick, 2000).

Though there certainly are unique challenges in rearing a child with ID, there has recently been increasing recognition that individuals with ID can uniquely benefit the family system (Hodapp & Dykens, 2012). According to Hodapp and Dykens (2012), some families report that having a child with an ID can lead to a fuller or richer life, and that they take fewer things for granted. Likewise, a growing body of research regarding siblings of individuals with ID suggests that there are many positive advantages for the family system (Hodapp & Dykens, 2012).

There is increasing recognition that well-being of families must be a treatment consideration for children. Family preferences for a child's treatments, as well as the way that a particular intervention fits within the existing family milieu, must be taken into consideration. Research suggests that family members who engage in active problem solving and open communication regarding their child with ID tend to have better family outcomes (Hodapp & Dykens, 2012). Additionally, there is a widespread belief that families themselves will benefit from direct intervention. The way in which family members are supported, educated, and empowered will need to be adjusted as a child ages. A growing body of literature indicates that parents of young children receive maximal benefit from home visits or interventions that are situated in the home context. As children age, support for parents may migrate to group formats, most often through the school. Finally, it will be critical for researchers to ascertain how child, parent, and family characteristics influence child, parent, and family outcomes (Hodapp & Dykens, 2012).

ETIOLOGY

Although theories differ on the exact role of genes and environment in the etiology of ID, we do know that ID can result from a number of risk factors, including

genetics, environmental variables, and combinations of the two. Historically, a demarcation was drawn between mild ID and more severe and profound levels of impairment: Mild ID was thought to be due to more familial or cultural causes and risk factors, while severe to profound ID was thought to be due to some type of genetic or other organic insult (see Simonoff, Bolton, & Rutter, 1996, for a discussion of this historical conceptualization). As our understanding of the interactions between genes and the environment evolves, a more commonly held assumption is that mild forms of ID represent the lower end of the normal IQ distribution. This distribution results from the interaction of many genetic and nongenetic factors. Conversely, more severe forms of ID are thought to be due to "catastrophic events, such as perinatal asphyxia and prenatal infections, or more often, specific genetic causes including chromosomal abnormalities or defects of single genes" (Ropers, 2008, p. 241). Indeed, this view is well represented and supported in studies examining genetic etiology in samples with ID. It has been estimated that currently a conclusive genetic or metabolic diagnosis can be made in approximately 50–65% of patients with moderate to severe ID, but only 20% of those with mild ID (van Bokhoven, 2011).

Some forms of ID have clear genetic links (e.g., Down syndrome); however, the cause is not as clear for the majority of ID cases. Indeed, for a large number, the etiology is likely to remain a mystery. Nevertheless, several identified organic causes and risk factors related to the periconceptual, prenatal, perinatal, and childhood periods have been linked to an increased risk of ID (see Table 13.2). Studies have also identified a number of environmental factors as contributory (Murphy, Boyle, Schendel, Decouflé, & Yeargin-Allsopp, 1998). In this section, we review each of these various factors and their implications for assessment and treatment.

TABLE 13.2. Etiology of Intellectual Disability by Time of Onset

Category	Examples
	Periconceptual onset
Genetic/chromosomal	Down syndrome, Williams syndrome
Sex-linked single-gene	Fragile X syndrome, Lesch–Nyhan syndrome
Metabolic	Hypothyroidism
Segmental autosomal	Prader–Willi syndrome, Angelman syndrome
	Prenatal onset
Nutritional deficiency (e.g., folic acid)	Neural tube deficits (e.g., spina bifida, meningomyelocele)
Infection	Toxoplasmosis, cytomegalovirus, rubella, herpes, group B streptococcus
Maternal metabolic problem	Hypothyroidism
Substance exposure	Alcohol, anticonvulsants, lead
	Perinatal onset
Premature birth	Gestational age <37 weeks
Asphyxia	
Low birth weight	Greatest risk <3 pounds
	Postnatal/childhood onset
Infections	Meningitis, encephalitis
Environmental exposure	Lead
Injuries	Severe traumatic brain injury (falls, vehicle accidents, sports injuries, assaults)
Deprivation	Extreme poverty, disordered parenting

Note. Based on McDermott, Durkin, Schupf, and Stein (2007) and Percy (2007).

Genetic Factors

To date, over 1,000 genetic conditions have been associated with ID (Abbeduto & McDuffie, 2010). Although (as noted above) it was once thought that organic causes were mostly associated with more severe disabilities, we now recognize that individuals with these genetic conditions present with a wide range of intellectual and adaptive functioning and behavioral characteristics. Indeed, those with Down syndrome, fragile X syndrome, Williams syndrome, and other genetic etiologies account for as many as 30–50% of those with mild ID (Simonoff et al., 1996). Genetic factors include causes that affect the usual number of chromosomes; these can involve either an extra chromosome (as in most cases of Down syndrome) or deletions on part of a chromosome. A number of common genetic disorders are also X-linked, meaning that there are mutations on the X chromosome. Mutations in more than 90 X-linked genes are currently known to cause ID and account for about 10% of cases (Mefford, Batshaw, & Hoffman, 2012). One such example is fragile X syndrome.

These genetic disorders have some common characteristics associated with them, which include not only genetic and physical features, but also behavioral characteristics. Table 13.3 specifies the relative prevalence of some of the more common genetic syndromes, as well as some of the associated characteristics. While it is important to recognize that there will be many individual differences among those with a particular genetic syndrome, especially in reference to behavioral characteristics, it is often helpful for clinicians and researchers working with this population to be aware of the increased likelihood of particular characteristics. We discuss two of the more common syndromes below: Down syndrome and fragile X syndrome.

Down Syndrome

Down syndrome is the most common genetic cause of ID (Lovering & Percy, 2007). Approximately 95% of those with Down syndrome have an extra chromosome 21 (i.e., trisomy 21—a total of three rather than the normal two chromosomes 21). The risk of having trisomy 21 increases with maternal age (Wu & Morris, 2013; see Table 13.4). In a smaller group, a portion of the extra chromosome 21 is attached to another chromosome (i.e., translocation chromosome). Most cases are not inherited and occur spontaneously; these errors typically occur during cell division in the ovary or testicles (Lovering & Percy, 2007). Down syndrome is often diagnosed during pregnancy on the basis of fetal ultrasound and/or additional maternal triple/quad screening (DeVore & Romero, 2003).

In addition to their genetic profile, those with Down syndrome have a unique developmental profile and trajectory. They are at higher than normal risk for a

TABLE 13.3. Common Genetic Syndromes and Characteristics

Syndrome	Prevalence (per 1,000)	Common characteristics
Down syndrome	1.7	Difficulty with language production; slowed rate of development; social strengths
Fragile X syndrome	0.5 (males) 0.2 (females)	Social anxiety; hyperactivity; strength in simultaneous processing
Williams syndrome	0.13	Relative strength in language; deficits in visual–spatial processing; hypersociability
Prader–Willi syndrome	0.04–0.13	Early failure to thrive; proneness to obesity; food preoccupation; obsessive–compulsive behaviors
Angelman syndrome	0.5–.10	Ataxic gait; severe developmental delay; seizure disorders; happy demeanor
Lesch–Nyhan syndrome	0.0026	Severe self-injury; severe intellectual disability

Note. Based on Abbeduto and McDuffie (2010); Dykens, Hodapp, and Finucane (2000); and Percy (2007).

TABLE 13.4. Risk of Down Syndrome by Mother's Age

Age (years)	Average specific risk per 1,000
Under 20	0.67
20–24	0.70
25–29	0.83
30–34	1.53
35–39	5.44
40–44	18.31
45 and older	28.12

Note. From Wu and Morris (2013). Copyright 2013 by the Nature Publishing Group. Adapted by permission.

number of associated medical conditions; these include congenital heart defects, hearing loss, ophthalmic conditions, hypothyroidism, dental conditions, and obesity. Several distinctive physical features are also associated with Down syndrome, such as a flat-looking face, small ears and mouth, a protruding tongue, and an upward slant to the eyes (Dykens et al., 2000). The trajectory of Down syndrome is marked by a decline in IQ over childhood (Dykens et al., 2000). Those afflicted also struggle with language development. Conversely, research has supported the common observation that those with Down syndrome tend to have relatively good social skills and tend to have less disruptive behavior than many other forms of ID. Research on the families of those with Down syndrome find that they tend to cope better than those with children with other types of ID; some use the term "Down syndrome advantage" to illustrate this difference between those with Down syndrome and others forms of ID (Dykens et al., 2000).

Investigators are currently attempting to extend the research on the various health and associated risks linked to Down syndrome by identifying biomarkers (e.g., genetic, epigenetic, metabolic), which may be able to predict who is at risk to develop a specific comorbidity. These will provide specific targets for therapeutic development (McCabe & McCabe, 2013). One such example is the body of research emerging in regard to the increased risk of Alzheimer's disease associated with Down syndrome. Thus far, an increased risk of Alzheimer's disease has been associated with polymorphisms in a number of genes (McCabe & McCabe, 2013). Additionally, the early onset of menopause, thought to be linked to the triplication on chromosome 21, seems to put women with Down syndrome at a particularly high risk for early-onset Alzheimer's disease (Zhao et al., 2011).

Fragile X Syndrome

Fragile X syndrome is the most common inherited form of ID (Murphy et al., 1998). The disorder is so named due to observation of a fragile site at the tip of the X chromosome of some who have this disorder. The gene at this site is the fragile X mental retardation 1 (FMR1) gene, which produces a protein important for brain development and function (Finucane et al., 2012). Further discussion of the presumed mechanism for fragile X appears in the "Current Issues and Future Directions" section, where pharmacological interventions are described. The effects of fragile X syndrome on IQ are variable. However, available research indicates that the majority of males and 50% of females with the full mutation have ID (Mazzocco, 2000). Both males and females show relative strengths in daily living skills and self-help skills, in comparison to other domains of adaptive functioning. Some common characteristics are gaze avoidance, attention deficits, shyness, and social anxiety (Dykens et al., 2000). Some physical features are also commonly associated with fragile X, but it is important to note that they are nonspecific and may be found in those without the disorder (Dykens et al., 2000). These include a long, narrow face and prominent ears. There are few medical problems associated with fragile X; most notable are seizures, which occur in 10–20% of those with the syndrome (Berry-Kravis, 2002).

Prenatal and Perinatal Factors

Several factors associated with the prenatal environment are known either to cause, or at least to increase the risk of, ID in the fetus (Murphy et al., 1998). The most common environmental factors associated with ID (especially mild ID) are malnutrition during pregnancy, prenatal infections, fetal alcohol syndrome, exposure to other toxic compounds, premature birth, and peri- and postnatal asphyxia or other trauma (Patel, Greydanus, Calles, & Pratt, 2010). Maternal nutritional deficiency in folic acid is associated with neural tube deficits such as spina bifida and meningomyelocele—medical conditions that often result in ID. Maternal metabolic disorders, such as hypothyroidism, have also been linked with a number of risks to the fetus. Additionally, children born to mothers with untreated hy-

pothyroidism score lower on IQ tests than children of healthy mothers (Poppe & Glinoer, 2003). Infections during pregnancy, such as toxoplasmosis, cytomegalovirus, rubella, herpes, and group B streptococcus, likewise have the potential to alter the brain development of the fetus and can result in significantly impaired functioning.

Maternal exposure during pregnancy to substances such as alcohol, lead, and anticonvulsant medicines has been associated with impairments in cognitive functioning. Depending on the timing and dose of the toxic substance, the effects can range from severe ID to more subtle difficulties in learning or memory (Percy, 2007). Maternal alcohol use is the most common preventable cause of ID worldwide (Nulman, Ichowicz, Koren, & Knittel-Keren, 2007). One issue that makes alcohol avoidance challenging is that not all pregnant women *know* that they are pregnant, and alcohol exposure is riskiest in the first trimester. The terms "fetal alcohol syndrome" and "fetal alcohol spectrum disorder" have been used to describe a range of physical, cognitive, behavioral, and learning disabilities caused by prenatal exposure to alcohol. The word "spectrum" is used in the latter term because an individual may have some or all of the characteristics, resulting in varied levels of impairment. One study (Streissguth et al., 2004) found that 24% of individuals with fetal alcohol syndrome had IQs less than 70, and IQs ranged from profound deficits to the average to above-average range.

In addition to prenatal maternal nutrition, illnesses, and toxic events, a number of perinatal factors have been associated with risk of ID. Infants born prematurely and those with low birth weights are at risk for learning and cognitive deficits. In general, rates of disability increase with decreasing gestational age and birth weight. Rates of neurodevelopmental disorders are highest in those with extremely low birth weights (i.e., less than 1,500 grams or 3.3 pounds); studies have found that 22–45% of infants born at 23–25 weeks' gestation have a significant disability (Stephens & Vohr, 2009). Other birth complications associated with ID are asphyxia and intrauterine infections.

Environmental and Social Risk Factors

Factors that are known to have an impact on intellectual functioning in childhood include insults to the brain through significant infections (e.g., meningitis, encephalitis), severe traumatic brain injury (e.g., falls, vehicle accidents, sport-related trauma, assaults), and epilepsy. Lead and mercury exposures have also been consistently linked with decreases in intellectual functioning. Baghurst and colleagues (1992) found that lead exposure was inversely related to IQ in their sample of 494 children age 7, even after they controlled for a large number of variables; these included sex, parents' level of education, maternal age at delivery, parents' smoking status, socioeconomic status, quality of the home environment, maternal IQ, birth weight, birth order, feeding method (breast, bottle, or both), duration of breast feeding, and whether the child's natural parents were living together.

Risk factors in children's environments have also been linked with increased risk of ID. These include (1) biomedical factors, such as malnutrition; (2) social factors, such as impaired child–caregiver interaction, chronic illness in the family, lack of adequate stimulation, and family poverty; and (3) educational factors, such as impaired parenting, delayed diagnosis, inadequate early intervention or special education services, and inadequate family support (Schalock et al., 2010). Historically, research has found strong inverse relationships between socioeconomic status (measured by parental education level, family income, parents' occupations, or some composite measure) and the prevalence of ID, particularly mild ID. A positive association between the quality of the home learning environment and a child's IQ has also been found (Murphy et al., 1998).

Guralnick (2005) has summarized how best to conceptualize these environmental risk factors. In his view, it is important to note that although environmental risk factors can and do make independent contributions to ID, they often operate in conjunction with biological conditions. Additionally, it is important in the majority of cases to recognize that the cumulative effect of all causal factors is what produces the greatest threat to young children's intellectual development.

DUAL DIAGNOSIS (PRESENCE OF BOTH ID AND MENTAL HEALTH DISORDERS)

A growing body of literature indicates that children and adolescents with ID have significantly higher rates of emotional and behavioral problems than their peers without ID (e.g., Baker, Blancher, Crnic, & Edelbrock, 2002; Emerson, 2003; Linna et al., 1999; Stores, Stores, Fellows, & Buckley, 1998). Prevalence studies

have reported that approximately 30–50% of children and adolescents with ID exhibit emotional and behavioral problems (Dekker & Koot, 2003; Emerson, 2003; Tonge & Einfeld, 2003). This is an enormously higher rate than that found in the general population. For instance, Dekker, Koot, Ende, and Verhulst (2002) found in a study comparing Child Behavior Checklist scores of children with and without ID that 50% of those with ID had Total Problem scores in the clinically significant range, compared to only 18% of those without ID.

In a population-based study of children ages 5–15 years with and without ID, Emerson (2003) found that 39% of those with ID were diagnosed with one or more *International Classification of Diseases*, 10th revision (ICD-10) psychiatric disorders. Most common were disruptive behavior disorders (25%), anxiety disorders (8.7%), and hyperkinesis or attention-deficit/hyperactivity disorder (ADHD; 8.7%). A small proportion had depression (1.5%). Other studies have found varied rates (e.g., Dekker & Koot, 2003; Einfeld, Ellis, & Emerson, 2011; Tonge & Einfeld, 2003). However, some consistent patterns have emerged. Studies have found that those with milder ID tend to show higher rates of disruptive and emotional disorders and more improvements in symptoms over time. Conversely, those with more severe ID have high rates of stereotypy, self-injury, and social isolation, and are less likely to show symptom improvements (Witwer & Lecavalier, 2008). Children with mild to moderate ID tend to have more antisocial/disruptive behaviors (Einfeld et al., 2006; Koskentausta, Iivanianen, & Almqvist, 2004; Molteno, Molteno, Finchilescu, & Dawes, 2001) and internalizing problems (Borthwick-Duffy, Lane, & Widaman, 1997) than those with more severe ID. In their longitudinal study, Einfeld and colleagues (2006) found that those with mild to moderate ID were likely to have higher scores on the Disruptive subscale of the Developmental Behaviour Checklist than those with severe and profound ID. Molteno and colleagues (2001) reported that children with mild ID (n = 127) had significantly higher scores than those with profound ID (n = 38) on the Antisocial Behaviour subscale of the Developmental Behaviour Checklist.

Difficulties with diagnostic assessment due to ID and associated language impairments make diagnostic practices and research in this area complex and have led to a wide range of prevalence rates. In typically developing youngsters, clinicians rely to a certain extent on children's verbal reports of experiences and emotions. Individuals with ID often have qualitative impairments in receptive and expressive language. Even mild impairments in language can make discussion of abstract concepts and subtle abnormalities in emotion difficult to detect and assess (Fletcher, Loschen, Stavrakaki, & First, 2007). The lack of speech in some with ID has made it difficult to determine the presence of many DSM-IV symptoms (Einfeld & Aman, 1995). The cognitive deficits may lead these individuals to have difficulty understanding and expressing the more complex cognitive phenomena that occur in some conditions (e.g., anxiety disorders; Cooray, Gabriel, & Gaus, 2007; Findlay & Lyons, 2001; Fletcher et al., 2007). Consider, for example, the problems in ascertaining the presence of major depression in a child with limited language. In such a case, determining the presence of depressed mood; lack of pleasure in previously enjoyed activities; and feelings of agitation/restlessness, guilt, and loss of energy could all be daunting.

Two historical consequences of these obstacles seen in the ID population are "diagnostic overshadowing" (Reiss, Levitan, & Szysko, 1982) and the reliance on behavioral equivalents. In diagnostic overshadowing, the clinician incorrectly attributes unusual behavior to an individual's developmental disability. The developmental disability has the potential to overshadow other psychiatric diagnoses in the eyes of clinicians and researchers, thereby resulting in a lack of sensitivity to the other psychiatric disorders.

Lack of language and intellectual impairment often require evaluators to rely on third parties for basic information on the behavior and emotions of individuals with ID. Because of this, many within the ID field have resorted to using "diagnostic equivalents" (Hurley, Levitas, Lecavalier, & Pary, 2007). That is, they equate DSM criteria with proposed alternatives that are compatible with these individuals' limited communication and cognitive disability. These equivalents are based on observable behaviors. Guidelines for incorporating behavioral equivalents into psychiatric diagnosis in ID have emerged (Fletcher et al., 2007; Royal College of Psychiatrists, 2001). Some have suggested that behavioral equivalents for depression include property destruction, aggression, self-injury, spitting, yelling, refusing preferred activities, loss of response to reinforcers, and stealing or obsessing about food (Charlot et al., 2007). However, there is a paucity of research supporting the validity of these symptoms or behavioral equivalents (McBrien, 2003). The research conducted to date has found equivocal results (e.g., Marston, Perry, &

Roy, 1997; Matson et al., 1999; Reiss & Rojahn, 1993; Tsiouris, Mann, Patti, & Sturmey, 2003).

Attempts to validate assessment of psychopathology in ID are faced with formidable barriers. On the one hand, clinicians have resorted to behavioral equivalents because of poor language and limited self-reporting ability in patients with ID. On the other hand, there are currently no objective clinical tests with which to validate these presumed indicators, leading to studies that are incapable of validating diagnostic methods. One promising area that has emerged within general psychopathology research is the identification of biomarkers associated with clinical profiles. Measurement of physiological variables such as heart rate, cortisol, and electrodermal activity (or galvanic skin conductance) may provide an objective measure of arousal state and stress in those with ID who might not otherwise be able to communicate their distress. Currently there is limited research on such markers in ID; however, such studies would appear to have great potential to influence the assessment and treatment of those with ID.

One recent study explored potential biomarkers associated with self-injury in a sample of individuals with ID. Symons, Wolf, Stone, Lim, and Bodfish (2011) compared salivary levels of biomarkers for the hypothalamic–pituitary–adrenal axis (cortisol) and the sympatho-adrenomedullary system (a-amylase) between individuals with ID with and without self-injurious behavior. They found significantly elevated cortisol in those with self-injurious behaviors. Additionally, there were significant differences in a-amylase between those with stereotypic movement disorder and self-injury on the one hand, and those with self-injury and no stereotypic movements on the other.

Another potential avenue toward a better understanding of the presentation and predisposition for psychopathology in ID is that of endophenotypes. Within the larger field of psychopathology, it is largely recognized that most forms of mental illness have some type of heritable aspect, which interacts with other genetic and environmental factors to increase the risk for disorders (Lenzenweger, 2013). As detailed above, a great deal of research has been conducted on the etiology of ID in subsamples (e.g., individuals with Down syndrome or fragile X syndrome). However, there is certainly something to be gained from examining liability for anxiety, depression, and many other mental illnesses in those with ID. It is particularly important that these studies not be limited to those cases with known genetic etiologies.

CURRENT ISSUES AND FUTURE DIRECTIONS IN PRACTICE AND RESEARCH: SOME EXAMPLES

Throughout this chapter, we have detailed many of the great advances the field of ID has made within the past few years—from better knowledge of etiology to improved assessment and treatment. We discuss recent and potential future advances further in this section.

Genetic Research

The most notable advances are within the field of genetics and the greater understanding of the connections among genes, brain, and behavior. To date, mutations in more than 450 different genes have been associated with ID; it is expected that this number may increase by three- to fourfold in the next years, due to advancing genetic lab technologies (van Bokhoven, 2011). Biomarker research (see below) has extended beyond that of examining the genetic etiology of ID to examining endophenotypes and the associated liabilities of those with particular genetic profiles. We cannot help appreciating the great potential this research has if it maintains its current trajectory.

New Approaches to Drug Research

Hints of what the future may hold in regard to drug treatments are well illustrated by the research in fragile X syndrome. Recently there has been a great deal of interest in the causal mechanisms of fragile X syndrome and several other forms of developmental disability. Research has isolated that the phenotype of fragile X syndrome is a consequence of the cytosine–guanine–guanine (CGG) repeats within the FMR1 gene (Erickson et al., 2011). More than 200 repeats of the CGG sequence lead to silencing of the FMR1 gene and absence of the fragile X mental retardation protein (FMRP) (Erickson et al., 2011). This absence, in turn, is associated with excessive neurotransmission of group 1 metabotropic glutamate receptor 5 (mGluR5). There appears also to be a down-regulation of gamma-aminobutyric acid (GABA; inhibitory) pathways in the central nervous system. Many features of fragile X syndrome are consistent with overactivation of the mGluR5 pathway, including seizures, "electrical excitability" on electroencephalograms, cognitive handicap, increased anxiety, and incoordination (Erickson et al., 2011). It is thought that the degree to which an indi-

vidual is affected by fragile X syndrome is related to how much the FMRP is reduced, and this is thought to fluctuate among individuals with fragile X syndrome (Bhakar, Dölen, & Bear, 2012).

Importantly, researchers have been able to mimic the fragile X syndrome phenotype in the laboratory by "knocking out" the FMR1 gene in mice and fruit flies (Wijetunge, Chattarji, Wyllie, & Kind, 2013). Both species then demonstrate characteristics consistent with fragile X syndrome in humans (including characteristic cognitive deficits, repetitive behavior, reduced seizure threshold, and neuroanatomical/physiological changes). It is of high interest that various drugs, including mGluR5 antagonists, are able to rescue behavioral and cognitive functioning in many animal models (Wijetunge et al., 2013). This has led to great excitement within the developmental disabilities community and within sectors of the pharmaceutical industry. To date, a number of pharmacological compounds have been or are being assessed. These include the mGluR5 antagonists fenobam and AFQ056 (*http://fraxa.org/toward-a-cure/clinical-trials*); the GABA agonist arbaclofen; and other compounds only identified by pharmaceutical company numerals (Wijetunge et al., 2013). Other drugs studied include lithium (targeting downstream mGluR5 signaling); a GABA agonist; and other agents that target metalloproteinases. These human clinical trials have met with variable levels of success, but results from many (perhaps most) trials are not available yet. Needless to say, these are exciting times: Not only have animal researchers reversed the fragile X syndrome phenotype pharmacologically, but a significant number of laboratories are striving for the same in individuals who show the full fragile X syndrome phenotype. Unlike the blunt instruments of yesteryear, which were intended to reduce comorbid behavioral symptoms of fragile X syndrome, these experimental agents being used in fragile X syndrome are very specifically targeted and are intended to offset the main elements of the disability. Early reports on mGluR blockers have been somewhat discouraging to date (Pollack, 2013). The importance of this work is that neuroscientists are learning more and more about the neurobiological disorder, including its presumed mechanisms, and that both industry and university scientists see possible avenues to halt the progression of impairment and perhaps even reverse aspects of the disability. It is a whole different mindset in the way that one looks at developmental disability.

Indeed, if one examines current entries on the website *clinicaltrials.gov*, one sees that several investigations now underway for ASD and for Down syndrome are using targeted treatments in a similar way. These investigations are being designed in hopes of reversing the core elements of these very severe conditions. Furthermore, it is possible that the study of the more specific genetic conditions may yield unanticipated gains, such as discovery of a final common pathway leading to various pathologies. As noted by Bear, Huber, and Warren (2004), who formulated the mGluR theory of etiology for fragile X syndrome, "it seems reasonable to anticipate that other disorders with similar symptoms might be traced to defects elsewhere in the same molecular pathways. . . . [O]ther types of human developmental disorder, including autism, have many of the same core characteristics as Fragile X" (p. 375).

Biomarker Research

As our understanding of the relationship between biology and behavior improves, we have seen an increase in the research on biomarkers in the field. The Symons and colleagues (2001) study, which examined cortisol and a-amylase in individuals with ID and self-injury, is an excellent example of how use of such markers may be able to move forward our assessment and understanding of psychopathology in those with the most severe forms of ID. Researchers to date have found this population an especially difficult one in which to assess co-occurring conditions and monitor the treatment of such conditions, in light of these individuals' significant communication deficits. As a result, often they are excluded from research studies. The reliance on variables aside from self-report will enable a new line of research for this challenging population.

Studies of Risk Factors for ID

Research on risk factors for ID continues to advance and become more refined. Whereas once the discussion was about general factors of race and poverty, current research has identified more complex explanations of risk. For example, racial disparities in ID rates have long been hypothesized to be related to factors such as assessment bias or poverty. However, a more complicated picture seems to be emerging. This is illustrated in a study by Christian and colleagues (2013). One risk factor for ID is preterm birth, which we know occurs twice as often in black women as in their white counterparts (Christian et al., 2013). There appears to be an interaction among stress, minority status, and

the biological response to these factors. Christian and colleagues found that black women have more robust stress-induced inflammatory responses. They posit that it is the biological response to stress that ultimately puts black mothers at risk for preterm labor. This also subsequently puts their children at risk for ID. Studies such as these have the potential to shape future prevention and treatment research. As a field, we have begun to understand that research should not be conducted on the child in isolation. Rather, it is important to consider multiple factors, such as socioeconomic status, family stress, social support, parental physical and mental health, and environmental risk factors (e.g., Emerson, 2012; Hodapp & Dykens, 2012).

Interdisciplinary Research and Service Delivery

Still another area that has seen great growth is that of service delivery models. There is a growing sentiment that we must become more interdisciplinary not only in our service delivery, but in our research (e.g., Hodapp & Dykens, 2012; G. King et al., 2009). This is illustrated well in the National Science Foundation's (2013) informational webpage on interdisciplinary research: "NSF has long recognized the value of interdisciplinary research in pushing fields forward and accelerating scientific discovery. Important research ideas often transcend the scope of a single discipline or program." Although several definitions for interdisciplinary practice and research exist, most conceptualizations involve the following elements: (1) a team of professionals from related disciplines; (2) shared goals among the team members; (3) team members' uniquely contributing expertise towards a particular goal; and (4) team members' adhering to recommendations from other team members regarding the goals (G. King et al., 2009). Thus interdisciplinary clinical and research teams are characterized by interdependence and an exchange of information, knowledge, and skills (Costarides, Shulman, Trimm, & Brady, 1998).

Treatments that are interdisciplinary arguably provide numerous benefits to children with ID and their families. Chief among these benefits is the likelihood that children with ID served by an interdisciplinary team experience better service and exhibit better outcomes (Yeager, 2005), particularly in rural areas (Fertman, Dotson, Mazzocco, & Reitz, 2005). In addition, interdisciplinary treatments can help to reduce fragmentation in services, improve service coordination, and increase the likelihood of providing unified and consistent messages to families (Carpenter, 2005). Many professionals feel that interdisciplinary collaboration is more efficient, less of a burden to families, and good for overall professional development (G. King et al., 2009).

Although interdisciplinary service has been part of the education of those with ID (Costarides et al., 1998; G. King et al., 2009), this model is only beginning to generalize to other service areas and to research. Surprisingly, having multiple disciplines investigate common areas of ID interest is a relatively new phenomenon. Hodapp and Dykens (2012) reported that a growing body of work seeks to combine behavioral, neurological, psychological, and genetic expertise. These disciplines are coming together to create an increasingly sophisticated field of "behavioral phenotyping," in which researchers study the behavioral effects of different genetic disorders (Hodapp & Dykens, 2012). Behavioral studies of ID now frequently use magnetic resonance imaging, and one of the major national funding bodies (the National Institute of Child Health and Human Development) now even holds an annual Research Training conference (Hodapp & Dykens, 2012).

Research on Transitions through Life Stages

Researchers and clinicians have begun to recognize that issues surrounding the transition from school age to adulthood are in need of further attention and research activities. In fact, the emergence of postsecondary education programs within the United States for students with ID is increasing, due to federal funding, legislation, and advocacy efforts of families, service providers, and persons with ID themselves (Izzo & Shuman, 2013). The concept of "transition planning" for adults with ID refers to the process of coordinating school programs, adult service agencies, and natural community supports during the time period when individuals' roles change from that of students to that of adults (Cobb & Alwell, 2009).

Since adult transition planning has been mandated in education, overall adult adjustment outcomes tend to be better than they were previously for those with ID. Studies have found that with vigorous advocacy and transition support, the hours, pay rates, and types of jobs held by youth with mild IDs tend to improve after 2 years from graduating from high school. Commonly held jobs include maintenance, food service, and retail positions, as well as some trade jobs such as plumbing and carpentry (Snell et al., 2009). Indeed, there is evi-

dence that many people with milder forms of ID can be gainfully employed in the community when given adequate training and on-the-job supports (Mank, 2007).

Despite the improvements made through mandated adult transition programming, there still remain numerous areas in need of improvement. In one follow-up study, unemployment rates among those with mild ID were four times those of same-age comparison groups without ID (Maughan, Collishaw, & Pickles, 1999). In one study of over 500 students with ID, students with ID were determined to be less likely to live independently.

Moreover, adolescents and young adults with ID often do not receive the same careful, mandated planning and assistance to address changes in other aspects of their lives, such as transitions to adult health care providers, psychologists, and other service providers. This transition becomes especially problematic when those with ID have co-occurring health conditions or mental health diagnoses; significant limitations in the availability of services for such individuals have been found. Often health care and mental health providers will baulk at treating individuals with ID, citing their lack of experience with the population. Examples of optimal health care transitioning are often limited to individual clinics and are not present in hospitalwide or regional planning (Kennedy & Sawyer, 2008).

To improve transition outcomes, there is increasing recognition that there must be active collaboration among clinical service developers, university training programs, and research initiatives (Kennedy & Sawyer, 2008). As a field, we need to investigate comprehensive models for adult transitions (Cobb & Alwell, 2009). Successful anecdotal instances of optimal educational and health care transition exist. However, we do not possess rigorous data proving their effectiveness (Cobb & Alwell, 2009); nor do we know the differential effectiveness of various adult transition programs.

Research and Services for All Individuals with ID

While we researchers are advancing our understanding of genetic syndromes, it is also important that we not forget about the *entire* population of those with ID. Recently, there has been a tendency to concentrate research on etiology, assessment, and treatment within small subsamples, such as those with Down syndrome, other genetic conditions, or ASD. Although there are certainly strengths to this type of research (e.g., reduction of error variance by focusing on more homogeneous samples), it inherently leaves out a very large population: those with ID of unknown etiology (i.e., idiopathic ID). Despite our numerous advances, there is a large subset of individuals whose ID is of unknown origin. While these individuals are heterogeneous in etiology and presentation, they also share a number of commonalities with those whose ID has a clear etiology: They are at risk for co-occurring psychopathology, struggle with communication and problem solving, and often continue to require significant supports into adulthood. As such, there continues to be a need to advance knowledge in this population as well. First, this is an ethical issue; just like others with ID, those with idiopathic ID deserve our attention and the potential for treatment. Moreover, by excluding these individuals, we as researchers may be losing the opportunity to study the true breadth of certain phenomena in ID.

One example, which demonstrates both the potential impact of this tendency and its shortcomings, is the field of ABA in ASD. Over the last 20 years, there has been growing support for the use of intense ABA therapy in young children with ASD (see Klinger, Dawson, Barnes, & Crisler, Chapter 11, this volume). Myriad other therapies also employ operant conditioning procedures to treat children with ASD (e.g., Dawson et al., 2010; Kasari, Freeman, & Paparella, 2006). The forms of intensive early intervention are usually marked by (1) the use of one-to-one therapy, (2) frequent provision for periods exceeding 20 hours per week, and (3) durations that may extend to several years (e.g., Lovaas, 1987; Smith, Eikeseth, Klevstrand, & Lovaas, 1997). Consequently, they can be very expensive (e.g., Chasson, Harris, & Neely, 2007; Motiwala, Gupta, & Lilly, 2006). Usually there is a "curriculum," which comprises the learning of small steps or mini-skills that collectively help a child develop necessary activities of daily living and even academic skills. What is interesting about ABA and related therapies in ASD is that its advocates claim that permanent and major gains are often made (including periodic recovery from ASD itself), and that the children's IQs, often significantly delayed in ASD, can be normalized with ABA (Lovaas, 1987).

We are not aware of any therapies of this intensity and duration that are broadly used in children with ID and without ASD symptoms. How do we account for this? Do the principles of operant conditioning not apply to children with ID alone? Are children with ASD uniquely different from those with ID, such that ABA principles work in one condition (ASD) but not the other (ID)? Or are parents and other family mem-

bers of children with ASD better able to lobby politically for the services that they believe their children need? At this point, most of the early intervention that children with ID receive is not intense, is delivered in a group format, and is far cheaper on a per capita basis than the ABA therapies advocated for treating children with ASD (Mandell, Cao, Ittenbach, & Pinto-Martin, 2006).

As citizens, we like to think of ourselves as living in an egalitarian society, and yet this major discrepancy exists in the amount of resources and effort provided to children with these two conditions. This is like a "Shakespearean silence" begging to be recognized, and we believe that it is only a matter of time before advocates for children with ID alone begin to demand similar attention and resources. We have no idea what form intensive early intervention may take for children with non-ASD ID. However, we feel that society cannot ignore this disparity indefinitely, and we look forward to the potential therapies that will eventually be ushered in. If indeed these therapies are as effective in ASD as claimed, the potential gains in the mental capacity of children with ID could be substantial, and the eventual impact for individuals with ID could be monumental. In the end, this issue is not so much scientific as one of fairness. It will be fascinating to see how the arguments are played out.

SUMMARY AND CONCLUSIONS

In summary, ID refers to a group of conditions defined by the presence of significantly subaverage IQ (usually below about 70 on an individually administered test), significant deficits in adaptive behavior, and occurrence during the developmental period (variously defined as before 18 or 22 years, depending on jurisdiction). Curiously, this means that disability caused by severe head trauma at, say, the age of 17 years would be categorized as ID, whereas the same injury at the age of 22 years would be classed as a form of dementia.

One oddity of ID is that it can wax and wane over the lifespan. For instance, an individual's ID may become most obvious during the school years (when the child is being maximally challenged intellectually), whereas later adaptation may be adequate (e.g., when the adult makes an excellent adjustment to the workplace and at home). ID may be the product of a huge array of potential causes. These may include genetic determinants, illnesses, brain trauma, toxins, poor environment, and adverse caregiver–child interactions. Furthermore, these determinants may occur *in utero*, at the time of birth, or in the early years of life, and they may interact with one another to produce a more adverse outcome. Consequently, one sees that we are emphatically *not* dealing with a single condition called ID. Rather, we are working with a near-infinite number of disabilities, which are expressed in a multitude of ways in different people. It is small wonder that an optimal approach to identifying and planning services for persons with various forms of ID is through interdisciplinary teams of professionals.

People with ID are at higher risk for a number of adverse outcomes, and one of these is the co-occurrence of psychiatric, emotional, and behavioral conditions. Prominent among these are disruptive behavior disorders, ADHD, anxiety conditions, and major depressive disorder. Because of many clients' intrinsic language limitations, limited self-insight, and difficulty conveying abstruse concepts, deriving an accurate diagnosis of comorbid mental disorders can be fraught with difficulty and uncertainty.

Recent diagnostic systems have endeavored to emphasize the additional supports that people with ID require from their communities. The intent in placing an emphasis on supports—rather than on deficiencies—is to make clear that one main objective of the diagnostic process be made explicit. It is clear that affected individuals need more than the ID diagnosis. They also need the *services* that will help them to approach their fullest potential.

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CHAPTER 14

Learning Disabilities

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It has now been over 50 years since that fateful meeting in 1963 at the conference on the "Exploration into Problems of Perceptually Handicapped Children," during which parents, educators, and policy specialists agreed on the term "learning disabilities" (LDs) to describe a large group of individuals who had significant academic learning deficits despite average or better intelligence. These advocates essentially launched a new field of study in special education, or at least integrated and redirected a number of factions studying various dimensions of the same phenomenon. They named their new organization the Association for Children with Learning Disabilities. Over the past five decades, much research has been conducted in the field of LDs, and many scientific accomplishments have been made. Yet, despite these apparent advancements, this is still a field without a consensus definition, with no known cause or identification marker, and with plenty of disagreement and controversy as to who has or does not have LDs. As this chapter reveals, there continues to be much debate over how to assess, identify, and treat individuals with presumed LDs.

As incongruous as it may seem, despite our not being able to agree on how to define, diagnose, or accurately count LDs, this is the largest category of students in special education, and it receives the most research and fiscal attention in the country. Children identified with LDs now represent over one-third of all children receiving special education services in the United States (National Center for Educational Statistics, 2012), with approximately 5% of all U.S. public school students identified as having one (Cortiella, 2011). In the years since publication of the previous edition of this chapter (Lyon, Fletcher, & Barnes, 2003), tremendous progress has been made in understanding and treating LDs.

It appears that those of us in the LD field have a somewhat similar idea about what constitutes LDs in a general sense, but there historically has been much disagreement as to the specifics of who has an LD and who does not, and how we can tell the difference. Even today, 50 years after the term was introduced, we have new models of determining LDs—whether one follows a response-to-intervention (RTI) approach as used in the educational system; the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association [APA], 2013) guidelines as used in the mental health disciplines; or current research definitions. So while we use this one term, and review much of the research that flows from this term, readers should know that we are referring to a wide range of studies using a variety of definitions and assessment systems that attempt to make inferences and generalizations about a very heterogeneous population of individuals.

That said, in this chapter we first provide a brief history of the field, with a focus on the origins of current

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policy-based definitions of LDs. Subsequent sections address in detail the core features of specific types of LDs. As noted earlier, LDs do not constitute a homogeneous disorder. In fact, LDs by definition refer to deficits in one or more of several domains, including reading disabilities, mathematics disabilities, and disabilities of written expression. Because each type of LD is characterized by distinct definitional and diagnostic issues, as well as issues associated with heterogeneity, each is covered separately in this chapter. Thus, for each LD domain, a review of critical background information, constructs, and research and policy trends is provided. More specifically, the review of each major LD domain is organized to address (1) a review of current definitional and diagnostic issues confronting each specific type of disability within the domain; (2) the epidemiology and developmental course of the disability; (3) core processes that have been identified for each disability; and (4) a review of the neurobiological mechanisms hypothesized to cause and/or contribute to the specific type of LD, when any have been identified. The chapter concludes with a brief review of current issues and a look toward the future.

HISTORY

A number of sources are available that provide overarching reviews of the field's scientific, social, and political history and development. These include works by Danforth (2009), Doris (1993), Hallahan, Pullen, and Ward (2013), and Torgesen (1991). These works trace the origins of the field in a comprehensive and detailed fashion, and they should be consulted if readers desire a more complete historical perspective on LDs. In general, these commentaries indicate that the field of LDs developed in response to two major needs.

First, the field is linked closely with the need to understand individual differences in learning and performance among children and adults displaying *specific* deficits in spoken or written language, while maintaining integrity in general intellectual functioning. This unexpected pattern of strengths and *specific* weaknesses in learning was first noted and studied by physicians and psychologists, thus giving the field the biomedical and psychological orientation that has always characterized it. Second, the LD movement developed as an applied field of special education driven by social and political forces, and in response to the need to provide services to youngsters whose learning characteristics were not being adequately addressed by the educational system. Each of these historical contexts is reviewed briefly.

LDs and the Study of Individual Differences

Gall's Influence

As Torgesen (1991) and Mann (1979) have pointed out, interest in the causes and outcomes of inter- and intra-individual differences in cognition and learning can be traced to early Greek civilization. However, the first work that had clear relevance to today's conceptualizations of LDs was conducted by Gall in the context of his work on disorders of spoken language in the early 19th century (Wiederholt, 1974). Unfortunately, today Gall is mainly remembered for his advocacy of the pseudoscience of phrenology, in which bumps on the head were taken to indicate levels of different personality traits and mental faculties (Goodwin, 2009). It is often forgotten that Gall was correct in a related claim: that different faculties are localized in different areas of the brain.

The relevance of Gall's observations to present conceptualizations of LDs was summarized by Hammill (1993). According to Hammill, Gall noted that some of his patients could not speak but could produce thoughts in writing, thus manifesting a pattern of relative strengths and weaknesses in oral and written language. In addition, Gall established that such patterns of strengths and weaknesses were a function of brain damage, and that brain damage could selectively impair one particular language capability but not affect others. Thus the clinical roots were established for the present-day observation that many children with LDs manifest "specific" deficits rather than pervasive or "generalized" deficits. Finally, Gall argued that it was essential to rule out other disabling conditions, such as intellectual disability or deafness, that could impair a patient's performance. Within this context, the origins for the "exclusion" component of current definitions of LDs are evident.

Early Neurology and Acquired Language Disorders

A number of other medical professionals also began to observe and report on patients demonstrating intraindividual strengths and weaknesses that included specific deficits in linguistic, reading, and cognitive abilities. For example, Broca (1863, 1865) provided important observations that have served to build the foundation

of the "specificity" hypothesis in LDs. Broca (1865) reported that "expressive aphasia," or the inability to speak, resulted from selective (rather than diffuse) lesions to the anterior regions of the left hemisphere—lesions primarily localized in the second frontal convolution.

In the latter 1800s and early 1900s, additional cases of unexpected cognitive and linguistic difficulties within the context of otherwise normal functioning were reported. For example, Hinshelwood (1917) described one 10-year-old youngster as follows:

> The boy had been at school three years and had got on well with every subject except reading. He was apparently a bright and in every respect an intelligent boy. He had been learning music for a year and had made good progress in it. . . . In all departments of his studies where the instruction was oral he had made good progress, showing that his auditory memory was good. . . . He performs simple sums quite correctly, and his progress in arithmetic has been regarded as quite satisfactory. He has no difficulty in learning to write. His visual acuity is good. (pp. 46–47)

Thus, by the beginning of the 20th century, evidence from several sources contributed to a set of observations that defined a unique type of learning difficulty in adults *and* children— specific rather than general in presentation, and distinct from disorders associated with sensory handicaps and subaverage general intelligence. As Hynd and Willis (1988) have summarized, the most salient and reliable observations included the following: (1) The children had some form of congenital learning problem; (2) more male than female children were affected; (3) the disorder was heterogeneous with respect to the specific pattern and the severity of deficits; (4) the disorder might be related to a developmental process affecting primarily left-hemisphere central language processes; and (5) typical classroom instruction was not adequate in meeting the children's educational needs. More recent evidence has supported some of these observations, but many have not been validated, as is made evident in later discussions.

Orton and the Origins of Dyslexia

During the 1920s, Samuel Orton extended the study of reading disabilities with clinical studies designed to test the hypothesis that reading deficits were a function of a delay or failure of the left cerebral hemisphere to establish dominance for language functions. According to Orton (1928), children with reading disabilities tended to reverse letters such as "b/d" and "p/q," and words such as "saw/was" and "not/ton," because of the lack of left-hemispheric dominance for the processing of linguistic symbols.

As Torgesen (1991) pointed out, neither Orton's theory of reading disabilities, nor his observation that reversals were symptomatic of the disorder, have stood the test of time. However, Orton's (1928, 1937) writings were highly influential in stimulating research; mobilizing teacher and parent groups to bring attention to reading disorders and other LDs that had a deleterious impact on children's academic, behavioral, and social development; and prompting the development of instructional techniques for teaching reading-disabled children. Moreover, Orton's influence on present-day conceptualizations of LDs can be seen indirectly in his early attempts to classify, within the same conceptual and etiological framework, a *range* of language and motor disabilities in addition to reading disabilities (Doris, 1993).

The Straussian Movement and the Concept of Cerebral Dysfunction

Whereas Orton's contributions are linked primarily to the development of scientific and clinical interest in reading disabilities (particularly dyslexia), it was the work of Strauss and Werner (1943) and their colleagues during the period after World War II that led directly to the emergence of the more general category of LDs as a formally recognized field (Doris, 1993; Rutter, 1982; Torgesen, 1991). This work built on an earlier series of attempts to understand the behavioral difficulties of children who subsequently were described as hyperactive; in this series of clinical observations, children's overactivity, impulsivity, and concrete thinking were attributed to brain damage, in the absence of physical evidence for an injury to the brain. Strauss and Werner expanded this concept in research involving children with intellectual disability. They were particularly interested in comparing the behavior of children whose intellectual disability was associated with known brain damage to that of children whose disability was not associated with neurological impairment, but was presumably familial in nature. Strauss and Lehtinen (1947) reported that children with intellectual disability and brain injury manifested difficulties on tasks assessing figure–ground perception, attention, and concept formation in addition to hyperactivity, whereas non-

brain-damaged children with intellectual disability performed in a manner similar to typically developing children and were less likely to show behavioral overactivity. Within the context of these studies, Strauss's group subsequently observed patterns similar to those of children with intellectual disability and brain injury in children with average intelligence, but behavioral and learning difficulties. They attributed to these children a syndrome they called "minimal brain injury" (MBI). From these studies, the concept of "minimal brain dysfunction" (MBD) emerged in the 1960s (Clements, 1966), with an emphasis on the Straussian thesis that MBI or MBD could be identified solely on the basis of behavioral signs even when physical and neurological examinations were normal.

Kavale and Forness (1985) reported that the research and writings of Strauss and his colleagues had a significant influence on the development of the LD paradigm, through ideas that included the following:

1. The locus of an LD is within the affected individual, and thus represents a medical (disease) problem.
2. LDs are associated with (or caused by) neurological dysfunction.
3. The academic problems observed in children with LDs are related to psychological processing deficits, most notably in the perceptual–motor domain.
4. The academic failure of children with LDs occurs despite the presence of normal intelligence; that is, there is a discrepancy between IQ (average or above) and academic achievement (subaverage).
5. LDs cannot primarily be due to other handicapping conditions.

We would add to this list the idea that brain dysfunction can be identified solely through behavioral signs even in the absence of a history of neurological disease, and we would also note the linking of behavioral characteristics of hyperactivity with LDs. Strauss and Werner's writings had a tremendous impact on the thinking and careers of several behavioral scientists who, in the 1950s and 1960s, were studying children who failed to learn in school despite having normal intelligence.

Cruickshank, Myklebust, Johnson, and Kirk and the Concept of LDs

Foremost among the behavioral scientists involved in the early conceptualization and study of LDs were William Cruickshank, Helmer Myklebust, Doris Johnson, and Samuel Kirk, all of whom propelled the field away from a focus on etiology toward an emphasis on learner characteristics and educational interventions to address learning deficits. For example, Cruickshank and his colleagues (Cruickshank, Bentzen, Ratzburg, & Tannenhauser, 1961; Cruickshank, Bice, & Wallen, 1957) were instrumental in studying and recommending modifications in classroom environments to reduce stimuli hypothesized to be distracting for children with learning and attention deficits. Likewise, Helmer Myklebust and Doris Johnson, working at Northwestern University, conducted numerous studies of the effects of different types of language and perceptual deficits on academic and social learning in children, and were among the first to develop well-designed intervention procedures for the remediation of disabilities in skills related to school learning (Johnson & Myklebust, 1967). However, it was Samuel Kirk who had the greatest influence on the formal recognition of LDs as handicapping conditions. In fact, it was Kirk who proposed the term "learning disabilities" in a 1963 conference devoted to exploring problems of perceptually handicapped children. Kirk (1963) stated:

> I have used the term "learning disabilities" to describe a group of children who have disorders in the development of language, speech, reading and associated communication skills needed for social interaction. In this group, I do not include children who have sensory handicaps such as blindness, because we have methods of managing and training the deaf and blind, I also excluded from this group children who have generalized intellectual disability. (pp. 2–3)

Thus, by 1963, this new field was moving toward the formal designation of LDs as handicapping conditions. This movement was based largely on the arguments of Kirk and others that children with LDs were indeed different with respect to learning characteristics from children with intellectual disability or emotional disturbance; that these learning characteristics resulted from intrinsic (i.e., neurobiological) rather than environmental factors; that LDs were "unexpected," given the children's strengths in other areas; and that children with LDs required specialized educational interventions. What is interesting is that the field received its initial momentum on the strength of clinical observation and advocacy. Only in the past 20 years has a systematic research base begun to emerge.

LDs as an Applied Field Molded by Social and Political Forces

As has been noted, the creation of the applied special education category of LDs in the 1960s reflected a belief by physicians, behavioral scientists, educators, and parents that some children had learning handicaps that were not being addressed effectively by extant educational practices (Zigmond, 1993). The fact that LDs were initially and formally identified as handicapping conditions on the basis of advocacy rather than systematic scientific inquiry is certainly not uncommon in either educational or public health domains. In fact, in the United States, the majority of scientific advances are typically stimulated by vocal critics of the educational or medical status quo. It is rare that a psychological condition, disease, or educational problem is afforded attention until political forces are mobilized by parents, patients, or other affected individuals expressing their concerns about their quality of life to their elected officials. Clearly this was the case in the field of LDs, where parents and child advocates successfully lobbied Congress to enact legislation in 1969 via the Education of the Handicapped Act (Public Law No. 91-230). This law authorized research and training programs to address the needs of children with specific LDs (Doris, 1993).

The diagnostic concept of LDs gained significant momentum during the 1960s and 1970s. As Zigmond (1993) has explained, the proliferation of children diagnosed as having LDs during these two decades was related to multiple factors. First, the label of "LDs" was not a stigmatizing one. Parents and teachers were certainly more comfortable with the term than with etiologically based labels such as "brain injuries," "MBD," and "perceptual handicaps." Second, receiving a diagnosis of an LD did not imply low intelligence, behavioral difficulties, or sensory handicaps. Quite the contrary, children with LDs manifested difficulties in learning *despite* having average to above-average intelligence and intact hearing, vision, and emotional status. The fact that youngsters with LDs displayed robust intelligence gave parents and teachers hope that difficulties in learning to read, write, calculate, or reason mathematically could be surmounted if only the right set of instructional conditions and settings could be identified. Advocacy efforts fueled a series of consensus conferences, two of which are most noteworthy: one on MBI and the other on LDs. Both attempted to define the disabilities widely believed to hamper the educational behavioral performance of many children in schools under a single overarching concept.

Definition of MBD

In the 1960s, the twin strands of individual differences and applications through social and political advocacy joined together, initially through efforts to define this syndrome of unexpected behavioral difficulties and underachievement due to factors intrinsic to a child. The first significant effort involved the development of a definition of MBD in 1962. In a meeting organized by what is now the National Institute of Neurological Disorders and Stroke, along with the Easter Seals Society, a formal definition of a syndrome called "minimal brain dysfunction" was formulated:

> The term "minimal brain dysfunction syndrome" refers . . . to children of near average, average, or above average general intelligence with certain learning or behavioral disabilities ranging from mild to severe, which are associated with deviations of function of the central nervous system. These deviations may manifest themselves by various combinations of impairment in perception, conceptualization, language, memory, and control of attention, impulse, or motor function. (Clements, 1966, pp. 9–10)

This definition essentially substituted "dysfunction" for "injury," recognizing the etiological implications of terms like "injury." It identified children with MBD as heterogeneous, with both behavioral and learning difficulties. As we have noted above, the definition stipulated that brain dysfunction could be identified solely on the basis of behavioral signs.

Federal Definition of LDs

Not surprisingly, the development of the definition of MBD led to reactions among educators and other professionals working in schools. In 1966, the U.S. Office of Education organized a meeting in which the participants formally defined Kirk's (1963) concept of "learning disability," as follows:

> The term "specific learning disability" means a disorder in one or more of the basic psychological processes involved in understanding or in using language, spoken or written, which may manifest itself in an imperfect

> ability to listen, speak, read, write, spell, or to do mathematical calculations. The term includes such conditions as perceptual handicaps, brain injury, minimal brain dysfunction, dyslexia, and developmental aphasia. The term does not include children who have learning problems, which are primarily the result of visual, hearing, or motor handicaps, or intellectual disability, or emotional disturbance, or of environmental, cultural, or economic disadvantage (U.S. Office of Education, 1968, p. 34)

The resemblance of this 1966 definition of an LD to the 1962 definition of MBD (Clements, 1966) is striking. The notion of MBD as an "unexpected" disorder not attributable to mental deficiency, sensory disorders, emotional disturbance, or cultural or economic disturbance was retained, reflecting work over the previous 60 years. Etiological terms were dropped and replaced by educational descriptors. The implicit attribution to intrinsic factors within a child was retained as the definition was clearly intended to be inclusive of MBD and other formulations derived from neurology and psychology (Doris, 1993; Rutter, 1982; Satz & Fletcher, 1980).

The most significant attribution for the pivotal importance of this definition is the fact that it continues as the federal definition of an LD. It has persisted through a series of parental and professional advocacy efforts that led to the provision of special education services for children with LDs. This occurred initially through the 1969 Children with Specific Learning Disabilities Act. The statutory definition of LDs in the 1969 Act then appeared in the Education for All Handicapped Children Act of 1975 (Public Law No. 94-142), and also was reflected in the 1997 reauthorization of the Individuals with Disabilities Education Act (IDEA). This definition has persisted despite the fact that it does not specify any inclusionary criteria for LDs. It essentially says that LDs are heterogeneous and not due to low intelligence and other exclusionary conditions. In a sense, the disorders became legitimized and codified in public law mostly on the basis of what they were not.

The absence of inclusionary criteria became an immediate problem in 1975, with the passage of Public Law No. 94-142 and the expectation that states would identify and serve children with LDs. In response to this problem, the U.S. Office of Education (1977) published recommendations for procedures for identifying LDs that included the notion of a discrepancy between IQ and achievement as a marker for LDs, as follows:

> . . . a severe discrepancy between achievement and intellectual ability in one or more of the areas: (1) oral expression; (2) listening comprehension; (3) written expression; (4) basic reading skill; (5) reading comprehension; (6) mathematics calculation; or (7) mathematic reasoning. The child may not be identified as having a specific learning disability if the discrepancy between ability and achievement is primarily the result of: (1) a visual, hearing, or motor handicap; (2) mental retardation; (3) emotional disturbance, or (4) environmental, cultural, or economic disadvantage. (p. G1082)

The use of IQ–achievement discrepancy as a marker for LDs has had a profound impact on how LDs are conceptualized. There was little research at the time validating an IQ–achievement discrepancy model, but researchers, practitioners, and the public continue to assume that such a discrepancy is a marker for specific types of LDs that are unexpected and categorically distinct from other forms of underachievement. However, as we discuss below, the evidence base for its validity as a central feature of LD classification is weak to nonexistent.

Probably the most important recent development in the LD field has been the RTI movement, which proposes a radical reconceptualization of the nature of LD. RTI is a general approach to education that, according to Brown-Chidsey and Steege (2005), consists of three "Big Ideas": high-quality instruction for all students, frequent assessment of skills, and data-based decision making. Rather than viewing disability identification and special education as a first-line solution to referrals for academic failure, RTI advocates propose frequently monitoring all students' academic skill development and providing increasingly intensive academic interventions as needed, without assuming an internal disability condition or formally providing "special education" under relevant laws. The RTI approach has the potential, then, to reduce official LD prevalence drastically, by recasting apparent LDs as students' inadequate responses to instruction. In this view, such a problem is just as likely to be due to the curriculum as to a child's inherent nature, and it may be best solved by trying other, more intensive instructional strategies. We discuss RTI and its philosophical foundations more in the next section. For now, we note that despite the RTI movement's recent influence, the research studies reviewed in this chapter generally have *not* used RTI as a way of identifying participants.

THE NATURE AND IDENTIFICATION OF LDs

LDs are different from many of the other disorders covered in this text, in that they represent not only clinical conditions, but also a discrete special education policy category. In addition, more than perhaps any other disorders, LDs are defined in large part by how they are identified. A student's LD can even be "cured" simply by moving to a school district with more stringent standards for identification, whereas this rarely if ever happens with other disorders. Similarly, when special education laws change (as they have, greatly, since the previous edition of this chapter), there are large changes to the LD population—since very different groups of students are identified as having LDs, depending on the precise identification criteria that are applied (Shifrin, 2010).

As Lovett and Hood (2011) have noted, psychiatric disorders can be conceived of in either *realist* or *operationist* ways. The realist conception views disorders as real, existing, latent entities that may be present whether or not they cause observable symptoms. In contrast, the operationist conception views disorders as merely the sum of their observable symptoms, with the disorder labels meaning nothing more than the operational definition (set of measurement results) for each disorder. Obviously, any disorder can be thought of, for specific purposes, in a realist or operationist way, but LD seems better conceived of as an operationist concept. This does not mean that LDs do not have a neurological basis; obviously, *all* behavior has such a basis. Instead, taking an operationist stance with regard to LD categories recognizes that there is an inevitable degree of arbitrariness in the criteria for diagnosing LDs, and so the criteria should be set based on pragmatic policy considerations rather than attempts to detect "true, underlying" LD conditions. Moreover, we should not make clinical decisions based on suspected "silent" cases of LD that are not causing obvious symptoms or impairment at the moment; if a child functions academically *as if* he or she has no LD, we should not generally search for one.

Methods of Identifying LDs

The historical concepts reviewed above set the stage for current debates over the nature and identification of LD. Today, there are three general perspectives on how to understand and assess for LDs: the cognitive processing (CP), RTI, and low-achievement (LA) approaches.

Supporters of the CP approach vary widely in the specifics of their views, but they are united in suggesting that cognitive measures must be used (in addition to academic skills measures) to identify students with LDs. The IQ–achievement discrepancy model was an early and popular version of the CP approach. As Kavale (2002) has noted, the idea of comparing IQ and academic achievement goes back to the 1920s, when the comparison was used to detect underachievement. In the 1960s and 1970s, underachievement relative to IQ came to be viewed as the hallmark of LD; even today, despite its many problems, the IQ–achievement discrepancy continues to be used, especially by private clinical evaluators, when diagnosing LD. Specific methods of determining the presence of a discrepancy vary (e.g., in the size of the discrepancy required, which tests are used, and which scores are examined), but the general model of looking for a discrepancy is fairly common. The approach has a compelling logic: If a student has an average or above-average IQ, but poor academic performance in some area that cannot be explained by an exogenous variable, there may be a specific "learning disability" keeping the student from using his or her intelligence to learn the academic skills.

Despite its storied history and wide popularity, very few researchers actually defend the IQ–achievement discrepancy model. The conceptual, statistical, and practical problems have been detailed *ad nauseam* in the literature (e.g., Aaron, 1997; Fletcher, Lyon, Fuchs, & Barnes, 2007; Lovett & Gordon, 2005; Sternberg & Grigorenko, 2002; Stuebing et al., 2002). Among other problems, discrepancy scores are unreliable; discrepancies do not predict students' underlying profile of relevant cognitive skills; and discrepancies do not predict which interventions will work for students. Now that IQ–achievement discrepancies have fallen out of fashion, today's CP proponents generally advocate the use of more complicated diagnostic models, such as cross-battery assessment based on the Cattell–Horn–Carroll theory (Flanagan, Ortiz, & Alfonso, 2013). These proponents often note that the still-unchanged federal definition of LD refers to "basic psychological processes," and suggest that LD must be identified by measuring cognitive skills directly. For instance, if a student is referred for poor reading performance, a CP proponent would be likely to measure reading performance by using standardized, norm-referenced reading

achievement tests, but the proponent would *also* probably measure the cognitive abilities thought to contribute to reading performance—abilities such as phonological processing or rapid naming. The CP proponent would also typically measure other cognitive abilities thought to be unrelated (or less related) to reading. If the student showed deficits in reading performance, as well as in related cognitive abilities, but not in less related cognitive abilities, this pattern of scores would be viewed as strong evidence toward an LD diagnosis. The logic of this more complex CP model is again clear: If a student has low achievement in an academic subject area, along with comparable deficits in cognitive abilities that are necessary for achievement in that area, while his or her other cognitive abilities are intact, there appears to be a specific learning *dis*ability (shown in the cognitive deficit) that "explains" the low academic achievement.

In contrast to the CP approach, the RTI approach must be understood in an indirect way, since it is not designed *primarily* to identify students with LD. Instead, RTI is an approach to schoolwide academic skill development, applicable (in theory) to all students. Specific RTI models, like specific CP models, vary widely, but they share many common elements. First, all students in a school are taught academic skills within high-quality, research-based curricula, and the students' skill levels are closely monitored. Next, students whose academic skills are not showing sufficient growth over time are identified, and these students are given more intensive instruction (this is an *intervention* given to students who are not responding appropriately to the same instruction that their peers are responding to). These identified students continue to have their academic skills monitored, and if the skills are still not showing sufficient growth, the students are given still more intensive, individualized instruction. Only when a student repeatedly fails to respond to instruction is an LD diagnosis considered.

In a sense, the major difference between the CP and RTI approaches is the issue of timing: In the CP approach, interventions are given after an LD diagnosis is made on the basis of CP data, whereas in the RTI approach, interventions are given as part of the process to determine if an LD is present. Similarly, in theory the two approaches could easily be integrated, since interventions can be attempted early, after low achievement is noticed; a comprehensive evaluation could be done only if a student fails to respond to the interventions (Hale, Kaufman, Naglieri, & Kavale, 2006).

However, despite the close connections and potential for integration, many logistical issues divide CP and RTI proponents. For instance, CP proponents tend to prefer extensive norm-referenced measures of cognitive and academic skills, whereas RTI proponents usually advocate monitoring academic skills through brief curriculum-based "probes" that measure very specific skills, using materials very similar to those used during instruction. More generally, CP proponents often come from a neuropsychological conception of LDs, whereas RTI proponents come from a behavioral approach to education.

The differences between CP and RTI proponents have led to considerable debate over the past decade (e.g., Batsche, Kavale, & Kovaleski, 2006; McKenzie, 2009; Reynolds & Shaywitz, 2009). At times the debate has been heated, with the two sides seeming to talk past each other, and occasionally even accusing each other of questionable motives. CP proponents have argued that RTI procedures are incapable of identifying LDs, since LDs are defined in terms of deficiencies in basic psychological processes that RTI procedures do not measure. Meanwhile, RTI proponents have argued that the measures used by CP proponents have little or no clinical utility, since poor readers (or students who are poor at math or writing) need intensive remediation regardless of their cognitive profiles, and evidence-based interventions should be used to promote skill development regardless of one's cognitive profile. We ourselves see strengths and weaknesses in each position, and although a detailed discussion of the advantages and disadvantages of CP and RTI models is beyond the scope of this chapter, we note the distinction because LDs are unique among disorders covered in this text. They are more often identified by schools than by private practitioners, and they are more often identified by using procedures from special education regulations than by using clinical criteria.

Finally, we note a diagnostic approach that seems to best encapsulate the operationist conception of LDs: the low achievement approach. For example, Siegel (1992) suggested that an achievement score (e.g., reading) below the 25th percentile could be used to indicate an LD in reading. More recently, Dombrowski, Kamphaus, and Reynolds (2004) have advocated for a cutoff at the 16th percentile. An achievement test standard score below 85, along with impairment in the real-world academic setting, would be sufficient to identify an LD, once certain other causes of low achievement

(e.g., intellectual disability) are ruled out. Dombrowski and colleagues argue that such a method would be relatively easy to apply systematically and would obviate many of the problems associated with discrepancy approaches. Furthermore, the LA approach would target those students in most need of educational assistance. Interestingly, of the three approaches noted in this section, the new DSM-5 definition discussed next seems most aligned with the LA method—that is, an emphasis on both low achievement test scores and functional academic impairment.

DSM-5 Definition of Specific Learning Disorder

The APA has historically used the terms "learning disorders" and "academic skills disorders" in its DSM to identify LDs. In the most recent version, DSM-5 (APA, 2013), the term has been changed to "specific learning disorder" (SLD). This modified diagnostic category now has four criteria, and may cause impairment in up to three domains: reading, mathematics, and written expression. Another diagnostic specifier in the recent version has to do with rating the severity of the disorder as mild, moderate, or severe. The exact criteria are provided in Table 14.1.

As in previous definitions, SLD is still believed to be a neurodevelopmental disorder that produces cognitive abnormalities, which underlie learning deficiencies in reading, writing, and math. The basis for the diagnosis, however, is not biological; rather, it is supposed to result from a synthesis of developmental, familial, educational, medical, and school report evidence, along with psychoeducational assessment. One change from DSM-IV-TR (APA, 2000) is the focus on "symptoms" (Criterion A) of difficulties in learning keystone academic skills (e.g., reading words or spelling inaccurately, excessive grammar or punctuation errors, problems with applying math facts and solving math problems). This criterion is much more detailed than it was in DSM-IV-TR. The focus is on problems that can be observed, described, specified, and measured. In this spirit, it should be noted that there no longer is a subcategory of "learning disorder not otherwise specified." Instead, the academic skill areas as explicitly noted in DSM-5 are assumed to be exhaustive, and a student without skill deficits in any of those areas does not have SLD.

Also, the new DSM-5 definition puts more emphasis on the impairment of academic skills (Criterion B). This criterion moves DSM-5 in line with the Americans with Disabilities Act (ADA) standard for determining a disability. The criterion states that "affected academic skills are substantially and quantifiably below those expected for the individual's chronological age" (APA, 2013, p. 67). This essentially is the "average-person standard" that has been applied in disability discrimination law for years. DSM-5 no longer takes the position that a person's impairment is related to his or her IQ or level of schooling. In other words, an academic achievement score is not compared to an IQ score (the outdated discrepancy notion), or to the achievement of peers attending law or medical school. The guidelines further suggest that academic skills that are well below average should be at least 1.5 standard deviations below the population mean (standard score of <78, or below the 7th percentile). A more lenient threshold can be considered when "learning difficulties are supported by converging evidence from clinical assessment, academic history, school reports, or test scores" (APA, 2013, p. 69). It should be noted that the DSM-5 definition does not directly discuss use of the IQ–achievement discrepancy model, and only indirectly addresses the RTI model. Its statement that the diagnosis is formulated from a clinical synthesis of information seems to encompass all possible sources of information and avoid the argument of what diagnostic model works best. That said, the focus on impairment (well below average) in achievement relative to one's age level, instead of one's aptitude, seems to align with the position of Dombrowski and colleagues (2004) and against the discrepancy model.

This version of the definition also seems to put less emphasis on age of diagnosis (Criterion C) than some other definitions do, noting that learning difficulties may not become fully manifest until academic demands exceed one's capacities. This seems to suggest that a person might first receive the SLD diagnosis in college or graduate school. The definition also seems to imply that a "mild" SLD may be present even if the student has compensated or functioned well in school with appropriate accommodations and support services. This is similar to the ADA Amendments Act of 2008 regulations, which argue that a person may still have a disability even if mitigating measures (e.g., accommodations, interventions, medications) allow the person to function normally.

In addition to these changes, Criterion D essentially covers all exclusionary criteria: It states that the learning difficulties must not be the result of intellectual

TABLE 14.1. DSM-5 Diagnostic Criteria for Specific Learning Disorder

A. Difficulties learning and using academic skills, as indicated by the presence of at least one of the following symptoms that have persisted for at least 6 months, despite the provision of interventions that target those difficulties:

1. Inaccurate or slow and effortful word reading (e.g., reads single words aloud incorrectly or slowly and hesitantly, frequently guesses words, has difficulty sounding out words).
2. Difficulty understanding the meaning of what is read (e.g., may read text accurately but not understand the sequence, relationships, inferences, or deeper meanings of what is read).
3. Difficulties with spelling (e.g., may add, omit, or substitute vowels or consonants).
4. Difficulties with written expression (e.g., makes multiple grammatical or punctuation errors within sentences; employs poor paragraph organization; written expression of ideas lacks clarity).
5. Difficulties mastering number sense, number facts, or calculation (e.g., has poor understanding of numbers, their magnitude, and relationships; counts on fingers to add single-digit numbers instead of recalling the math facts as peers do; gets lost in the midst of arithmetic computation and may switch procedures).
6. Difficulties with mathematical reasoning (e.g., has severe difficulty applying mathematical concepts, facts, or procedures to solve quantitative problems).

B. The affected academic skills are substantially and quantifiably below those expected for the individual's chronological age, and cause significant interference with academic or occupational performance, or with activities of daily living, as confirmed by individually administered standardized achievement measures and comprehensive clinical assessment. For individuals age 17 years and older, a documented history of impairing learning difficulties may be substituted for the standardized assessment.

C. The learning difficulties begin during school-age years but may not become fully manifest until the demands for those affected academic skills exceed the individual's limited capacities (e.g., as in timed tests, reading or writing lengthy complex reports for a tight deadline, excessively heavy academic loads).

D. The learning difficulties are not better accounted for by intellectual disabilities, uncorrected visual or auditory acuity, other mental or neurological disorders, psychosocial adversity, lack of proficiency in the language of academic instruction, or inadequate educational instruction.

Note: The four diagnostic criteria are to be met based on a clinical synthesis of the individual's history (developmental, medical, family, educational), school reports, and psychoeducational assessment.

Coding note: Specify all academic domains and subskills that are impaired. When more than one domain is impaired, each one should be coded individually according to the following specifiers.

Specify if:

315.00 (F81.0) With impairment in reading:

Word reading accuracy
Reading rate or fluency
Reading comprehension

Note: *Dyslexia* is an alternative term used to refer to a pattern of learning difficulties characterized by problems with accurate or fluent word recognition, poor decoding, and poor spelling abilities. If dyslexia is used to specify this particular pattern of difficulties, it is important also to specify any additional difficulties that are present, such as difficulties with reading comprehension or math reasoning.

315.2 (F81.81) With impairment in written expression:

Spelling accuracy
Grammar and punctuation accuracy
Clarity or organization of written expression

315.1 (F81.2) With impairment in mathematics:

Number sense
Memorization of arithmetic facts
Accurate or fluent calculation
Accurate math reasoning

(continued)

TABLE 14.1. *(continued)*

Note: *Dyscalculia* is an alternative term used to refer to a pattern of difficulties characterized by problems processing numerical information, learning arithmetic facts, and performing accurate or fluent calculations. If dyscalculia is used to specify this particular pattern of mathematic difficulties, it is important also to specify any additional difficulties that are present, such as difficulties with math reasoning or word reasoning accuracy.

Specify current severity:

Mild: Some difficulties learning skills in one or two academic domains, but of mild enough severity that the individual may be able to compensate or function well when provided with appropriate accommodations or support services, especially during the school years.

Moderate: Marked difficulties learning skills in one or more academic domains, so that the individual is unlikely to become proficient without some intervals of intensive and specialized teaching during the school years. Some accommodations or supportive services at least part of the day at school, in the workplace, or at home may be needed to complete activities accurately and efficiently.

Severe: Severe difficulties learning skills, affecting several academic domains, so that the individual is unlikely to learn those skills without ongoing intensive individualized and specialized teaching for most of the school years. Even with an array of appropriate accommodations or services at home, at school, or in the workplace, the individual may not be able to complete all activities efficiently.

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disability, sensory deficits, other medical or neurological conditions (e.g., pediatric stroke), lack of language proficiency, psychosocial adversity, or inadequate educational instruction. These exclusionary criteria are discussed separately below.

LD Identification in Special Education

As a special education policy category, LD is governed by the Individuals with Disabilities Education Improvement Act of 2004 (still abbreviated as IDEA; Public Law No. 108-446), as well as state and local educational agencies' regulations. IDEA still uses a conception of LD from the federal definition reviewed earlier (i.e., "a disorder in one or more of the basic psychological processes"), but whereas earlier versions of IDEA had prescribed use of the "severe discrepancy" method of identification, the 2006 regulations for implementing IDEA make clear that states "must not require the use of a severe discrepancy between intellectual ability and achievement" (34 C.F.R. §300.07(a)). The regulations further indicate that states must permit RTI methods and *may* permit "other alternative research-based procedures" for LD identification. In essence, states can either require that schools use RTI, and *must* at least permit RTI as an alternative (Herr & Bateman, 2013). Moreover, states can still use an IQ–achievement discrepancy to classify a student as having LD; they just can't use the lack of a discrepancy to stop identification of a student.

Exclusionary Factors

Intellectual Disability

Every significant definition of LD has incorporated exclusionary criteria that should be addressed in order to "rule out" conditions that could cause the same symptoms of a learning disorder. These include intellectual disability, sensory acuity loss, other mental or neurological disorders, lack of language exposure/proficiency (e.g., English as a second language [ESL]), psychosocial adversity, or inadequate educational instruction.

We have used the phrase "unexpected academic underachievement" to distinguish LD from other causes of learning failure, such as intellectual disability, global developmental delay, or autism spectrum disorder. For example, intellectual disability often limits one's capacity to read, write, and compute; however, this is not regarded as an LD because the limitations in academic achievement are not specific, but are part of a generalized delay in cognitive development. Thus intellectual disability must be ruled out before the LD diagnosis can be made. In this regard, knowledge that a person's intellectual ability is at least within the average range is needed to make a diagnosis. There is no boundary on the high end of the IQ continuum, so most

people believe that even an intellectually gifted individual could theoretically meet criteria for LD, *if* his or her academic skills were low when compared to age expectations, not just low for IQ expectations. As noted in DSM-5 and by various scholars, students with valid LD diagnoses should demonstrate functional impairment in comparison to their same-age peers (see Gordon, Lewandowski, & Keiser, 1999; Lovett & Lewandowski, 2006). In summary, high IQ is not considered to be an exclusionary factor, whereas low IQ ($<70 \pm 5$) is exclusionary.

Sensory Disorders

It should be fairly obvious that totally deaf and/or blind individuals will have learning challenges. Even students with various lesser hearing impairments have been shown to experience reading problems. Research has shown that hearing-impaired children tend to have weaker vocabulary (e.g., Pittman, Lewis, Hoover, & Stelmachowicz, 2005) and lower levels of reading comprehension (e.g., Traxler, 2000) than peers. In fact, Wauters, Van Bon, and Tellings (2006) found that only 4% of their hearing-impaired Dutch sample (ages 7–20) was reading at an age-appropriate level. Similarly, a number of visual conditions other than total blindness (e.g., strabismus, color-blindness) can interfere with typical instructional methods and learning. Of course, there are theories of reading disabilities that are based on visual (e.g., visual tracking, contrast sensitivity) and auditory (e.g., temporal auditory processing) system dysfunction. The task of the LD diagnostician is to rule out primary sensory disorder (e.g., acuity loss), yet still consider the possibility that auditory or visual processing problems underlie an LD. DSM-5 suggests ruling out uncorrected visual or auditory acuity losses as explanations for SLD, while ruling in other perceptual explanations.

Mental Health Disorders

As noted above, an LD diagnosis must be differentiated from normal variations in academic achievement and from other disorders that might trigger learning difficulties. Clearly, intellectual disability and severe sensory deficits (e.g., blindness) can significantly impede learning. But in these cases there is another primary disability responsible for the learning problems. Perhaps less obvious would be learning difficulties related to other mental health disorders, such as attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder, anxiety disorders, depression, or conduct disorder. Students may suffer from one or more of these disorders, each of which is capable of having a negative impact on learning. For example, ADHD does not always cause academic achievement problems, but in an estimated 20–30% of cases there is sufficient evidence to diagnose both disorders (see Barkley, 2006). Similarly, some students with autism spectrum disorder may also qualify for the LD diagnosis if their academic problems are not based on IQ, communication deficits, or lack of appropriate instruction. Although a careful assessment may be able to make sound differential diagnoses and determine whether LD exists over and above another disorder, the picture is clouded by secondary mental health effects that often accompany LD. Considerable research has shown that students with LD are at greater risk for behavior problems (e.g., Hinshaw, 1992), social problems (e.g., Swanson & Malone, 1992), anxiety (e.g., Nelson & Harwood, 2011), low academic self-concept (e.g., Bear, Minke, & Manning, 2002), and poor motivation (e.g., Bender & Wall, 1994), as well as symptoms of clinical maladjustment and depression (e.g., Martinez & Semrud-Clikeman, 2004). These findings complicate the diagnostic decision, as the evaluator must decide whether the mental health disorder is primary, secondary, or co-occurring. This is probably the most difficult of the exclusionary criteria to assess.

Lack of Adequate Instruction

A recent report by UNICEF (see *www.unicef.org/factoftheweek/index_45364.html*) indicates that the number of children currently not attending school worldwide is 72 million, many of whom are receiving no formal education. Certainly it makes no sense to label students as having LDs if they are not receiving an education. Similarly, it is argued that children whose instruction has not been adequate should be excluded from the LD category. Of the different exclusionary criteria for LDs, instructional factors have been the least frequently examined, but are perhaps the most important. The opportunity-to-learn exclusion presumed that the field has a good understanding of what constitutes adequate instruction. At the time the federal definition was adopted, this was not the case. Consensus reports (National Reading Panel, 2000; Snow, Burns, & Griffin, 1998) have since made it clear that we do know a lot about teaching children to read. At least in reading,

which accounts for most forms of LD, consideration of the students' response to high-quality intervention should be part of the definition of LD.

Here again, the RTI model directly addresses this exclusionary factor, whereas the discrepancy model does not. A central tenet of an RTI approach is that adequate universal instruction is provided and student progress is frequently evaluated. Students who do not make satisfactory progress continue to be monitored while deficient skills are more specifically targeted with evidence-based interventions. If a student does not respond to these interventions, more intensive interventions are applied with integrity. Through this process of tiered interventions of increasing specificity and intensity, the question of adequate instruction should be well addressed. All of this assumes that the RTI model is being implemented appropriately and comprehensively. If so, we should have some assurance that a student's lack of academic progress is not due to inadequate instruction, leaving open the possibility that an LD exists.

Psychosocial Adversity

Although all current definitions of an LD state that the academic deficits encompassed by the disorder cannot be attributed to economic disadvantage and cultural factors (including race or ethnicity), limited information exists regarding how race, ethnicity, and cultural background might influence school learning in general and the expression of different types of LDs in particular. Wood, Felton, Flowers, and Naylor (1991) conducted a longitudinal study of specific LDs (in reading) within a random sample of 485 children selected in the first grade and followed through the third grade. They found that at the first-grade level, race did not appear to be an influential variable in reading development once vocabulary ability was accounted for. However, by the end of the third grade, race had become a significant predictive factor even when the most powerful predictors—first-grade reading scores—were also in the prediction equation. In attempting to understand this race effect, they assessed a number of additional demographic factors, including parental marital status, parental education, parental status as a welfare recipient, socioeconomic status (SES), the number of books in the home, and occupational status. The presence of any or all of these demographic variables in the prediction equation "did not remove the race effect from its potency as an independent predictor of third-grade reading" (Wood et al., 1991, p. 9).

There has been a long-standing issue of disproportionality with regard to race and disability categorization, as well as participation in special education programs. For example, a report on the condition of education by Planty, Hussar, and Snyder (2009) indicated that Native American, African American, and Hispanic groups were at greater risk for the LD category than European Americans or Asian Americans. In part, the differences may be related to minority status that is linked to socioeconomic disparities, including poverty, restricted access to health services, or adverse social conditions (Donovan & Cross, 2002; Hosp & Reschly, 2004; Oswald, Coutinho, & Best, 2002). This possible "diagnosis bias" could be partly a result of non-LD factors that lower academic achievement, and in an effort to get such children extra assistance, the LD category is applied (inaccurately) by a school system.

A major issue in all of this is that environmental variables that are excluded as potential influences on LD can and do interfere with the development of cognitive and linguistic skills that may lead to low achievement (Lyon et al., 2001). Parents with reading problems, for example, may find it difficult to establish adequate home literacy practices because of the cumulative effects of their reading difficulties (Wadsworth, Olson, Pennington, & DeFries, 2000). Children who grow up in economically disadvantaged environments are already behind in language development when they enter school (Hart & Risley, 1995). This delay may interfere with the development of reading, writing, and math skills. Thus the assessment of LD should carefully parse social, economic, and cultural factors from cognitive characteristics known to define true LDs. This is a problem for the LA model of LD categorization.

Language Proficiency

In 2011, English language learners (ELLs) made up 10% of public school students (approximately 4.7 million students in grades K–12) in the United States (Aud et al., 2011). This is a large number of students who have varying degrees of English language proficiency, and certainly a proportion of these students struggle with academic work, including taking standardized tests. This struggle continues throughout development, as shown by Hendricks (2013), who compared college students who learned English as a first versus second language (ESL) on a host of reading-related variables. She found that the ESL students tended to perform less well than native English speakers on measures of read-

ing speed, vocabulary, word recognition, and comprehension. These students also had much less exposure to education and reading in English. Hendricks noted that some of the achievement profiles of the ESL students looked very similar to those of college students with LDs, and that they struggled with many of the same issues. Ortiz (2011) has written about the problems of differential diagnosis among ESL students who may or may not have LDs. The legal definitions of LD, as well as DSM-5, view a diagnosis of LD as separate from a language proficiency issue. That means that academic difficulties specifically related to ESL must be ruled out of the diagnosis. It is interesting that in many states ELLs can receive test accommodations due to their language proficiency status, but this does not mean that they qualify for an LD diagnosis or special education. The LD diagnosis must be differentiated from any language proficiency problem, and that is a subject for another chapter (see Ortiz, 2010).

For children with mental deficiency, sensory disorders, and emotional disturbance, there are other classifications in IDEA that can lead to services. Likewise, students with medical and neurological disorders that affect learning can access specialized services without the need of LD identification. For children who are deemed culturally, economically, or socially disadvantaged, compensatory education programs are available. And students who are considered ELLs also can qualify for certain services according to specific state educational policies (e.g., test accommodations). Students with traumatic brain injury or ELLs should not be considered as having LDs even if there are similarities in test performance (e.g., slow reading fluency). The science of LDs is moving toward being more specific and less encompassing. Thus differential diagnosis should always be a consideration, whether it results in excluding certain conditions or acknowledging comorbid conditions.

Heterogeneity and Comorbidity

LDs are clearly domain-specific, meaning that disabilities involving reading, math, and written expression are different in terms of phenotypic descriptions and intervention needs. Although many children have more than one of these disorders, there are prototypes for subgroups of children with isolated disabilities in the domains of reading and math. The problem is that the categories in federal regulations do not line up well with the domains that have emerged from research. Moreover, this heterogeneity alone makes difficult the proposition that LDs can be subsumed under a single overarching conceptualization.

The heterogeneity of LDs is illustrated in several ways. First, it is important to recognize that many children have LDs in more than one domain, and that multiple LDs tend to produce poorer outcomes than a single LD (Martinez & Semrud-Clikeman, 2004). Second, LDs are often diagnosed in conjunction with other disorders, such as ADHD (Barkley, 2006), oppositional defiant disorder (DeLong, 1995), depressive disorders (San Miguel, Forness, & Kavale, 1996), and a host of other comorbid conditions. Third, having an LD places one at greater risk for a variety of mental health problems, including behavioral, emotional, and social difficulties that result in increased anxiety, lower academic self-concept, and more peer rejection (Gadeyne, Ghesquiere, & Onghena, 2004). The various types of LDs, the different ways in which they are expressed, and the range of concomitant variables make this diagnostic category one in which no two individual profiles are alike. This heterogeneous expression of LDs may parallel the finding that "generalist genes" are associated with LDs. That is, the same genes responsible for LDs are also responsible for normal variation in learning abilities, affect various aspects of the disabilities, and are likely to affect multiple areas of learning (Plomin & Kovas, 2005). It seems that both the genotypic and phenotypic sides of LDs are multiple, general, and variable. It is no wonder that assessment and treatment have become increasingly individualized.

As noted in the DSM-5 definition of SLD (see Table 14.1), certain LD subgroups have been identified in research. These subgroups include several forms of reading disabilities, involving word recognition, comprehension, and fluency; various forms of math disabilities, involving understanding of number concepts, calculation accuracy/fluency, and reasoning; and disorders of written expression, which include technical issues such as grammar and punctuation, poor spelling (possibly related to poor phonology and a reading disorder), and difficulties with writing clarity, organization, and quality. The following sections review research knowledge on these three domains of LDs, as well as specific subtypes.

Before covering these specific subtypes, we should discuss briefly an LD construct not covered in detail: nonverbal learning disability (NVLD, also called nonverbal learning difficulty or disorder). NVLD is primarily associated with the work of Rourke (e.g., 1989)

and is said to involve deficits in reading comprehension, mathematics, and early handwriting skills, as well as social/emotional skills (Hulme & Snowling, 2009). The cognitive/neuropsychological theory underlying NVLD is that some kind of right-hemisphere dysfunction is present, leading to all of the (seemingly unrelated) deficits (Pennington, 2009).

There are many scholars who continue to promote the NVLD construct as a useful clinical diagnosis (e.g., Casey, 2012), while other scholars question its validity and clinical utility (e.g., Spreen, 2011). Certainly the key question is whether NVLD exists as something more than a set of comorbid disorders that are already well characterized under other labels (Pennington, 2009). While we await further research to determine this, we stand by our operationist position elucidated earlier in the chapter. Since we view LDs primarily in terms of their symptoms and consequent impairment, we place less emphasis on labels and encourage clinicians to describe a child's deficits in concrete, detailed terms, rather than using terms like NVLD to "explain" the deficits.

READING DISABILITIES

General Definitional Issues

According to the Centers for Disease Control and Prevention (Boyle et al., 2011), the prevalence of LDs in children ages 3–17 years from 1997 to 2008 was 7.66%. It is estimated that most of these students have reading disabilities. Lerner (1989) reported that 80% of all children served in special education programs have problems with reading, while Kavale and Reese (1992) found that over 90% of children in Iowa with the LD label had reading difficulties. Both studies indicated that most children who have reading problems experience difficulty with word-level skills. Not surprisingly, we have considerably more research-based knowledge about reading disabilities—including neurobiological and cognitive correlates, subtypes, and core characteristics, as well as evidence-based, effective intervention methods—than about other types of LDs.

As noted in federal guidelines (e.g., IDEA), there are two broad forms of reading disabilities. One involves more basic reading problems, such as difficulty understanding the relationships among sounds, letters, and words; another involves difficulties with reading comprehension, due to an inability to grasp the meaning of words, phrases, and paragraphs. These forms of reading disabilities may be manifested in problems with recognizing or decoding letters and words; with reading speed and fluency; or with various forms of comprehension of words (i.e., vocabulary), sentences, or text. Much of the research happens to be centered on three aspects of reading: word recognition, fluency, and comprehension; as such, this section is organized around these three reading subdomains. Before we begin, it should be noted that terms such as "reading disability," "reading disorder," and "dyslexia" generally mean the same thing. From here on in this chapter, we generally use the term "reading disability" (RD).

Word Recognition

Definitional Issues

Reading is a developmental process that starts with recognizing letters and attaching certain sounds to them. Children are taught the letters of the alphabet, the different sounds letters can make, and the symbol–sound combinations made by certain letter strings. Children are also taught to recognize short words and associate the picture/shape of each word with its pronunciation, as well as with a pictorial representation of the meaning of the word. The hope is that students will learn to associate visual symbols with sound representations, so they can immediately sound out words or decode a string of letters part by part until the word is fully read. Because letters can make more than one sound, students have to learn rules of phonics and apply them in order to decode words. The accuracy and fluency with which these sound–symbol combinations can be made often differentiates the skilled from the less skilled reader. We have known for some time that individuals with RDs have difficulty with this process, such as reading pseudowords (Bruck, 1988; Siegel & Ryan, 1988).

Experts refer to this ability to read words as "word recognition" or "word decoding." In some cases, word reading is referred to as "sight word reading." Here the student may rely on familiarity with the orthography of the word and make an automatic recognition; alternatively, the student may apply rules of phonics to "sound out" or decode the word. It would appear that sight and sound approaches are interdependent, and that reliance on one or the other may have to do with the type and familiarity of the word being read.

Obviously, even these basic reading skills depend on certain intact sensory and perceptual processes. A

good reader needs intact vision and eye movements, as well as hearing and auditory processing. There are theories of RDs built around the dysfunction of basic visual and auditory processes, and we discuss these in more detail below. But as noted in the National Reading Panel (2000) report and in most of the reading literature since that report, phonological explanations for RDs have primacy over visual explanations, and phonics-based interventions have shown more efficacy than visually based reading approaches (National Reading Panel, 2000; Swanson, 1999). The English language is a phonologically based system; thus phonological awareness, processing, and memory have become important constituents of the RD assessment and intervention endeavors.

The emphasis on phonological processing issues as underlying RDs may be related to another well-established comorbidity with RDs: Research has confirmed a relationship between speech and language deficits and RDs, with the former typically preceding emergence of the latter (Catts, Adlof, Hogan, & Weismer, 2005; Liberman, Shankweiler, & Liberman, 1989; Scarborough, 1990). In fact, the commonality of LDs in reading, writing, spelling, speaking, and math word problems has tempted some authors to theorize that LDs constitute a set of language-based disorders (Vellutino, 1979). Whether or not one adopts this position, there certainly is no denying the connection between phonological deficits and RDs. Studies have noted that phonological deficits persist into adulthood (Bruck, 1992; Ransby & Swanson, 2003). To be more specific, Swanson (2013) recently synthesized results from several meta-analytic studies of RDs, and he concluded that difficulties on measures of phonological processing, naming speed, and verbal memory are pervasive across age.

Developmental Course

RDs in general reflect persistent deficits rather than a developmental lag in linguistic and reading skills (Francis, Shaywitz, Stuebing, Shaywitz, & Fletcher, 1996; Lyon, 1994). For example, longitudinal studies have shown that of children classified as having RDs in the third grade, 74% remained thus classified in the 12th grade (see Shaywitz, 2003). Others have shown that word-reading difficulties persist in adults with RDs, as do underlying phonological processing deficits (Ransby & Swanson, 2003). Clearly these data reflect a pessimistic outcome for youngsters with LDs who have difficulties learning to read.

At least three factors could be responsible for the lack of progress made by students with early phonological deficits. First, most of these students were identified through the use of a discrepancy between IQ and reading achievement in the eligibility process, and many children are not thus identified until the third grade—the point at which their achievement has suffered enough to demonstrate the required discrepancy between the ostensible predictor (IQ) and reading skills. It is not coincidental that the largest increase in those eligible for special education in the LD category occurs in the 12- to 17-year age range. As Fletcher and colleagues (1998) have indicated, initiating intervention after a child has failed for 2–3 years does not bode favorably for realistic gains in reading. Rojewski and Gregg (2011) have noted that a significant number of adults with LDs lack the print and/or digital media skills necessary for success in postsecondary schools.

Second, teaching interventions that are most efficacious for readers with LDs are only now being systematically implemented in most schools. Moreover, many of the children followed in longitudinal studies were provided with several different types of interventions, without attention to how these intervention effects may have interacted. Given this lack of systematic program planning and teaching, it is not surprising that only 20–25% of children made gains in reading.

Third, it is quite possible that the motivation to learn to read diminishes with time, given the extreme effort that many readers with RDs put into the learning process without success, resulting in protracted periods of failure. As we know from meta-analyses (Camilli, Wolfe, & Smith, 2006; Hammill & Swanson, 2006; National Reading Panel, 2000), the treatment effect sizes for reading interventions in children are modest (d = 0.12–0.41), and these do not consider issues of maintenance and generalization of improved reading skills. Unfortunately, we know much less about the development of reading skills in adults or the efficacy of targeted intervention programs for them. This is certainly an area that begs for attention.

Core Processes

As could be expected, given the continuous and heterogeneous distribution of reading behaviors associated with reading abilities and disabilities, both single-cause

and multiple-cause theories have been advanced to represent the nature and etiologies of RDs. The hallmark academic deficits characterizing children with RDs are difficulties in decoding and the ability to read single words (Lovett, Barron, & Frijters, 2013; Olson, Forsberg, Wise, & Rack, 1994; Perfetti, 1985; Stanovich, 1986). These lead to the profound disturbance of reading ability that forms the core of most types of RDs. Stanovich (1994) places the substantial importance of word recognition vis-à-vis reading comprehension within the following perspective: "Reading for meaning [comprehension] is greatly hindered when children are having too much trouble with word recognition. When word recognition processes demand too much cognitive capacity, fewer cognitive resources are left to allocate to higher-level processes of text integration and comprehension" (p. 281). One could certainly argue that timed passage reading comprehension may be the biggest problem confronting poor readers because it encompasses the need for accurate word reading, fluent text reading, and working memory, as well as understanding of word, sentence, and passage meanings. Of course, it makes sense that the most complex and subsuming reading function will elicit the most difficulty for an impaired reader, whether the underlying problem is decoding, fluency, or understanding. Only recently have researchers been systematically treating these underlying processes collectively within an RTI approach (see Vaughn, Swanson, & Solis, 2013).

Despite our understanding of the complexities of reading, it is not surprising that the ability to read single words accurately and fluently has been the most frequently selected research target in the study of RDs (see Fletcher et al., 2007). Again, and as we discuss later, this is not to diminish the role of reading comprehension as an academic and cognitive skill to be taught and acquired. However, word recognition is not only a prerequisite behavior to comprehension; it is a more narrowly circumscribed behavior and is not related to the numerous nonreading factors typically associated with comprehension (Wood et al., 1991). Therefore, it offers a more precise developmental variable for study. With students in middle and high school, there seems to be a greater need to provide concurrent instruction in word reading and text comprehension (see meta-analysis by Edmonds et al., 2009). Presumably, as word-decoding skill improves, it should account for less of the variance in overall reading ability, while reading comprehension takes on greater salience.

PHONOLOGICAL PROCESSING

There seems to be wide agreement that a core deficit in RD involves faulty phonological processing, including difficulties in detecting, matching, segmenting, blending, combining, and manipulating the 44 phonemes in the English language (Blachman, 1997, Liberman & Shankweiler, 1991). Early reading instruction, especially phonics training, relies heavily on the integrity of students' phonological processing abilities, and assessments of early reading progress have historically focused on these subskills (e.g., Boder, 1971; Good & Kaminski, 2002; Lindamood & Lindamood, 1998; Wagner, Torgeson, & Rashotte, 1999). We know that early problems with phonological decoding can persist into adulthood (Bruck, 1992) and that the gap between poor and good readers tends to widen over time (Rayner, Foorman, Perfetti, Pesetsky, & Seidenberg, 2001). Thus, it is important to address these deficits early and intensively.

RAPID AUTOMATIZED NAMING

A somewhat related underlying core deficit in RD seems to be impairment in rapid automatized naming (RAN). Research on cognitive factors associated with RD have shown that such students exhibit difficulties in rapidly (and automatically) naming letters, pictures, objects, colors, and words (e.g., Korhonen, 1995; Scarborough, 1998; Semrud-Clikeman, Guy, Griffin, & Hynd, 2000). Furthermore, RAN has been shown to predict reading growth and other reading outcomes (Manis, Seidenberg, & Doi, 1999). The problem seems to be a lack of automaticity in quickly naming a particular stimulus. Bowers and Wolf (1993) explained the deficit as a problem in the temporal integration of the visual and auditory stimuli. In other words, a student is unable to attach a letter or word sound automatically and quickly to a visual stimulus (i.e., a letter, word, or object). RAN has become a common task in reading assessment batteries such as the Comprehensive Test of Phonological Processing (Wagner et al., 1999), though it has spawned more assessment tasks than it has specific reading interventions. There has been some debate about the RAN construct, especially concerning whether it is distinct from phonological processing and contributes independent variance in the prediction of reading deficits (see Vukovic & Siegel, 2006). Because deficient RAN is essentially a speed deficit, it may be

more related to reading fluency than accuracy. In their review of the role of RAN in reading, Georgiou, Parilla, Cui, and Papadopoulos (2013) concluded that RAN has been shown to strongly predict reading acquisition, and continues to predict reading performance after speed of processing has been controlled. They also noted that RAN can be a cognitive marker for RDs, in addition to phonological awareness and other variables.

VISUAL PROCESSING DEFICITS

For many years there have been attempts to tie visual-perceptual difficulties to RDs (Cruickshank & Hallahan, 1973; Frostig, Lefever, & Whittlesey, 1964; Kephart, 1971; Vellutino, 1979). In fact, prior to 1980, visual-deficit-based explanations for dyslexia tended to dominate the literature. However, while it is common to observe the presence of difficulties with copying or matching geometric designs in comparisons of children with and without RDs, there is little evidence that the spatial processing problems are causally linked to RDs (Vellutino, Fletcher, Snowling, & Scanlon, 2004). Most visual-perceptual theories and treatments proved untenable and fell out of favor.

This same trend is apparent with regard to sensory deficits in the visual modality as an explanation for RDs. In the visual area, there are studies using psychophysical methods involving visual persistence, contrast and flicker sensitivity, and the detection of motion thresholds; these studies are often interpreted to suggest a deficiency in the temporal processing of visual information (Stein, 2001). Such deficits have been related to specific difficulties in the magnocellular visual pathway. The magnocellular pathway is responsible for operations of the transient visual channel, which provides short, previsual responses to stimuli that are low in spatial frequency and move rapidly. In contrast, the parvocellular visual pathway is related to operations of the sustained visual channel, which provides a longer duration response to slow-moving stimuli that have high spatial frequency. In reading and other visual tasks, these two systems inhibit one another. Various findings have suggested that individuals with reading difficulties have ineffective transient system inhibition that interferes with the saccadic suppression of visual information. This leads to persistence of retinal image, so that the words on a page may seem jumbled (Lovegrove, Martin, & Slaghuis, 1986; Stein, 2001). Although it is clear that individuals with RDs differ from typically achieving individuals on measures involving the visual system, it is not clear how the magnocellular system can be involved in word recognition. The print itself is stationary, not moving. If words are jumbled when a person is scanning words, then the task would seem to involve the perception not of individual words, but of groups of words as a person reads text (Iovino, Fletcher, Breitmeyer, & Foorman, 1999). The magnocellular system operates when a person is reading continuous text; the core problem in RD involves the identification of words in isolation. Thus it is difficult to see how such a theory can explain the core reading problems associated with RDs.

Other efforts to explain the visual processing difficulties observed in children with RDs relate these difficulties to the processing of the orthographic components of written language and assume that such deficits are not related to phonological decoding. Such explanations relate to the sometimes irregular relationship of the pronunciation of words and their representation in print. It is well established that the relationship of phonology and orthography in English is sometimes inconsistent, and that English spellings are commonly irregular (Rayner et al., 2001). Thus it is hypothesized that the visual system is related to the ability to immediately process words that cannot be sounded out automatically—a representation of the dual-route theory of reading. In this theory, words can be either accessed through a phonological route or recognized immediately through a visual route that bypasses the need for phonological processing (Castles & Coltheart, 1993). Talcott and colleagues (2000) found correlations between visual motion sensitivity and orthographic processing even when variance due to phonological processing and IQ was covaried from the relationship. However, this relationship was true for all children, regardless of the presence of a disability. In addition, there was no evidence that the relationship of orthographic processing to word recognition was stronger than the relationship of phonological processing. Eden, Stern, Wood, and Wood (1995) performed similar analyses, in which they observed that measures of visual processing continued to contribute independently to prediction of reading skills after IQ and phonological processing were partialed out of the relationship; however, the amount of variance accounted for was relatively small. Therefore, it appears that visual processing hypotheses do not provide robust explanations for the core reading problems experienced by children with RDs. While the ability to form, store, and access orthographic representations of letters and words is important in reading, it appears

that neither reading deficits nor reading interventions are best addressed by singular visual approaches. Even though orthography is important, it is phonology that gets most of the attention in reading assessment and intervention.

Neurobiological Factors

The hypothesis that LDs are "unexpected" stems in part from the belief that if children who experience low achievement due to such factors as economic disadvantage and inadequate instruction are excluded from the LD category, the cause in those who have low achievement not due to the exclusions must be intrinsic to the children. The history of research on LDs from the very beginning reflects this assumption and was significantly influenced by concepts like MBD. Although the emphasis on constitutional factors is only implicit in the federal definition of LDs through the subsuming of disorders represented by MBD and brain injury, it is explicit in other definitions. To illustrate, consider the National Joint Committee on Learning Disabilities (NJCLD, 1988) definition: "These disorders [LDs] are intrinsic to the individual, presumed to be due to central nervous system damage, and may occur across the life span" (p. 1). Similarly, the World Federation of Neurology definition explicitly indicates that dyslexia is "dependent upon fundamental cognitive disabilities, which are frequently of constitutional origin" (Critchley, 1970, p. 11).

As we have noted in our review of the history of LDs, the intrinsic nature of LDs was inferred from what was then known about the linguistic and behavioral characteristics of adults with documented brain injury. As the field progressed, definitions of LDs continued to attribute them to intrinsic (brain) rather than extrinsic (e.g., environmental, instructional) causes, even though there was no objective way to adequately assess the presence of putative brain damage or dysfunction. It was believed that technology would someday resolve this mystery. This conviction was reinforced by numerous indirect associations between LDs and neurological dysfunction (e.g., less right-handedness, "soft" neurological signs, fine and gross motor incoordination, perceptual difficulties, and other characteristics seen in individuals with cerebral palsy and epilepsy), as well as by anomalies on electrophysiological measures (e.g., Duffy, Denckla, Bartels, & Sandini, 1980, Dykman, Ackerman, Clements, & Peters, 1971; Taylor & Fletcher, 1983). At this writing, the correlative connection between LD and neurobiological underpinnings is much stronger, suggesting that LDs in general and RDs in particular have a neurobiological locus (see Shaywitz & Shaywitz, 2013).

BRAIN STRUCTURE AND FUNCTION

Research on brain structure involves either postmortem studies or the use of imaging techniques such as (functional) magnetic resonance imaging ([f]MRI). There are a few postmortem evaluations of the brain anatomy of adults with a history of RD. Obviously these cases are rare, as RD is not regarded as lethal. These studies, largely by a group led by Galaburda (1993), have involved a total of 10 brains accumulated over several years. The findings indicated that individuals with dyslexia are characterized by differences in the size of specific brain structures (e.g., planum temporale) and the presence of specific neuroanatomical anomalies (Filipek, 1996; Galaburda, 1993; Shaywitz et al., 2004).

Evaluations of cortical structures in adults with a history of reading problems as children have found that the planum temporale, a structure on the plane of the temporal lobe, is symmetrical in size in the left versus right hemisphere (Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985; Humphreys, Kaufmann, & Galaburda, 1990). In postmortem studies of adults who presumably did not have reading problems, this structure is often larger in the left hemisphere than the right hemisphere (Geschwind & Levitsky, 1968). Because this area of the left hemisphere supports language function, the absence of this anatomical difference has been viewed as a partial basis for language deficiencies that should lead to reading problems. In addition, microscopic examinations of cortical architecture have shown minor focal distortions called "ectopias." While also common in individuals with no history of dyslexia, these ectopias are more common than would be expected in individuals with a history of dyslexia. They are also more common in the left hemisphere.

Altogether, postmortem studies have found clear evidence of anomalies at both subcortical and cortical levels. However, these studies are limited because the reading characteristics, educational histories, and important factors that influence brain organization, such as handedness, are difficult to ascertain in a postmortem study. For example, it is not possible to correlate the size of the planum temporale or the frequency/location of ectopias with reading performance in a post-

mortem study, so it is difficult to establish the role of these findings in causing RDs.

Given the difficulties involved in ascertaining brains for postmortem evaluation, as well as the limitations of any postmortem study mentioned above, investigators have turned to MRI/fMRI for the evaluation of potential differences in brain structure. The use of MRI is desirable because it is noninvasive and is safe for children. The addition of functional imaging has allowed the imaging of brains during various reading and other tasks, permitting further differentiation between the brains of children with LDs and of other children.

Dozens of imaging studies have been conducted in the past 10–15 years that are too numerous to review in this brief chapter. Eckert (2004) provided a review of some of these studies and noted that findings tend to support structure–function differences in the left inferior frontal gyrus, inferior parietal lobule, and cerebellum. However, he also noted that the nature of atypical anatomical findings will depend on an individual's pattern of impairments as demonstrated on measures of phonology, orthography, and fluency. Indeed, recent research has moved from general neurobiological differences between students with and without RDs to more specific brain activation differences associated with certain reading impairments in phonology and orthography (Temple et al., 2001), spelling (Richards, Berninger, & Fayol, 2009), and fluent reading (Shaywitz & Shaywitz, 2005).

Shaywitz and Shaywitz (2013) have recently summarized the research on neural systems of reading. They describe three left-hemisphere areas believed to be related to reading. These include an occipitotemporal region that specializes in visual word form, but may also serve to synthesize orthographic, phonological, and semantic inputs (Price & Devlin, 2011). This system seems to be crucial for the rapid, automatic and fluent identification of words. Another system seems to be located in the parietotemporal region. This system is where visual and auditory pathways interface (including Wernicke's area) to aid in the function of word analysis. If a word is seen and not immediately identified in the posterior system, this system is likely to assist with decoding. Wernicke's area is also noted for its role in language comprehension, so presumably this region adds meaning to words being read. In general, research investigating posterior regions of the left hemisphere in RDs shows a failure of these systems to function normally during reading tasks (Rumsey et al., 1992; Salmelin, Service, Kiesila, Uutela, & Salonen, 1996; Shaywitz et al., 2002; Temple et al., 2001). The third system involves the inferior frontal gyrus (including Broca's area). This system is believed to play roles in both word analysis and word articulation. Heim, Eickhoff, and Amunts (2008) found that this brain region was activated by tasks involving phonological, semantic, and syntactic verbal fluency. In general, the research has shown less activation of the left posterior regions in individuals with RDs, and overactivation in the frontal region (Richlan, Kronbichler, & Wimmer, 2011; Shaywitz, 2003). It is as if the more automatic posterior systems fail, and a reader with an RD must compensate by using the deliberate frontal system.

It is often assumed that reading is strictly a left-hemisphere task, but we should note studies that have found the right hemisphere to play a significant role in understanding reading disability. A number of studies have noted overactivation in the right inferior frontal gyri of individuals with RDs (Georgiewa et al., 2002; Hoeft et al., 2010; Milne, Syngeniotis, Jackson, & Corballis, 2002). It may be that in a person with an RD, greater activation in the right hemisphere is necessary to compensate for inefficiencies in left-hemisphere reading areas; or perhaps this overactivation reflects the brain needing to work a little harder to accomplish reading tasks. It seems clear that we still have a long way to go before we fully understand the neural mechanisms working and not working in the brains of individuals with RDs.

GENETICS

Genetic studies of reading ability stem from many years of observing that reading problems run in families. Reading problems clearly occur across family generations. The risk in the offspring of a parent with an RD is eight times higher than in the general population (Pennington, 1999). Yet studies of the heritability of RDs show both genetic and environmental influences (for a review, see Petrill & Plomin, 2007). As Grigorenko (2001) has pointed out, three areas of research converge in demonstrating that RDs have a heritable component. These areas involve both twin and family studies of individuals in families with members who have RDs, along with linkage studies examining the role of specific genes that congregate within families that have significant heritability.

As reviewed by Grigorenko (2001) and Olson, Forsberg, Gayan, and DeFries (1999), 25–60% of the parents of children who have reading problems also display

reading difficulties. The rate is higher in fathers (46%) than in mothers (33%). Children who have parents with reading difficulties are at much higher risk relative to the general population. The rates range from about 30 to 60%, depending on the method of ascertainment. If ascertainment depends on the parent's or school's identifying a child as having an RD, the rate is closer to 30%. If the child and parent are actually evaluated by research instruments, the rate is significantly higher.

Other approaches to twin studies of reading achievement also support the heritability of RDs. These studies have employed statistical methods that help separate the variance in reading skills according to heritability and environmental factors (see the meta-analysis by Grigorenko, 2004), showing that 45–65% of the variance in word recognition can be attributed to genetic factors, whereas approximately 69% of the variance in phonemic awareness and 75% of the variance in spelling are due to genetic factors. In addition, the studies reviewed by Grigorenko (2004) also show that both shared (9–37%) and nonshared (13–26%) environments exercise a significant influence on various reading skills.

The final item of evidence comes from linkage studies that attempt to identify specific genes related to RDs. There are dozens of candidate genetic markers, which we will not attempt to delineate in this chapter. Linkage findings in dyslexia have been relatively consistent across studies in comparison to findings for other disorders, especially for chromosome regions 1p34–p36, 6p21–p22, 15q21, and 18q11. Two candidate genes, DCDC2 and K1AA0319, seem to be of most significance for dyslexia. Both were identified through systematic investigation of LD mapping within DYX2 on chromosome 6p22 and replicated in independent samples (see review by Schumacher, Hoffmann, Schmal, Schulte-Korne, & Nothen, 2007).

The genetic studies do provide strong evidence for the heritability of reading difficulties and help explain why reading problems have always been known to run in families. It is important to recognize that the evidence suggests that environmental factors are also important. More specifically, it appears that environmental influences can moderate genetic influences on outcomes (i.e., gene–environment interaction). Petrill (2013) summarizes three possible models of gene–environment interaction: (1) Negative environmental influences catalyze underlying genetic risk, which lowers learning outcomes; (2) positive environments (e.g., high SES, teaching quality) promote higher and positive genetic influence, thus raising learning outcomes; and (3) some individuals are genetically sensitive to extremely positive or negative environments, which can differentially affect learning outcomes. There is modest research support for each of these models. In contrast, however, a recent twin study found no evidence of gene–environment interaction in reading ability (Kirkpatrick, Legrand, Iacono, & McGue, 2011). It appears that the field has a long way to go in order to specify what genes have what influence on certain types of reading phenotypes under which environmental conditions. However, given the strong link between genetics and RDs, we remain hopeful that a growing understanding of these phenomena will someday allow us to effectively detect, treat, and possibly prevent reading problems.

Reading Comprehension

Definitional Issues

Reading comprehension is defined as "the process of simultaneously extracting and constructing meaning through interaction and involvement with written language" (RAND Reading Study Group, 2002, p. 11). There is considerable research support in the elementary school population that component reading skills such as fluency, decoding skill, vocabulary, and phonemic awareness are strongly tied to reading comprehension (Braze, Tabor, Shankweiler, & Mencl, 2007; Fuchs, Fuchs, Hosp, & Jenkins, 2001; Martino & Hoffman, 2002; McKeown, Beck, Omanson, & Perfetti, 1983; Medo & Ryder, 1993; National Reading Panel, 2000; RAND Reading Study Group, 2002). Research has documented that students who perform better on measures of reading comprehension utilize more metacognitive strategies (Risemberg & Zimmerman, 1992; Ruban & Reis, 2006; Schunk, 2005; Vermetten & Lodewijks, 1997). Other factors specific to the reader that have been demonstrated to have a positive or negative impact on reading comprehension are motivation, domain knowledge, and anxiety (Cantor, Engle, & Hamilton, 1991; Engle, Cantor, & Carullo, 1992; Hembree, 1988). Lastly, we cannot forget higher cognitive processes such as working memory, strategy use, and test-taking skills.

Some studies have examined the adequacy of different models in explaining reading comprehension (Cromley & Azevedo, 2007; Gottardo & Mueller, 2009; Gough & Tumner, 1986). These models examine combinations of individual skills (e.g., decod-

ing, vocabulary, listening comprehension) that may explain individual differences in reading comprehension. One such model is the "simple view of reading" (SVR), which posits that reading comprehension is the result of a combination of decoding and listening comprehension ability (Gough & Tumner, 1986). Research has indicated that the SVR model predicts the development of reading comprehension for both native English-speaking students and ELL students (Gottardo & Mueller, 2009).

Research has demonstrated that the format used in assessing reading comprehension has an impact on what variables predict performance (e.g., vocabulary, decoding, and fluency) (Cutting & Scarborough, 2006; Keenan, Betjemann, & Olson, 2008). Keenan and colleagues (2008) found that decoding was more predictive of reading comprehension performance on tasks using a cloze method (in which a reading passage is presented to students with key words missing, and they must insert words to construct the meaning of the text), whereas listening comprehension was more predictive of performance on passage comprehension measures. This suggests that various measures of reading comprehension may not necessarily be measuring the same skill(s). Additionally, these findings suggest that the importance of different contributing factors to reading comprehension is affected by the format of the test rather than reading comprehension as a construct. These findings call into question the construct validity of some reading comprehension measures.

There is always concern about how well reading comprehension tests measure processes specific to the comprehension of written language, as opposed to other language processes that must be in place in order for reading comprehension to occur. Measures of word recognition accuracy have a relatively transparent relationship between the content of the tests and performance requirements for word reading. However, standardized reading comprehension tests differ from everyday reading contexts along several potentially important dimensions, including passage length, immediate versus delayed recall, and learning and performance requirements (Pearson, 1998; Sternberg, 1991). The available assessments vary in what a child is asked to read (sentences, paragraphs, pages); in the response format (cloze, open-ended questions, multiple-choice, think-aloud); in memory demands (answering questions with and without the text available); and in the specific aspects of comprehension that are assessed (gist understanding, literal understanding, inferential comprehension). At this time, a single assessment may not be adequate, as it is difficult to determine the source of a child's comprehension difficulties based on a single measure (Francis, Fletcher, Catts, & Tomblin, 2005).

Epidemiology and Developmental Course

Estimates of specific reading comprehension difficulties from epidemiological studies are not available. Sample-specific studies of children who have age-appropriate word recognition skills but poor reading comprehension range from 5 to 10%, depending on the exclusionary criteria used to define the groups (e.g., Cornoldi, DeBeni, & Pazzaglia, 1996; Stothard & Hulme, 1996). Leach, Scarborough, and Rescorla (2003) found that 20% of children with reading problems had specific comprehension difficulties. Unfortunately, the prevalence rates of an RD in reading comprehension are affected by the definition of the construct employed, the measures used to categorize it, the cutoff scores selected, and the extent to which the disability has been separated from general low achievement or cognitive functioning.

In general, research has demonstrated that decoding is more closely related to reading comprehension in younger readers (Braze et al., 2007; Cutting & Scarborough, 2006). Catts and colleagues (2005) found that as age and reading ability increase, vocabulary and listening comprehension become more predictive of reading comprehension. In particular, research suggests that as age and reading skill increase, vocabulary may become more predictive of overall reading comprehension (Braze et al., 2007, Cromley & Azevedo, 2007). This may be especially true for ESL students, who may struggle with English vocabulary. Braze and colleagues (2007) expanded the SVR model to include vocabulary and found that it explained unique variance in reading comprehension for older, more advanced readers (i.e., high school students), even after decoding and listening comprehension skills were accounted for.

Some have argued that poor decoding, vocabulary, and/or fluency skills cause students to read less, thus reducing their exposure to text. Their sight word vocabularies do not keep pace with those of other students, and they fall farther behind over time (Cunningham & Stanovich, 1999). This pattern has been referred to as the "Matthew effect" (Stanovich, 1986). For a number of reasons, both developmental and hierarchical, it is likely that specific reading comprehension problems

are more apparent in older children and emerge after the initial stage of learning to read.

Core Processes

Research on reading comprehension difficulties has used three major experimental designs in an attempt to identify core deficits. One design compares age-matched children who are good at decoding but poor at comprehending with children who are good at both (chronological-age design). A second design compares children who are good at decoding/poor at comprehending with younger children matched for level of reading comprehension to the older disabled children (reading-level match design). The third design attempts to train children in skills hypothesized to contribute to the reading comprehension deficit, to determine whether training actually improves reading comprehension.

The findings from the three methods are consistent. Children with good decoding/poor comprehending may have more basic deficits in vocabulary and understanding of syntax that impair their reading comprehension (Stothard & Hulme, 1992, 1996). Other studies have shown that even when vocabulary and syntax are not deficient, deficits in reading comprehension still arise (Cain, Oakhill, & Bryant, 2000; Nation & Snowling, 1998) because of difficulties with inferential reasoning and text integration, metacognitive skills related to comprehension, and working memory (Cornoldi et al., 1996; Oakhill, Cain, & Bryant, 2003). In contrast, phonological skills, short-term memory, and verbatim recall of text are typically not deficient (Cain & Oakhill, 1999; Cataldo & Cornoldi, 1998; Nation, Adams, Bowyer-Crane, & Snowling, 1999; Oakhill, 1993; Stothard & Hulme, 1992).

Reading comprehension is the ultimate goal of learning to read. It is at the end of the developmental chain of reading events, and it subsumes all reading subskills that precede and support it. So the core processes already discussed for word recognition must also underlie comprehension. Phonological processing, naming speed, orthography and sight word reading, word recognition, semantic processing, and vocabulary development all contribute to one's ability to read text and comprehend. In addition, we must now consider functions such as language skills, listening comprehension, working memory, inferencing, and metacognitive skills, all of which serve to facilitate reading comprehension.

It is well established that difficulties in listening comprehension parallel problems with reading comprehension (Shankweiler et al., 1999; Stothard & Hulme, 1996). Most studies comparing reading and listening comprehension in normative samples show high levels of overlap. Children cannot understand written language any better than they can understand oral language. It is possible that dissociations of listening and reading comprehension occur in some cases, so that reading comprehension is better than listening comprehension. This would seem most likely in older children and adults, but there is little research demonstrating these dissociations. Regardless, any language or cognitive difficulties that hinder oral language comprehension will also affect individuals' ability to read text or even to comprehend text read to them.

Neurobiological Factors

We have already discussed the neurobiological factors associated with various aspects of RDs in word recognition. There is little research in this area that focuses specifically on brain and genetic factors involved in reading comprehension. It is clear from work in neuropsychology that damage to the left hemisphere in most people can affect reading comprehension, but of course a deficit in reading comprehension could be related to phonological processing weaknesses, word-reading deficits, language processing problems, and even executive functioning deficits such as poor working memory (Cutting, Materek, Cole, Levine, & Mahone, 2009).

Within the left hemisphere, as noted earlier, there are several sites considered to show brain activation differences in those with and without RDs. The site having most research evidence seems to be an occipitotemporal region close to Wernicke's area (Richlan et al., 2011), which typically shows hypoactivation in individuals with RDs. Wernicke's area is known to subserve language comprehension functions, and damage to this area can significantly affect language comprehension. Gernsbacher and Kaschak (2003) noted that the comprehension of sentences involves Wernicke's area as well as Broca's area and superior and middle temporal regions, including homologous regions in the right hemisphere. Rimrodt and colleagues (2009) also examined brain activation via fMRI in students with and without RDs, while controlling for the influence of word recognition components of the sentence comprehension task. As in previous studies, they found that better word- and text-reading fluency were associated

with greater left occipitotemporal activation. In addition, the group with RDs showed more activation in left middle and superior temporal gyri, as well as bilateral insula, right cingulate gyrus, right superior frontal gyrus, and right parietal lobe. More specifically, activation in the right supramarginal gyrus was negatively correlated with reading comprehension. Because reading comprehension is a complex task made up of so many subskills, it makes sense that a rather extensive brain network supports this activity, and that damage in a variety of places can impair reading comprehension. It seems that less skilled readers may need to rely more on right-hemisphere functions (e.g., visualization strategies) to facilitate reading comprehension.

There is sparse research on the genetic factors involved in reading comprehension. However, the limited research seems to support some dissociation between comprehension and word reading. The genetic evidence points to both shared, or common, genetic influences and to independent influence on comprehension and word reading (Keenan, Betjemann, Wadsworth, DeFries, & Olson, 2006). These authors note that the genetic evidence seems to support the SVR model proposed by Hoover and Gough (1990). Other research (Harlaar et al., 2010) indicated that 75% of the variance in reading comprehension was due to genetic factors, 66% of which could be attributed to a unitary genetic factor and 9% to independent genetic influences related to listening comprehension and vocabulary. The genetic research suggests that reading comprehension is largely a distinct reading process that may give rise to a specific form of reading disability. These genetic findings are also consistent with the view of Nation (2005), who has suggested that comprehension and word-reading deficits are distinct from one another. It seems clear that genes play an important role in reading, and seem to be differentially involved in reading skills such as word reading and comprehension. Research has yet to tease apart the gene–environment interactions that affect comprehension, as well as how different measures of reading comprehension influence genetic findings.

Reading Fluency

The question of whether there is a subgroup of RD characterized specifically by difficulties in reading fluency is controversial. Wolf and Bowers (1999), Lovett, Steinbach, and Frijters (2000), and others have argued for a "rate deficit" group that does not have problems primarily in the phonological domain, but often has difficulties with comprehension because of a more general difficulty in rapidly processing information. The subtyping study of Morris and colleagues (1998) found evidence for a rate deficit subtype that was not phonologically impaired, but that showed difficulty on any task that required speeded processing. These tasks included measures of RAN, visual attention, and rapid articulatory movements. As Wolf and Bowers (1999) hypothesized, this subtype also had difficulties with reading fluency and comprehension, but not word recognition. More recently, Meisinger, Bloom, and Hynd (2010) also found that a significant number of children with RDs displayed reading fluency deficits but no difficulty reading single words. These students also tended to have problems with rapid naming and comprehension. In this section, we review evidence on definitional issues, core processes, and interventions pertaining to RD in fluency.

Definitional Issues

Reading fluency, as defined by the National Reading Panel (2000), is the ability to read text quickly, accurately, and with appropriate expression (prosody). Most reading fluency measures at least check on comprehension, so that the task is not merely tapping reading speed. Perhaps the most widely used measures of reading fluency in the schools involve timed passage reading. Students are asked to read instructionally appropriate reading probes/passages for 1 minute; the number of words read correctly becomes their reading rate score. These quick and content-valid measures can be used frequently to monitor students' reading fluency progress. This curriculum-based measurement approach has become standard assessment practice for RTI models (Deno, 2003).

The critical question for a rate deficit subtype is similar to that identified for reading comprehension, which is whether processes associated with accuracy of word recognition can be differentiated from speed of either word decoding or text reading. Here there is ample evidence that these are dissociable processes, and that fluency can also be differentiated from comprehension. However, all three processes are highly correlated, especially in younger children or in those who have reading difficulties. We do know that dysfluent readers have trouble with content learning (Chall, Jacobs, & Baldwin, 2009), and that dysfluency affects students' ability to comprehend (Fuchs et al., 2001). It is also believed that reading fluency difficulties persist into adulthood

even after these individuals have learned to become accurate word readers (Shaywitz, 2003). Research seems to suggest that reading fluency and word reading are distinct and related skills, and that they probably make unique contributions to reading comprehension (Meisinger, Bloom, & Hynd, 2010). However, whether there is a separate type of RD in fluency seems to be a matter of debate. It seems that the rate deficit notion is complicated by a host of factors that could influence how fast someone reads (e.g., habit, style, effort, processing speed, working memory, attention, focus on comprehension). Despite the debate, current federal and DSM-5 definitions acknowledge reading dysfluency as evidence of an RD.

Core Processes

The core process that has received the most attention in the rate deficit subtype involves RAN. In reviewing research on RAN, it should be noted that some investigators find evidence for deficiencies on any speeded process (e.g., Waber et al., 2001; Wolff, Michel, Ovrut, & Drake, 1990). However, our brief review focuses primarily on the evidence that relates RAN to reading. There are essentially three lines of evidence supporting the relationship of naming speed as a separate contribution to reading difficulties. First, naming speed tasks, especially the ability to name letters rapidly, consistently contribute independently to variance in reading achievement beyond what can be attributed to phonological awareness ability. This finding is apparent not only in studies that attempt to predict longitudinal outcomes (Schatschneider, Carlson, Francis, Foorman, & Fletcher, 2002; Wolf & Bowers, 1999), but also in studies that examine the relationship of different latent variables through confirmatory factor analysis (McBride-Chang & Manis, 1996; Wagner, Torgesen, & Rashotte, 1994). Second, there are studies that compare children who have deficits in both phonological awareness and RAN to children who have only a single deficit (Lovett et al., 2000; Wolf & Bowers, 1999). These studies show that children with "double deficits" have more severe reading difficulties than children who have only single deficits. In general, research suggests that 60–75% of individuals with LDs have RAN deficits (Norton & Wolf, 2012).

Despite this evidence, researchers argue about whether rapid naming contributes to reading achievement independently of its phonological component (Vellutino et al., 2004). Obviously, any task that requires retrieving of information with an articulatory component has to involve phonological processing. As rapid naming tasks are moderately correlated with phonological awareness measures, this appears to be a reasonable conclusion. In this interpretation, naming speed is essentially a measure of how rapidly an individual can access phonologically based codes. The alternative view is that measures of naming speed involve nonphonological processes that are also related to reading (Wolf & Bowers, 1999; Wolf, Bowers, & Biddle, 2001). In order to complete RAN tasks, it is apparent that a variety of cognitive processes may be involved. As reviewed above, RAN tests seem to contribute independently to predicting reading outcomes, relative to the contribution of phonological awareness tasks, although some researchers doubt this contribution (Vellutino et al., 2004). It does appear that the contributions are much higher if the outcome is a measure of fluency, leading some to speculate that RAN may be just a proxy for an early reading speed measure (Schatschneider et al., 2002).

The third issue involves the apparent lack of specificity of RAN measures to reading difficulties. Waber and colleagues (2001) have demonstrated that unlike phonological awareness tasks, RAN measures do not differentiate children who have difficulties in other areas. For example, children with ADHD often have difficulties on measures of RAN (Tannock, Martinussen, & Frijters, 2000). Based on these types of data, Waber and colleagues have argued that these difficulties reflect common brain-based problems with timing or rapid processing that occur across all forms of learning impairment.

Studies of children with brain injury also provide evidence that the accuracy and speed of word recognition seems to be affected by this condition. Barnes, Dennis, and Wilkinson (1999) matched children with and without traumatic brain injury on their word-decoding accuracy. Comparisons of reading rate and naming speed showed that fluency was worse in children with traumatic brain injury, paralleling observations of non-brain-injured children with rate deficits (Waber et al., 2001; Wolf & Bowers, 1999). Although it is possible to differentiate accuracy and rate components on measures of phonological awareness and RAN, more research needs to be done on the presence of a subgroup specific to reading fluency. It is clear, however, that fluency must be considered independently of word-reading accuracy in evaluating the outcomes of reading intervention studies. Many reading studies currently

focus on fluency interventions (e.g., repeated reading, listening passage previewing) as a critical target for promoting reading skills, hence acknowledging both the importance of fluency and the large number of students who struggle with it.

Neurobiological Factors

Because the fMRI methodology does not have refined temporal resolution and is not conducive to reading aloud, it has not been used to examine brain activation during reading fluency tasks. Similarly, imaging studies have not focused exclusively on individuals with fluency deficits. There is some information about brain activation and speeded naming tasks for pictures and letters. Katzir, Misra, and Poldrack (2005) found that brain activation patterns were similar for naming and word-reading tasks, including brain regions such as the left inferior frontal cortex and left temporoparietal areas. They also found activation in areas associated with eye movements and attention.

Treatment studies also have shed some light on the neurobiology of reading fluency. Shaywitz and colleagues (2004) showed that phonological interventions with children experiencing decoding problems showed increased activation in left occipitotemporal regions, and they related this change to improved reading fluency. Simos and colleagues (2007) found that intensive treatment of decoding problems resulted in the "normalization" of brain activation, corresponding to improvement in rapid word recognition ability. Thus it appears that poor reading fluency is associated with hypoactivation in certain left-hemisphere regions, and that increased, or more normal, activation is seen after treatment has improved reading fluency.

Clinical neuropsychological studies also have tried to address brain-behavior correlates of reading fluency–dysfluency. Chang and colleagues (2007) compared 10 patients with periventricular nodular hyperotopia (PNH), a rare genetic brain malformation characterized by gray matter nodules along the lateral ventricles, to 10 individuals with diagnosed RDs and 10 controls. They found that those with PNH had specific deficits in reading fluency similar to those with RDs, although those with RDs had more significant phonological impairment. They showed that structural brain anomalies can be associated with reading fluency deficits, and that the disruption of white matter structure and organization seems to correlate with this deficit. There appears to be a connection between brain function and reading fluency involving some of the same areas as word reading and comprehension, but the specific nature of these brain–behavior relationships remains to be worked out.

MATHEMATICS DISABILITIES

Definitional Issues

Deficits in math among individuals with LDs have been less extensively reported in the historical literature, though they have been noted for as long as reading difficulties have. In general, clinicians and researchers have paid less attention to children and adults with math difficulties, possibly because illiteracy has been considered to be more of a problem to society than math deficiency (Fleishner, 1994). However, since the previous edition of this chapter, the research on mathematics disabilities (hereafter usually referred to as LD-Math) has blossomed. This is appropriate, given research showing that numeracy may be even more important than literacy in the world of work, especially in the increasing number of jobs requiring quantitative skills (Geary, 2013).

Current definitions of LDs acknowledge that impairment in the ability to learn math should be considered as one of the major disorders subsumed within the category if certain inclusionary and exclusionary conditions are to be met. As noted earlier in this chapter, the federal definition of LDs refers to disabilities in mathematical calculations and concepts, whereas the NJCLD (1988) definition of LDs refers to significant difficulties in "math abilities." The DSM-5 criteria for SLD mention four areas of mathematical skills that may be deficient: number sense, memorization of arithmetic facts, calculation skills, and math reasoning skills. The *International Classification of Diseases*, 10th revision (ICD-10; World Health Organization, 1992) provides research criteria for the identification of individuals with deficits in a highly specific domain termed "specific disorder of arithmetical skills." In the ICD-10 approach, the diagnosis of disorders of arithmetical skills is appropriate when such weaknesses occur against a background of normal reading and spelling development. All these definitions of LD-Math, like definitions of LDs in reading and written expression, are based on assumptions of normal or above-average ability to learn (as assessed by IQ measures), normal sensory function, adequate educational opportunity, and absence of developmental disorders and emotional disturbance.

The controversies over defining and identifying reading disabilities extend to LD-Math as well. Adding to this dilemma is the fact that "LDs in math," "developmental arithmetic disorder," "math disabilities," and "specific math disabilities" are typically broad terms used for a variety of impairments in math skills. In addition, as Fleishner (1994) has pointed out, in some cases the term "math LD" has been used synonymously with the term "dyscalculia," to denote *specific* deficits in calculation or mathematical thinking (see also Reigosa-Crespo et al., 2012). In these situations, there is often the assumption that oral language, reading, and writing are intact (e.g., see Strang & Rourke, 1985; World Health Organization, 1992). However, math deficits are frequently associated with other LDs (Fuchs, Fuchs, & Prentice, 2004; Pennington, 2009). It is clear that disorders of math calculations occur in isolation and, by definition, involve problems with concepts. Computational difficulty is a potential marker variable for some forms of LD- Math, though the underlying core processes may be different. Less clear is whether there is a separate disorder of math concepts that cannot be explained by difficulties with reading and language. Similarly, is a disability involving both reading and math a reading disability, a math disability, or a comorbid association? These issues are addressed below.

Epidemiology and Developmental Course

Obviously, the prevalence of LD-Math depends on the identification criteria used. In their review of the literature on LD-Math, Geary, Hoard, and Bailey (2011) noted that research studies typically require that a student with LD-Math "score below the 10th percentile on standardized mathematics achievement tests for at least two consecutive academic years" (p. 44), and approximately 7% of students will meet this criterion at some point in their K–12 schooling (Geary, 2011; Geary, Hoard, & Bailey, 2011; see also Shalev, 2007, for a review of the literature on LD-Math prevalence). We would note that Geary and colleagues' classificatory criterion is more stringent than what is often seen in clinical diagnosis, where "below-average" math achievement at only one point in time may lead to an LD-Math diagnosis, and where being "below average" may be defined as below the 16th or 25th percentiles, not the 10th. Geary and colleagues refer to students who consistently score between the 11th and 25th percentiles in math as exhibiting "low mathematics achievement" instead of having LD-Math. Research suggests that the distinction is worth making, as the two groups have different cognitive profiles (Murphy, Mazzocco, Hanich, & Early, 2007).

In terms of developmental course, there is little research, and none of it has followed students for very long periods. Shalev and her colleagues have conducted important longitudinal work in Israel. A 3-year study (grades 4–7) by Shalev, Manor, Auerbach, and Gross-Tsur (1998) reported that only 47% of those with math disabilities in grade 4 met criteria for such disabilities (arithmetic scores ≤ 5th percentile) in grade 7. Stability did not seem to increase with age; Shalev, Manor, and Gross-Tsur (2005) found that only 40% of those with LD-Math in grade 5 continued to meet criteria in grade 11. Admittedly, these studies used a very stringent cutoff (the 5th percentile), and Shalev and colleagues (2005) noted that the fifth graders with LD-Math still usually had low math achievement in grade 11—just not low enough achievement to meet the cutoff. Indeed, the authors still interpreted their results as showing that LD-Math is "persistent and enduring" (p. 123).

In the United States, Mazzocco and Myers (2003) followed 209 students from kindergarten to third grade, measuring their math achievement each year with multiple tests. Students were classified with LD-Math on the basis of more liberal criteria than those used in Shalev's studies. Mazzocco and Myers found that 63% of students who met LD-Math criteria at some point in the study exhibited "persistent" LD-Math (i.e., they met LD-Math criteria for at least 2 years). Thus, with more liberalized identification criteria, somewhat better stability was found, but the stability was still sufficiently low to underscore the importance of Geary and colleagues' (2011) insistence that low scores be found in two consecutive academic years.

Core Processes

The core processes that underlie LD-Math have been studied for as long, but not as extensively, as those in RDs. Early research tended to use neuropsychological models, which focused on comparisons of children with disabilities in reading, in math, and in both that have become the preeminent paradigm in math disabilities research. This research, which is discussed below in the section on subtypes, showed that children with impairments in both reading and math had pervasive problems with language and concept formation skills (Rourke, 1993).

More recent work on LD-Math has combined research strategies from the fields of cognitive development, mathematical cognition, and LDs. The leaders in this area include Brian Butterworth, David Geary, and Michelle Mazzocco. These researchers and their collaborators have found many replicable cognitive correlates of LD-Math, some of which appear to exert causal influence over mathematical skills. We review their work below, leaning especially heavily on Geary's excellent reviews of the literature.

It is useful to distinguish between domain-general cognitive deficits (deficits in skills that are not tied uniquely to mathematics) and domain-specific deficits.

Domain-General Deficits

One domain-general skill implicated in LD-Math is working memory. Swanson has long recognized working memory deficits as a part of the cognitive profile of LDs (for a review, see Swanson & Stomel, 2012), and students with LD-Math typically exhibit these deficits. Working memory generally refers to the ability to manipulate information representations in one's mind, while maintaining other passive information temporarily. Performing mental math calculations is a typical example of a working memory task; for instance, solving the multiplication problem 24×3 without a pencil and paper would require that the results from each step of the multiplication process (e.g., $4 \times 3 = 12$) be maintained as long as necessary while performing other cognitive tasks (e.g., retrieving from long-term memory that $2 \times 3 = 6$). In Baddeley's classic model of working memory (e.g., Baddeley, 1999), there are three working memory systems: the "phonological loop," which holds representations of auditory information; the "visuospatial sketchpad," which holds representations of visual information such as the shape and color of objects; and the "central executive," which supervises the other two systems.

Children with LD-Math show deficits on measures of all three of Baddeley's working memory systems (Geary, 2011; Geary, Hoard, Byrd-Craven, Nugent, & Numtee, 2007). Deficits in central executive processes may be especially determinative of math problems, since one of the central executive's jobs is to inhibit the retrieval of inaccurate or irrelevant information from memory (e.g., responding to "What is 3 times 3?" by answering "6," since 6 is 3 *plus* 3), and as we describe below, children with LD-Math often have trouble with this inhibition. Deficits in the phonological loop and the visuospatial sketchpad appear to relate to specific types of mathematics performance that are logically related to the perceptual modality of each working memory system. For instance, problems with the phonological loop may make it difficult to temporarily store the name of one number while performing a calculation with other numbers, whereas problems with the visuospatial sketchpad may lead to problems performing math tasks that require visual representations or are aided by such representations (e.g., geometry, understanding fractions).

A second proposed domain-general deficit is in processing speed, defined as "the ability to perform simple, repetitive cognitive tasks quickly and efficiently" (Schneider & McGrew, 2012, p. 119). Students with LDs are often found to have deficits on the processing speed tasks of IQ tests (e.g., Calhoun & Mayes, 2005), and they certainly exhibit slow speed in completing academic tasks (i.e., poor academic fluency). Even so, it has been difficult to determine whether students with LD-Math have slower processing speed per se (Geary, 2013). When these students take longer to respond to problems, it could result from the students' using inefficient problem-solving strategies that would take any student longer to use. Meanwhile, studies of speed in performing very basic math tasks (e.g., counting) have shown inconsistent results; in some studies students with LD-Math show a deficit, but in other studies they do not.

Finally, we should briefly note a possible domain-general deficit in general intelligence. Intelligence predicts academic achievement well, including mathematics achievement, and so an intelligence deficit in LD-Math is at least plausible. Students with LDs have, on average, somewhat lower IQs (Kavale & Forness, 1995), although this depends in part on the LD identification method chosen. Geary (2011) notes that students with LD-Math generally have IQs in the lower area of the average range of ability (between 90 and 100), but he doubts whether this can explain much of these students' performance deficits on math tasks, since their math performance is significantly lower than that of students with general low intelligence (IQ < 10th percentile). Butterworth and Reigosa (2007) are similarly skeptical, noting that intelligence deficits cannot be a necessary condition for LD-Math, since there are cases of severe math impairments in individuals with superior IQs. Finally, we would note that examining the effects of intelligence on LD-Math is difficult, since working memory is a large part of

general intelligence (cf. Conway, Getz, Macnamara, & de Abreu, 2011).

Domain-Specific Deficits

In the same way that deficits in phonological awareness are thought to underlie many RD cases, recent research has elaborated certain cognitive deficits that are specific to the domain of mathematics and that appear to underlie LD-Math (Geary, 2013). One area of deficit involves concepts of number. For instance, typically developing children can instantly determine the quantity of sets of fewer than four items, through a process called "subitizing," in which the items are not enumerated individually (as in counting). But children with LD-Math appear to have trouble with subitizing even three items (Koontz & Berch, 1996). Moreover, once they learn symbolic representations for quantity (digits), children can quickly say which of two numbers is larger (e.g., 12 or 21), but students with LD-Math are slower and less accurate than their peers at doing so (Rousselle & Noël, 2007). Similar deficits are found in estimating which of two sets has more items (Chu, vanMarle, & Geary, 2013; Mazzocco, Feigenson, & Halberda, 2011).

A second domain-specific deficit occurs in the area of counting (Geary, 2013). To use counting accurately, children have to count following certain rules, such as always saying the names of numbers in the correct order (i.e., not counting "1, 3, 4" while enumerating three items and concluding that there are four items). Some studies have found children with LD-Math to be worse at detecting violations of proper counting rules, although this finding is not consistent; it likely differs at different ages; and it may be due to domain-general deficits such as decreased working memory.

A final area of domain-specific deficits involves arithmetic processes (Geary, 2013). As children develop, they learn more strategies for solving arithmetic problems; for instance, they may use finger counting or verbal counting as an aid, or may rely on long-term memory for arithmetic facts. Children with LD-Math have higher rates of procedural errors when performing arithmetical operations, and even when their answers are accurate, they are more likely to use strategies associated with younger children, such as finger counting (Geary, 2011). Moreover, children with LD-Math have more problems learning and recalling basic math facts. Various possible cognitive mechanisms may underlie this memory deficit; one involves a failure to inhibit irrelevant associations that lead to inaccurate answers. As mentioned earlier, LD-Math has been found to involve deficits in the central executive system of working memory, and this system inhibits competing irrelevant associations. Therefore, when a child sees "3 + 4 = " he or she must inhibit the inaccurate answer "5," which is associated with the counting chain of "3 . . . 4 . . . "; children with LD-Math are more likely to provide such inaccurate answers.

Subtypes of LD-Math

Children who manifest LDs in math are believed to display deficits in some area of mathematics skill, but there are many such areas of skill—and thus whether it is theoretically interesting and clinically useful to classify students with LD-Math into tighter subtypes is an important question.

In his early work, Geary (1993) defined three subtypes. Students with the "procedural subtype" are characterized by their immature and error-laden use of rules for solving mathematics problems. They may confuse the order of steps when solving long-division problems, for instance. In contrast, students with the "semantic memory subtype" are characterized by trouble retrieving math facts from memory. These students cannot quickly and accurately recall that 3 + 4 = 7, and this causes problems when solving more complicated or applied problems. Finally, students with the "visuospatial subtype" are characterized by problems representing mathematical information in visual space. These students may be unable to line up columns of numbers for proper multidigit addition, and may even confuse numbers that are visually similar, such as 6 and 9. These are certainly distinct areas of cognitive skills, but in Geary's later work (e.g., Geary, 2011), he appears to view the subtypes as areas of deficit, rather than distinct syndromes that would lead to separate clinical diagnostic categories. Moreover, the validity of the visuospatial subtype has been questioned by, for instance, Fletcher and colleagues (2007), who note the lack of research establishing a unique link between spatial processing and mathematics performance.

An alternative approach to subtyping LD-Math, and one that lends itself more easily to operationalization, relies on the distinction between calculation and math word problems. Just as achievement tests have separate tasks measuring reading decoding and reading comprehension, they have separate tasks measuring calculation (thought to be a lower-level skill) and word prob-

lems (sometimes called "math reasoning" and thought to require higher-level skills). Fuchs and colleagues (2008) noted that while "a computation problem is already set up for solution, a word problem requires students to use the text to identify missing information, construct the number sentence, and derive the calculation problem for finding the missing information" (p. 30). These researchers found that deficits in the two areas of academic skills were associated with different patterns of cognitive deficits, suggesting the two as separate subtypes, along with a third subtype for students who showed deficits in both calculation and word problem solving. Different patterns were again found by Namkung and Fuchs (2012), indicating that using these subtypes may be a fruitful way to characterize students with LD-Math.

Still other attempts to characterize the population of children who manifest LDs in math contrasted these children with each other based on their reading performance. Thus "LD-Math with comorbid RD" could be viewed as a subtype of LD-Math. Swanson, Jerman, and Zheng (2009) performed a useful quantitative synthesis of research comparing students with LD-Math to those with RD, those with both types of LDs, and those without any LDs. Of particular interest to us is the comparison of LD-Math students with and without comorbid RD. On measures of working memory, students with only LD-Math were found to perform substantially better (d = 0.42 for visual–spatial working memory and 0.88 for verbal working memory). They also outperformed comorbid peers on measures of long-term memory (d = 0.58) and visual–spatial problem solving (d = 0.63). However, they actually exhibited *worse* performance than peers with comorbid RD on measures of attention (d = –0.31). All of these comparisons suggest that if a student meets criteria for multiple LDs, they should all be noted, since the combination of LD-Math with RD is generally associated with greater cognitive deficits.

Neurobiological Factors

Studies of adults with brain lesions show that fairly specific math skills can be lost or preserved, depending on the pattern of brain injury (Dehaene & Cohen, 1997). However, there are few studies of either brain structure or brain function in individuals with LD-Math, and some have used adults, for logistical reasons. Whether the development of math skills across different domains can be fractionated in ways apparent in studies of adults with brain injury is not clear. Also emerging are studies of the familial segregation and heritability of LD-Math, which are reviewed in this section.

Brain Structure and Function

Multiple frontal and parietal areas appear to be involved in processing of mathematical information, but recent work has focused on the intraparietal sulcus (sometimes called the horizontal intraparietal sulcus; the IPS or HIPS). This region has been repeatedly associated with mathematical skills (Ansari & Dhital, 2006), and, more recently, abnormalities in its structure and function have been associated with LD-Math (Butterworth, Varma, & Laurillard, 2011; for a review of fMRI studies, including those examining other brain areas, see Kaufmann, Wood, Rubensten, & Henik, 2011). One Swiss study (Rotzer et al., 2008) compared 12 children with LD-Math to 12 age-matched controls and found a variety of brain structure differences, including reduced gray matter volume in the right-hemisphere IPS. A Belgian fMRI study (Mussolin et al., 2010) found that unlike their nondisabled age-matched peers, children with LD-Math failed to show changes in IPS activation during a numerical comparison task, depending on how different the numbers were. Perhaps most intriguingly, Kadosh and colleagues (2007) used transcranial magnetic stimulation to disrupt activity in the IPS of adults with and without LD-Math. Disruption of activity in the right-hemisphere IPS led to numerical magnitude deficits in nondisabled adults that resembled LD-Math symptoms.

Genetic Factors

As in RDs, there is an emerging research base demonstrating heritable factors in LD-Math. First, it is clear that math disabilities are more common in certain families. Shalev and colleagues (2001) found that the prevalence of LD-Math was quite high in mothers (66%), fathers (40%), and siblings (53%) of probands with LD-Math. Shalev and colleagues concluded that the prevalence of LD-Math was about 10 times higher in those with family members who had LD-Math than in the general population.

However, family associations can be due to either genes or environment. Heritability studies have nonetheless found that genetic factors are important in LD-Math. In a twin study, Alarcon, DeFries, Light, and Pennington (1997) reported that 58% of monozygotic

twins shared a math disability, compared to 39% of dizygotic twins; this difference is not large, but suggests a genetic component to LD-Math. Knopik and DeFries (1999) arrived at a heritability estimate of 38%, also not especially high (compared to many other disorders) but substantial. More recent work has yielded similar estimates; Kovas, Petrill, and Plomin (2007) found heritability values for different math skills (not LD-Math per se) ranging from .30 to .45.

Finally, we would note that math deficits are seen in a variety of genetic disorders. In his review of this literature, Simon (2011) considered several genetic disorders whose phenotypes include math disabilities: velocardiofacial syndrome, Turner syndrome, fragile X syndrome, and Williams syndrome. It is possible that once the gene-to-behavior links in these disorders are better understood, we will have a better understanding of LD-Math.

DISORDERS OF WRITTEN EXPRESSION

Developmental disorders in the writing process have been discussed since the 1980s (Hooper et al., 1994). Wong (1991) has argued that deficits in written expression are clinically important, since they are frequently associated with RDs and/or are governed by similar metacognitive processes to include planning, self-monitoring, self-evaluation, and self-modification. Hooper and colleagues (1994) have reported that much of the research related to disorders of written expression and agraphia continues to employ case study methodology, and, in the main, continues to rely on the study of individuals with acquired brain damage. More recent studies have used improved theoretical models and larger samples. However, studies of written expression have not followed the lead of LD-Math research, and often do not separate children according to specific writing disabilities versus comorbidity with other LDs. This hampers definitional efforts. Altogether, as noted in the previous edition's chapter, disorders of written expression have lagged behind the interests in RDs and LD-Math. Truly, they remain the least well-understood LDs.

Definitional Issues

A review of the available definitions for disorders of written expression reveals that the complexity and multidimensionality of these disorders continue to be ignored by formal characterizations or definitions. There are still no clear operational definitions of written language expression that address all components of the written language domain (see Berninger, 1994, 2004, for discussions of these issues). Research on written language indicates that most, if not all, children with LDs have problems with at least one component of writing, whether it is handwriting, spelling, or written discourse. Hooper and colleagues (1994) and others (De La Paz, Swanson, & Graham, 1998; Englert, 1990; Graham & Harris, 2000) report that writers with LDs demonstrate deficits in deploying strategies during production of written text and also have problems in actually generating text. When compared to "good" writers, writers with LDs produce shorter and less interesting essays, produce poorly organized text at the sentence and paragraph levels, and are less likely to review spelling, punctuation, grammar, or the body of their text to increase clarity (Hooper et al., 1994). But even here the description of children as "writers with LDs" is difficult because most probably also have problems with oral language and reading development. A critical definitional issue relates to what is specific about disorders of written expression.

A number of authorities in this area have offered strategies to bolster definitions of LDs in written language (Graham & Harris, 2000; Mather & Wendling, 2011). Spelling, handwriting, and more general aspects of formulating and producing written text are seen as somewhat separate components of a disorder of written language. But, other than descriptions of these processes and of children with LDs in one or more of these areas, little work on definition and classification has been completed. Although it may be possible to identify children who have problems only in spelling and in handwriting as prototypes, children with problems only in "written expression" and in no other area appear difficult to identify. Given the complexity of the writing process and the fact that it is the last language domain to develop in children (Hooper et al., 1994; Johnson & Myklebust, 1967), it should not be surprising that deficits in written expression often co-occur with deficits in oral language, reading, and mathematics. However, Berninger, Mizokowa, and Bragg (1991) and Berninger and Hart (1992, 1993) have demonstrated that reading and writing systems can be dissociated. Some children have reading problems but not writing problems, and other children have writing problems but not reading problems. But these patterns are infrequent, and most (but not all) children with writing deficits also manifest

deficits in reading. Indeed, Berninger and May (2011) provocatively state that "Although many think of dyslexia as a specific reading disability, it is really a specific reading *and writing* disability" (p. 170, emphasis added).

A final definitional issue involves the measurement of writing skills. In the case of reading and mathematics, there is a clear, correct, consensus answer for each item on a test: Words are either read correctly or not, and answers to math problems are either correct or not. In the case of writing, things are more complicated, and can be somewhat subjective as well. At least in the case of spelling, there is always a "correct" conventional spelling. And even in the case of handwriting, there are scales of legibility that yield consensus. But in the case of the most complex writing skill, composition, it can be difficult to judge quality. Admittedly, there are grammatical conventions that can be graded—but when lengthier compositions are being graded, and issues of organization, diction, and style come up, it is not always easy to say precisely why writing is good or bad. Indeed, the poor reliability of essay grading has long been known (see e.g., Starch & Elliott, 1912).

Noting the challenges associated with measuring composition does not mean that we have no tools to measure it. Standardized, norm-referenced achievement tests include measures of composition, and some RTI systems use brief writing probes in which students' writing fluency (e.g., the number of words written in 3 minutes in response to a story prompt) is quantified. We merely point out that measures of composition quality differ in important ways from measures of reading and mathematics skills, making it difficult to characterize some students whose poor compositions lead them to have what we refer to hereafter as the LD-Writing label. We must, of necessity, put these measurement concerns to one side as we review the available literature on LD-Writing below.

Epidemiology and Developmental Course

In 1994, Hooper and colleagues pointed out that few epidemiological studies of LD-Writing had been carried out. Since then, unfortunately, little has changed, and the few studies that have been done differ in the degree to which they include individuals who have comorbid problems in reading. Texts list prevalence rates—for instance, Mather and Wendling (2011) tell us that "problems with written expression are estimated to occur in 2% to 8% of school-aged children" (p. 66)—but the empirical basis for claims such as these is small.

One epidemiological study was reported by Katusic, Colligan, Weaver, and Barbaresi (2009), who studied children born between 1976 and 1982 in Rochester, Minnesota. Three different LD diagnostic models were applied to these individuals' IQ and writing achievement scores: two different kinds of discrepancy models, and one based on low writing achievement (but also requiring an IQ of 80 or above). These investigators estimated the prevalence of LD-Writing as being between 7 and 15%, depending on which diagnostic model was used. (The low-achievement model led to the highest prevalence estimate.) These investigators also estimated the male–female gender ratio as being between 2:1 and 3:1, which is quite substantial.

A different approach to estimating prevalence was taken by Graham and Harris (2011), who examined data from the National Assessment of Educational Progress (NAEP). The NAEP is a criterion-referenced test where grade-level standards are established for different grades. In 2003, between 14 and 26% of students (depending on the grade level) fell below the cutoff for "basic" skills in the area of written language, suggesting that this many students were, in a sense, disabled in the area of writing. Of course, this does not take into account a variety of factors that could have led to low scores on the NAEP, including other medical or psychological conditions. In any case, the prevalence of writing problems is substantial, but high-quality epidemiological studies of LD-Writing are lacking.

Core Processes

Almost half a century ago, Johnson and Myklebust (1967) presented a developmental model of language learning, which posited that the ability to write is dependent upon adequate development in listening, speaking, and reading. Similarly, Hooper and colleagues (1994) indicated that written expression and its disorders are multidimensional in nature. In short, writing is, neuropsychologically speaking, an extremely complex and difficult skill. Therefore, deficits in a variety of domain-general processes could impair writing. Obviously, other academic deficits can also impair writing; for instance, poor reading skills will keep students from revising their writing appropriately and getting feedback when reading their own attempts at composition.

One way of exploring the cognitive bases of writing problems involves examining the writing process and products of struggling writers (we use the term "struggling writers" because many do not have official LD-Writing diagnoses). In their review of struggling writers' characteristics, Graham and Harris (2011) noted several salient facts. First, struggling writers showed less planning before beginning to write; instead, they started to generate text mechanically, without considering the endpoint of the composition. Second, despite the immediate text generation without planning, these writers finished with startlingly little text; they were not productive, generating very short compositions. Third, their text revision tended to focus on minor issues such as diction and grammar, rather than higher-level organizational issues. Fourth, they made many minor errors with regard to features such as spelling and punctuation (perhaps necessitating the low-level revisions just described). Finally, struggling writers showed less motivation, as measured by their lack of persistence when writing. When these five characteristics are considered, cognitive issues of executive functioning appear prominent.

A different way of exploring cognitive bases involves using cognitive assessment tools to predict writing achievement. Floyd, McGrew, and Evans (2008) used the norming sample of the Woodcock–Johnson Tests of Cognitive Abilities and Achievement to determine these predictive relationships. Crystallized ability (i.e., comprehension/knowledge) was the broad cognitive ability that had the strongest unique relationship with writing performance. In addition, several other broad cognitive abilities consistently added unique value in predicting writing: processing speed, and short-term and long-term memory. Floyd and colleagues also found that the various cognitive abilities were differentially important at different age levels, which is intuitive when one considers how writing assignments change markedly from the early elementary years through high school and beyond.

Recently, Flanagan, Alfonso, Ortiz, and Dynda (2013) considered the results from several studies (including that of Floyd et al., 2008) to integrate findings and summarize the relationships between cognitive abilities and writing achievement. Flanagan and colleagues aimed to consider specific, narrow cognitive abilities that were relevant, rather than merely broad abilities. Within the area of crystallized ability, these scholars concluded that language development, lexical knowledge, and general information were all important in children older than age 7. Within the area of short-term memory skills, memory span was especially important in predicting spelling skills, whereas working memory was important in predicting more advanced writing skills. Within the area of auditory processing, phonological processing skills were important in predicting writing achievement at earlier ages (under age 11). Finally, within the area of processing speed, perceptual speed was important in predicting composition skills at all ages.

As a final area of work examining the cognitive underpinnings of LD-Writing, we should note that recent research has emphasized the contribution of competent, fluent low-level skills (handwriting and spelling) to composition skills. For instance, Puranik and AlOtaiba (2012) found that handwriting and spelling added unique value to the prediction of composition skills when other predictors (e.g., cognitive ability) were statistically controlled. Similarly, Peverly (2006) reviewed research showing that handwriting speed was related to composition in adults. It appears that solid, automatic low-level skills free up working memory, allowing writers more mental workspace to be reflective and deliberate about their compositions.

Neurobiological Factors

Brain Structure and Function

Research on the neurobiological correlates of LD-Writing is in its infancy. Studies of acquired disorders show that reading and writing can be fractionated, as in the example of "pure alexia," in which a patient loses reading ability but maintains the ability to write. Berninger (2004) summarized a variety of findings from functional neuroimaging studies, showing that components involved in fine motor control and language generation can be related to areas of the frontal lobes and the cerebellum. These areas are well known to be involved in support of core processes that underlie writing, including motor control and planning, executive functions, and language. Barkley (1997) had used these findings earlier to help explain why many children with ADHD have problems with writing.

A recent series of studies by Todd Richards, Virginia Berninger, and their colleagues illustrates the complexities of research on the neurobiology of LD-Writing. In one study (Richards, Berninger, Stock, et

al., 2009), this team compared 8 "poor writers" (students who scored below average or below their IQ on any of several writing measures) to 12 "good writers." The students (all were tested in the summer between fifth and sixth grades) underwent fMRI imaging during different finger-tapping tasks, and the researchers found 42 (!) different brain regions that showed a statistically significant difference between the two groups. Activation in these areas (during the tasks) was then correlated with performance on various writing tasks, and many substantial correlations ($r > .40$) were found, widely distributed around the brain. In another study (Richards, Berninger, Winn, et al., 2009), the research team examined brain activation during different working memory tasks in good and poor spellers. Different activation levels were observed in several anterior areas (frontal and anterior cingulate cortex areas), suggesting that good spellers were more efficient in their processing of information. Similar efficiency differences were suggested by a third study (Richards et al., 2011) comparing good and poor writers' brain activation during letter-writing tasks. Although these studies often find differences in the activations of brain regions that have been associated in other research with writing-related functions, it is becoming clear that writing is a widely distributed brain function, limiting the clinical value of such studies.

Genetic Factors

There are few studies of the heritability of writing problems. Raskind, Hsu, Berninger, Thomson, and Wijsman (2000) found that spelling disorders, but not handwriting problems, aggregate in families. Other studies have found that spelling difficulties aggregate in families (Schulte-Korne, Deimel, Muller, Gutenbrunner, & Remschmidt, 1996). These findings are consistent with twin studies, which have found strong heritability of spelling abilities in twins, similar to that found for reading abilities (Bates et al., 2004; Stevenson, Graham, Fredman, & McLoughlin, 1987). Nothen and colleagues (1999) reported a locus for spelling (and reading) on chromosome 15, which has also been reported for dyslexia (see Grigorenko, 2001). As reading and spelling abilities are highly correlated and represent a common factor that shares heritability (Byrne et al., 2008), it remains to be seen how these findings really differ from those reported above for reading.

CONCLUSIONS AND FUTURE DIRECTIONS

This chapter has provided a review of past and recent research related to LDs in children. Within this context, the most productive research in LDs has been carried out in the reading area, particularly in the study of the relationship between specific linguistic skills such as phonological processing and word recognition abilities. The focus on this relationship in typically achieving populations versus those with RDs has led to an explosion of research on definition, core processes, neurobiological correlates, and intervention. In the past decade, the same thing has happened, on a smaller scale, for the case of LD-Math. Gaps continue to exist, especially in our knowledge of LD-Writing—in part due to conceptual and methodological issues discussed earlier, such as the poor separation of writing from other skills.

The past decade has witnessed many advances in our neurobiological understanding of learning disabilities. We know more than ever about brain–behavior correlates, particularly with regard to RDs. Imaging research is beginning to provide the neural signature for the processing deficiencies associated with various aspects of reading. This needs to be done with other forms of LDs. Genetic research is helping us understand both the general and specific ways in which genes influence one's psychoeducational abilities. Neuroscientific research has also begun to reveal how various learning interventions modify brain activation, perhaps making permanent positive changes in the direction of more normalized brain states. These neurobiological breakthroughs will only continue to aid the understanding of LDs, and perhaps someday will better inform the diagnosis and treatment of this heterogeneous group of disorders.

Another major advance that has occurred over the past decade in LD research has been the integration of assessment with instruction/intervention. Consistent with the RTI model, researchers now routinely perform studies by tracking large groups of students, determining the characteristics (cognitive, neurobiological, etc.) of those students who fail to respond to general classroom instruction (as measured by insufficient improvement in academic skills), and then evaluating the effects of different interventions on these students' academic skills. This "educational" model of LD research contrasts with the earlier, "clinical" model, in which students were identified as having LDs on the basis of a diagnostic assessment performed at a single point in time, and emphasis was placed on describing the pre-

cise subtype of LD rather than on providing evidence-based academic skill remediation.

This shift has led to an interesting schism in the field, as some researchers and practitioners (often those in medical settings and private practice) continue to rely on the older clinical model, while other researchers and practitioners (often those in school psychology and special education) have discarded it for the educational model. The continuing debates over RTI display this schism, as do programs of research that fail to cite each other even when the work is relevant. There is certainly room for both approaches in conducting research studies, although in practice it is difficult to fully reconcile the two approaches, especially since the RTI model is less about diagnosis or classification than it is about a general system of providing academic skill instruction and monitoring its effectiveness.

In the previous edition of this chapter, the authors despaired that "while research flourishes, practice lags behind" (Lyon et al., 2003, p. 574). With the adoption of RTI, the gap between research and practice is less pronounced. Indeed, although research has failed to support the outdated notions of IQ–achievement discrepancies, the details of RTI are continuing to be worked out—and some studies have cast doubt on the reliability and validity of certain measures and criteria used in RTI systems, leading us to sympathize with practitioners who are skeptical of RTI. The comprehensive CP diagnostic models have been worked out in much more detail, but they have not proven themselves to be so efficient that they should be used with any student referred for academic skills problems; nor have they led to interventions that produce more than small effects. We have yet to see a longitudinal, randomized treatment study that compares outcomes on students diagnosed (and treatments designed) by way of CP, RTI, LA, and discrepancy methods, and that day may never come. Although more work on the details of RTI awaits, we applaud the general approach of viewing LDs operationally—as deficits in students' response to academic instruction—and then focusing efforts on identifying effective interventions that facilitate academic skills.

It is time to move from an advocacy approach that sought recognition and access to special services for LDs, to an action approach that seeks research- and evidence-based, effective services for all forms of LDs. Advocacy has helped these children enter schools with protections. It is now time to advocate for results through the rigorous scaling up and implementation of what we know from research. This will require enhanced preparation of personnel at all levels, but especially of the teachers who instruct all children in general and those in special education particularly. Addressing this latter issue is the key to results for children with LDs.

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PART VI

INFANTS AND CHILDREN AT RISK FOR DISORDER

CHAPTER 15

Disorder and Risk for Disorder during Infancy and Toddlerhood

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Infant mental health always has had as a central premise that the developing young child must be understood in context. Class, culture, and even historical epochs are all important contexts for development; from the perspective of understanding psychopathology, however, the experience-near context of the infant's relationships with the primary caregivers is considered the most important context for assessment and intervention.

Nevertheless, this emphasis introduces some significant challenges to attempting to conceptualize and define disorders of infancy. Can infants be diagnosed as having within-the-person psychiatric disorders, or are their symptoms relationship-specific? To what degree should the caregiving contexts of infants' development be considered an integral part of a relationship disorder, as opposed to an associated feature of individual disordered behavior? Are disturbed behaviors in infants indicative of disorder per se, or do they merely indicate risk for subsequent disorder? To what degree are we to take into account here-and-now suffering, or must we also demonstrate links between infant developmental disturbances and subsequent disorders? How we answer these questions may lead us in different directions.

There are, in fact, two major and quite different traditions in infant mental health regarding how to conceptualize psychiatric disturbances in young children. These approaches make different assumptions about disturbances and seem likely to direct efforts at intervention differently as well.

One tradition (which has dominated research in developmental psychology and developmental psychopathology) suggests that infants may be considered as having a number of specific risk factors that increase, and/or protective factors that decrease, the probability that they will develop a given disorder in later childhood. These risk and protective factors may be biological (intrinsic), social (contextual), or both. Much of contemporary research has been devoted to detecting early "markers" of subsequent disorder, with the aim of delineating developmental pathways or trajectories of at-risk infants. For example, the recent emphasis on how early experiences get "under the skin" and lead to subsequent health and mental health problems exemplify a focus on risk factors and processes related to downstream outcomes (Hertzman & Boyce, 2010).

Another tradition (which has more clinical than empirical roots) suggests that infants may have formal psychiatric disorders, even in the first 3 years of

life. Research in support of this tradition has emerged mostly in the past decade or two, and much work needs to be done to test some of the assertions that have been made. Nonetheless, this approach to disorders of infancy appears to have widespread support (Egger & Angold, 2006; Gleason & Schechter, 2009; Zeanah, 2009).

The plan for this chapter is first to consider some of the conceptual controversies regarding relational versus individual approaches to diagnostic classification issues, which emerge with particular clarity in the study of disorders of infancy. Current competing approaches to diagnosis in infancy are discussed. Research relevant to the definitions and correlates of the various particular "disorders" of infancy is then reviewed—including research on common clinical problems not yet represented in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association [APA], 2013), such as regulatory disorders. In the final major section, longitudinal developmental research exploring both infant behavioral constellations and family characteristics that may constitute risk factors, precursors, or prodromal forms of later childhood disorders is selectively reviewed. Three particularly active areas of current research are considered: studies of the intergenerational transmission of patterns of relational behavior; research exploring the context and correlates of disorganized/disoriented infant attachment behaviors; and recent studies of early predictors of later psychiatric symptomatology, including aggressive behavior disorders, anxiety disorders, depressive and dissociative symptoms, and suicidality.

DIAGNOSTIC CLASSIFICATION IN INFANCY

The clinical tradition of examining disorders of infancy requires us to consider some of the special challenges of diagnostic classification relevant to this age group. Emde, Bingham, and Harmon (1993) noted that these challenges include the multidisciplinary nature of infant mental health, the developmental perspective inherent in infant mental health, the multigenerational focus of problems, and the prevention orientation of the field. These features complicate the diagnostic process in infancy, but the failure to include such features may also be responsible in part for the widespread dissatisfaction among clinicians with the approach to disorders of infancy taken by standard nosologies.

DSM-5 and Disorders of Infancy

DSM-5 was intended to be explicitly developmental in focus, considering how disorders manifest themselves at different stages in the life cycle. Unfortunately, research on disorders of early childhood is so limited that few of the changes from DSM-IV to DSM-5 will enhance its accessibility and usefulness for those treating young children. DSM-5 does include a preschool subtype of posttraumatic stress disorder (PTSD), which we review in detail later (see also Nader & Fletcher, Chapter 10, this volume), but this was included because of careful and systematic research that has been conducted about the phenotype of PTSD in the first few years of life. No other disorders have received the degree of careful empirical attention to developmental differences in how disorders are manifested. The challenge is to define other disorders as they manifest themselves in early childhood—in the knowledge that this means taking into account the rapid developmental change over the first 3 years of life, the possible developmental differences in symptom picture, and the likelihood of symptoms or syndromes specific to this developmental period.

The Zero to Three Scheme and Disorders of Infancy

One response to the lack of attention to these issues in traditional nosologies was the creation of a task force by Zero to Three, a national advocacy organization (*www.zerotothree.org*). This task force developed and published a more detailed classificatory scheme for disorders apparent in the first 3 years of life, known as the *Diagnostic Classification of Mental Health and Developmental Disorders of Infancy and Early Childhood*, or the *Diagnostic Classification: 0–3* (DC:0–3) for short (Zero to Three/National Center for Clinical Infant Programs, 1994). It adopted a multiaxial approach to diagnosis similar to that of DSM-III through DSM-IV (APA, 1980, 1987, 1994), although its axes were somewhat different. The DC:0–3 was revised in 2005 as DC:0–3R (Zero to Three/National Center for Clinical Infant Programs, 2005; see Table 15.1), updating several disorders, eliminating others, and attempting to use recent research to inform criteria whenever possible.

In DC:0–3R, Axis I defines clinical disorders of infancy and early childhood. The second axis includes a classification of "relationship disorders"—that is, types

TABLE 15.1. Diagnostic Classification: 0–3 (DC:0–3R)

- Axis I: Clinical disorders
  - Posttraumatic stress disorder
  - Deprivation/maltreatment disorder
  - Disorders of affect
  - Prolonged bereavement/grief reaction
  - Anxiety disorders of infancy and early childhood
    - Separation anxiety disorder
    - Specific phobia
    - Social anxiety disorder (social phobia)
    - Generalized anxiety disorder
    - Anxiety disorder not otherwise specified (NOS)
  - Depression of infancy and early childhood
    - Type I. Major depression
    - Type II. Depressive disorder NOS
  - Mixed disorder of emotional expressiveness
  - Adjustment disorder
  - Regulation disorders of sensory processing
    - Hypersensitive
      - Type A. Fearful/cautious
      - Type B. Negative/defiant
    - Hyposensitive/underresponsive
    - Sensory stimulation-seeking/impulsive
  - Sleep behavior disorder
    - Sleep-onset disorder (protodyssomnia)
    - Night-waking disorder (protodyssomnia)
  - Feeding behavior disorder (see Table 15.4)
  - Disorders of relating and communicating
  - Multisystem developmental disorder (MSDD)
  - Other disorders (DSM-IV-TR or ICD-10)
- Axis II: Relationship classification
- Axis III: Medical and developmental disorders and conditions
- Axis IV: Psychosocial stressors
- Axis V: Emotional and social functioning

of relationships with caregivers that are so disturbed as to constitute disorders. Nevertheless, a relationship disorder is believed to exist between a caregiver and infant rather than within the infant. The types of disordered relationships defined include "overinvolved," "underinvolved," "anxious/tense," "angry/hostile," "verbally abusive," "physically abusive," or "sexually abusive." In this classificatory system, a relationship disorder can occur with or without an Axis I disorder, and vice versa. Two tools are provided to aid the clinician. The Relationship Problems Checklist is used to document the degree of evidence supporting each type of relationship disorder. The Parent–Infant Relationship Global Assessment Scale allows the clinician to rate the level of relationship adaptation or disturbance. Ratings range from "well adapted" through "perturbed," "distressed," "disturbed," and "disordered," and finally to "grossly impaired" and "documented maltreatment." This scale is intended to be used after a clinical assessment of a dyad is completed, and to be based upon all observations of the intensity, frequency, and duration of disturbances to arrive at the rating.

The development of DC:0–3 and DC:0–3R has been an important advance, and this alternative diagnostic system has been widely adopted by clinicians. Nevertheless, neither DC:0–3 nor DC:0–3R has inspired much research; 20 years after the original publication, there are only a handful of studies examining the reliability and validity of the criteria for some of the disorders it defines. This is disappointing indeed, as a major hope for the system was to stimulate research. A significant problem is that although some disorders are described clearly with well-delineated decision rules (e.g., PTSD), others are vaguely defined (e.g., multisystem developmental disorder) or unclear with regard to how many criteria are needed to make a diagnosis (e.g., regulatory disorders). A major revision of the DC:0–3R approach is underway, with an anticipated publication date of 2016 for a revision.

With both the DSM-5 and DC:0–3R diagnostic systems, there is an implicit acceptance of the traditional biomedical model of a categorical typology of disorders. Nevertheless, we might reasonably ask whether a continuous or dimensional approach to psychopathology during infancy may have important advantages over a categorical or disorder approach, as some have suggested (Rutter, 1994). Some have advocated a continuous approach to diagnosis with older children as well, and indeed DSM-5 includes a severity dimension for most disorders (APA, 2013).

Another issue to be considered is whether disorders of infancy are better conceptualized as within individuals or as between infants and their primary caregivers. Sameroff and Emde (1989) have suggested that with a few notable exceptions, such as autism spectrum disorder, most disorders of early infancy are relationship disorders rather than individual disorders. Anchoring their approach in disturbances in the infant–caregiver relationship, and particularly in the caregiver's regulatory function for the infant, they have defined different levels of disturbance (relationship perturbations, disturbances, and disorders). Still, almost no research has addressed this approach in relation to diagnoses in infancy. However, in relation to risk factors for later diagnoses, developmental psychopathology researchers have repeatedly documented the role of parental regulation as a concurrent correlate and prospective predictor of childhood disturbance (see the last major section of this chapter).

In summary, the extant systems of classifying disorders of infancy are preliminary (in the case of DC:0–3R) or insufficiently relevant (in the case of DSM-5). An attempt to validate the classification systems and the specific criteria included for various disorders is a necessary next step. For the discussion that follows, we have selected for review common problems seen by infant mental health clinicians. We begin with problems typically believed to be more biologically rooted, such as regulatory disorders, and conclude with disorders believed to be more experientially rooted, such as PTSD and disinhibited social engagement disorder (DSED). Between these two poles of the spectrum are disorders believed to have more variable or mixed contributions from individual differences in central nervous system functioning and psychological experiences. Throughout the discussion we emphasize the ongoing importance of contextual factors, and especially the primary caregiving relationship, for the expression and experience of disorders during this early developmental period when the infant is dependent on primary caregivers for regulation of affect and arousal.

DISORDERS OF INFANCY AND TODDLERHOOD

Table 15.2 lists the DSM-5 diagnoses relevant to infants and toddlers that are reviewed in this chapter. In addition, several common problems encountered during infancy are not included in DSM-5. However, given the frequency of presentation of these problems and the controversies surrounding infant diagnosis, some are also reviewed below.

TABLE 15.2. DSM-5 Psychiatric Disorders and Conditions of the First 3 Years

Feeding and eating disorders
Rumination disorder
Pica
Avoidant/restrictive food intake disorder
Other specified feeding or eating disorder
Sleep–wake disorders (see Table 15.5)
Trauma- and stressor-related disorders
Posttraumatic stress disorder
Reactive attachment disorder
Disinhibited social engagement disorder

Regulation Disorders

Description of the Disorders

Regulation disorders are characterized by DC:0–3R as "the child's difficulties in regulating emotions and behaviors as well as motor abilities in response to sensory stimulation that lead to impairment in development and functioning" (Zero to Three, 2005, p. 28). According to DC:0–3R, three central features characterize regulation disorders, including a specific maladaptive behavioral pattern (e.g., excessive cautiousness), a sensory processing difficulty, and/or a motor difficulty. DeGangi, DiPietro, Greenspan, and Porges (1991) offer a broader clinical range of atypical behaviors associated with regulation disorders, including affective lability; feeding problems; an inability to regulate sleep–wake cycles; difficulty with transitions, changes in routines, and self-soothing; and hypersensitivities to stimulation. Specific sensory symptoms may include impaired or enhanced reactivity to auditory, visual, tactile, gustatory, vestibular, or olfactory stimulation, as well as temperature; impaired motor tone, motor planning skills, and fine motor skills; and decreased capacity to discriminate or integrate auditory–verbal or visual–spatial stimuli. Although such behaviors are common in infants younger than 6 months of age, their perseverance beyond this time frame may be maladaptive, especially when expressed across settings and within multiple relationships (Zero to Three, 2005). Marked

concerns associated with regulation disorders are that their presence may interfere with the infant or child's comfort and ability to interact with caregivers, adults, and peers alike; that they are predictive of problematic socioemotional, cognitive, and motor development; and that they may interfere with sensory integration.

Diagnostic Considerations

Regulation disorder of sensory processing is a diagnostic category unique to DC:0–3R (Zero to Three, 2005), and is thus not included in the diagnostic nomenclature of DSM-5 or the *International Classification of Diseases*, 10th revision (ICD-10; World Health Organization [WHO], 1992). DC:0–3R describes three types of regulation disorders of sensory processing: (1) hypersensitive (subtypes: fearful/cautious and negative/defiant); (2) hyposensitive/underresponsive; and (3) sensory stimulation-seeking/impulsive. For young children with the hypersensitive type of regulation disorder, auditory, visual, tactile, gustatory, vestibular, and/or olfactory stimulation is experienced as overpowering; however, the experienced intensity and duration of the aversive stimuli can be inconsistent throughout the day and across stimuli. Young children experiencing the hyposensitive or underresponsive type of regulation disorder appear uninterested in their surroundings and withdrawn from their social environment. Substantial sensory input is often required to trigger a response to social overtures or to their environmental surroundings. Finally, young children with the sensory stimulation-seeking and/or impulsive type of regulation disorder are drawn to and actively seek out sensory stimulation to satisfy their desire for sensory input. As a result of their craving for high-intensity sensory stimulation, children with this disorder often engage in inappropriate invasions into others' physical space (e.g., unprovoked aggression).

Regulation disorders may affect one or more areas of development and may range in severity from mild to severe. In the mildest form, infants may exhibit sleep, feeding, or elimination problems. In the most severe form, physiological or state repertoires are affected. For example, infants may have irregular breathing, startles, gagging, and so forth. Between these two extremes of severity, other difficulties may be found in the area of (1) gross and fine motor activity (e.g., abnormal tonus or posture, jerky or limp movements, poor motor planning); (2) attentional organization (e.g., driven behavior or perseveration on small details); or (3) affective organization (including predominant affective tone, range, and modulation of affective experiences).

Regulation disorders are diagnosed only in infants older than 6 months because transient difficulties with self-regulation (e.g., sleep problems) are common in young infants and typically resolve spontaneously by 6 months of age (DeGangi, Craft, & Castellan, 1991). Furthermore, in order for a diagnosis of a regulation disorder to be made, both behavioral and constitutional maturational elements must be present, and the difficulties in sensory, sensory–motor, or organizational processing capacities must affect daily adaptation and relationships (DeGangi, Craft, & Castellan, 1991; Greenspan & Wieder, 1993).

Currently, little is known regarding the reliability and validity of regulation disorders (Dunst, Storck, & Synder, 2006; Emde & Wise, 2003). The limited research on reliability and validity may be due to the lack of discrete boundaries between regulation disorders and other diagnoses in childhood (e.g., attention-deficit/hyperactivity disorder [ADHD]) (Egger & Emde, 2011). Furthermore, DC:0–3R does not provide operational criteria for the number or duration of symptoms required for a diagnosis of regulation disorders, which may hinder efforts at evaluation (Gomez, Baird, & Jung, 2004). Finally, although the concept of regulation disorders has been helpful clinically, there are no guidelines regarding who may suffer from regulation "difficulties" versus a regulation disorder per se.

Developmental Course and Prognosis

There are no documented adult equivalents of regulation disorders. DeGangi, Porges, Sickel, and Greenspan (1993) examined the natural history and prognosis of regulation disorders in a small sample of infants diagnosed with regulation disorders at ages 8–10 months. Of the nine infants followed up 4 years later, eight continued to have developmental, sensory–motor, and/or emotional and behavioral problems. In addition, when compared to preschoolers without diagnosed regulation disorders in infancy, those with infant diagnoses of regulation disorders were more likely to demonstrate differences on measures of cognitive abilities, attention span/activity level, emotional maturity, motor maturity, and tactile ability. The authors concluded that if left untreated, regulation disorders and the associated behavioral difficulties may persist.

Epidemiology

There is a dearth of research on the incidence and prevalence rates of regulation disorders. Although over 50% of infants and toddlers will experience a regulation difficulty in the area of feeding, sleeping, or crying at some point during their childhood (Schmid, Schreier, Meyer, & Wolke, 2010), the diagnosis of a regulation disorder itself is believed to be rare. The limited research evidence suggests that there may be an overrepresentation of males diagnosed with regulation disorders (DeGangi, Craft, & Castellan, 1991; Equit, Paulus, Fuhrmann, Niemczyk, & von Gontard, 2011). No information is yet available on either socioeconomic or cultural variations of regulation disorders.

Etiology

Although the etiology of regulation disorders is unclear, dysfunctions in the autonomic nervous system have been hypothesized; however, such dysfunctions may be physiological correlates of these disorders rather than etiological factors. In support of this hypothesis, DeGangi, DiPietro, and colleagues (1991) found that some physiological responses relating to vagal tone (heart period and cardiac vagal tone) differentiated 8- to 11-month-old infants with regulation disorders ($n = 11$) from infants without regulation disorders ($n = 24$). Specifically, the infants with regulation disorders tended to have higher baseline vagal tone and showed inconsistent vagal reactivity (i.e., heterogeneous response to sensory and cognitive tasks). These findings raise the possibility that infants with regulation disorders may have autonomic (parasympathetic) hyperirritability caused by defective central neural programs and mediated via neurotransmitters through the vagus nerve (DeGangi, DiPietro, et al., 1991; Porges, 1991).

In a study to identify early physiological correlates of regulation disorders, Zeskind, Marshall, and Goff (1996) studied the autonomic regulation of newborn infants found to be normal and healthy by routine physical and neurological examinations. They measured the children's cry threshold because characteristics of the cries of a newborn infant, such as threshold and sound, are sensitive to individual differences in the functional integrity of the infant's developing parasympathetic and sympathetic nervous system. In addition, Zeskind and colleagues completed a spectrum analysis of heart rate and made observations of the infants' behavior (e.g., cry reactivity, behavioral state, behavioral startles). Thirty-seven infants had a typical cry threshold (i.e., they required one rubber band snap to the sole of the foot to elicit crying), and 17 infants had a high cry threshold (i.e., they required three or more such snaps to elicit crying; high cry threshold has been described as reflecting nervous system dysfunction). Behaviors long described as characteristic of difficult temperament differentiated infants in the study (such behaviors include less biobehavioral rhythmicity; variations in self-regulation; and variations in the threshold, latency, and duration of infant reactivity and heart rate variability). Results provided evidence that infants with a high cry threshold showed a wide range of biobehavioral responses previously described as reflecting the homeostatic properties and regulation of an infant's autonomic nervous systems. However, the study did not follow the children beyond the neonatal period to examine whether the infants with high cry threshold developed regulation disorders nor how environmental regulation affected infant reactivity over time. No genetic etiological contributor has yet been hypothesized for these disorders.

In addition to central nervous system reactivity, it has been proposed that regulation disorders represent the extremes of normal variations in temperament. A recent study by Dale, O'Hara, Keen, and Porges (2011) examined the temperamental, physiological, and maternal behavior factors associated with regulation disorders. Dale and colleagues compared three groups of 9-month-old infants—those with no difficulties; those with difficulties in either self-regulation or hypersensitivities ($n = 25$); and those with difficulties in both ($n = 10$, classified as the regulation-disordered (RD) group)—on measures of parent-reported temperament, heart rate, and observed maternal and infant behavioral features. They found that infants in the RD group were more temperamentally difficult and also demonstrated atypical physiological activity, compared to those infants exhibiting no difficulties or to those exhibiting difficulties in either self-regulation or hypersensitivity. There were no significant differences in maternal behavior (e.g., physical behavior, quality of approach to infant, use of social cues to engage the infant) expressed toward infants in the RD group, compared to the other two groups. However, infants in the RD group were more likely to exhibit withdrawal behaviors (e.g., verbal and physical protests) in response to maternal approaches, compared to infants in the other two groups.

Environmental factors, especially ones associated with the caregiving environment, have been examined as root factors of regulation disorders. In contrast to the study by Dale and colleagues (2011), DeGangi, Sickel, Wiener, and Kaplan (1996) found that, compared to mothers of infants without regulation disorders, mothers of infants with regulation disorders showed less contingent responses, less physical proximity, and more flat affect during play interactions. Although findings from these studies do not point directly to an environmental etiology for regulation disorders, they suggest that the quality of the caregiving environment may contribute to the improvement or perpetuation of some regulation disorders.

Future Directions

To date, a few case vignettes of children affected by regulation disorders have been described (Barton & Robins, 2000; Benoit, 2000; Maldonado-Duran & Sauceda-Garcia, 1996). Clinically focused longitudinal studies are necessary to validate this diagnostic grouping and to determine the disorders' prevalence, developmental course, and prognosis. It will be essential for future research to examine the relative contributions of the autonomic nervous system, infant temperament, and the caregiving environment in the development of regulation disorders. The relationship between sleeping and feeding disorders and regulation disorders should be explored as well.

Failure to Thrive/Faltering Weight/ Faltering Growth

Description of the Disorder

Although there is no universally accepted definition of "failure to thrive" (FTT), also referred to as "faltering weight," "faltering growth," or "growth failure," FTT represents a symptom of the DSM-5 diagnostic criteria for avoidant/restrictive food intake disorder (see Table 15.3, later in this chapter) and of several feeding behavior disorders from the alternative classification system DC:0–3R (Zero to Three, 2005), which includes six subtypes of such disorders. We discuss feeding and eating disorders in a separate section below. FTT should not be viewed as a diagnosis unto itself (Cole & Lanham, 2011), but as a symptom of a wide range of childhood diseases and problems. Considerable heterogeneity exists with respect to characteristics of infants with FTT, their caregivers, and their family and social circumstances (see Benoit, 2009, for a review).

INFANTS WITH FTT

Because of their state of malnutrition, infants with FTT often look cachectic, are prone to recurrent infections, and show a decreased ability to recover from these infections (Sherrod, O'Connor, Vietze, & Altemeier, 1984). They may be developmentally delayed and exhibit unusual postures. They may look depressed, withdrawn, sad, apathetic, wary/hypervigilant, irritable, and angry. Some may have behavioral problems, including impaired communication skills and ADHD (Galler, Ramsey, Solimano, Lowell, & Mason, 1983). A retrospective population-based survey of 97 infants with FTT, identified by population screening at a median age of 15.1 months and compared to a control group of 28 infants without FTT who had similar levels of deprivation, showed that the parents of infants with FTT reported an early history of feeding problems more often than the parents of infants in the control group did. Despite the problems associated with retrospective accounts of earlier problems, the findings identify early feeding problems as a potential risk factor for the development of FTT (Wright & Birks, 2000). In a prospective study of 35 neonates with a median gestational age at birth of 34 weeks admitted to a neonatal intensive care unit for a minimum of 5 days, Hawdon, Beauregard, Slattery, and Kennedy (2000) examined risk factors for later feeding problems and identified 14 of 35 (40%) of infants with disorganized or dysfunctional feeding patterns. Compared to infants with normal feeding patterns at the original feeding assessment, these infants were six times were likely to have problems with vomiting, and three times more likely to cough when offered solids at 6 months old. By 12 months old, infants who had had disorganized and dysfunctional early feeding patterns were nine times more likely to cough with meals and four times less likely to tolerate lumpy textures. Hawdon and colleagues suggested that these feeding problems might contribute to FTT and psychosocial distress in some of these infants and their families.

CAREGIVERS OF INFANTS WITH FTT

Mothers of infants with FTT have been described (in both controlled and noncontrolled studies) as exhibiting

a wide variety of clinical problems, such as affective disorders, substance abuse, and personality disorders (e.g., Crittenden, 1987; Polan et al., 1991). However, conflicting findings continue to surround this area of research (see Benoit, 2009, for a review). In their controlled study of maternal attachment characteristics, Benoit and colleagues (Benoit, Zeanah, & Barton, 1989; Coolbear & Benoit, 1999) found that mothers of infants with FTT were more likely than their matched counterparts to be classified as insecure with respect to attachment on the Adult Attachment Interview (AAI; George, Kaplan, & Main, 1985) (see also Ward, Lee, & Lipper, 2000). These findings suggest either that mothers of infants with FTT are more passive, confused, and intensely angry than their matched counterparts when discussing past and current attachment relationships, or else that they dismiss attachment relationships as unimportant and noninfluential. Such patterns of responses are usually associated with insensitive caregiving (van IJzendoorn, 1995). Polan and Ward (1994) demonstrated that types of maternal touch that may promote growth or facilitate feeding are reduced in FTT, due (in extreme cases) to maternal and child touch aversion. Black, Hutcheson, Dubowitz, and Berenson-Howard (1994) showed that parents of children with FTT were less nurturing and more neglecting than parents of control children. However, findings from these studies do not elucidate the direction of effects.

FAMILY, CAREGIVING, AND SOCIAL CHARACTERISTICS OF INFANTS WITH FTT

Several controlled (Chatoor, Ganiban, Colin, Plummer, & Harmon, 1998; Crittenden, 1987; Valenzuela, 1990; Ward et al., 2000) and noncontrolled (Drotar et al., 1985; Gordon & Jameson, 1979) studies have documented increased rates of insecure attachment between infants with FTT and their mothers. Furthermore, Chatoor (1989) reported that compared to matched controls, infants with FTT interacted with their mothers in ways characterized by more conflict, less dyadic reciprocity, more struggle for control, and more negative affect (e.g., anger, sadness, frustration). In fact, mothers of infants with FTT used more abrupt, rough, and controlling interactions; fewer positive vocalizations; and more criticism or threats when interacting with their infants, and were generally less responsive and more intrusive than the control mothers (Berkowitz & Senter, 1987; Chatoor, Egan, Getson, Menvielle, & O'Donnell, 1987; Finlon et al., 1985). These findings identify an association between FTT and the quality of mothers' interactions with their infants with FTT, but not a direction of effect.

Some studies on FTT have reported that infants with FTT generally have a late birth order in a two-parent family (Benoit et al., 1989; Crittenden, 1987), with three to four children close in age (Benoit et al., 1989). Controlled studies have documented various family and marital/couple problems (Benoit et al., 1989; Crittenden, 1987) including inadequate housing, frequent moves, poverty, unemployment, substance abuse, violence, social isolation, and child maltreatment (Benoit, 2000).

Diagnostic Considerations

Several attempts at classification—for example, DC:0–3R (Zero to Three, 2005); DSM-5 (APA, 2013); ICD-10 (WHO, 1992); Chatoor, Dickson, Schaefer, and Egan (1985); Dahl and Sundelin (1986); Gremse, Lytle, Sacks, and Balistreri (1998); and Woolston (1985)—have been more or less successful in operationalizing diagnostic criteria to cover the spectrum of feeding disorders and FTT, or to distinguish between feeding disorders and FTT. As stated earlier, FTT is not a diagnosis unto itself (Cole & Lanham, 2011), but a symptom of a wide range of childhood diseases and problems, and it should be distinguished from constitutional small size (Ficicioglu & an Haack, 2009). FTT generally describes children whose current weight or rate of weight gain is significantly below that of other children of similar race, age, and sex (Tuohy, Barnes, & Allen, 2008); it has often been defined as weight for age that falls below the 5th percentile on multiple occasions, or as weight deceleration that crosses two major percentile lines on standard growth charts (Cole & Lanham, 2011). However, many other definitions have been used, with the end result being that there is no universally accepted definition of FTT and no consensus on which of several specific anthropometric criteria should be used to define FTT (Cole & Lanham, 2011; de Onis, Garza, Onyango, & Borghi, 2007; Ficicioglu & an Haack, 2009; Hosseini, Borzouei, & Vahabian, 2011; Jeong, 2011; Jolley, 2003; Olsen, 2006; Olsen et al., 2007; Raynor & Rudolf, 2000; Tuohy et al., 2008). Some authors even question the validity of this "diagnosis," given the absence of a concise and universally accepted definition (Hughes, 2007; Tuohy et al., 2008).

FTT has traditionally been dichotomized into "organic" (when an underlying health problem is thought

to cause or contribute to FTT) versus "nonorganic" (when no underlying health problem can be identified as contributing) groups. There is now greater awareness that this dichotomy can be misleading and should be abandoned in favor of considering the contribution of multiple possible factors in poor growth, even in cases where a major single underlying cause is identified (Tuohy et al., 2008). It is now recognized that FTT is usually caused by inadequate energy intake in diet, inadequate caloric absorption, and/or excessive caloric expenditure; that it is typically explained by multiple factors; and that it needs to be distinguished from constitutional small size.

Developmental Course and Prognosis

Although some literature suggests that even mild FTT is associated with significant adverse outcomes (Atalay & McCord, 2012; Corbett, Drewett, & White, 1996), the relevance of FTT to a child's future health and development remains controversial (Tuohy et al., 2008). In their systematic review, Rudolf and Logan (2005) concluded that children who had FTT were lighter and shorter than comparison children at follow-up (Boddy, Skuse, & Andrews, 2000). Concerns and conflicting findings related to impaired cognitive development, learning problems, lower intelligence, or developmental delay associated with FTT characterized earlier research (Corbett & Drewett, 2004; Corbett, Drewett, & Wright, 1996; Drewett, Corbett, & Wright, 1999), but more recent evidence suggests that the long-term impact of FTT on subsequent cognitive abilities may not be as serious as previously thought (Black, Dubowitz, Krishnakumar, & Starr, 2007; Emond et al., 2007; Rudolf & Logan, 2005). When FTT was examined in the general population, rather than in exclusively low-income families, no adverse cognitive effects were identified (Belfort et al., 2008).

Atalay and McCord (2012) have suggested that the neurocognitive deficits attributed to FTT are likely to result both from poor nutrition and from the well-documented detrimental effects of poverty and psychosocial stress on child development. If malnutrition becomes severe and chronic during the first year of life, a child's brain and neurological development may be permanently affected, making early recognition and prompt intervention critical (Jeong, 2011). In a nested case–control study within a large cohort (an area of northeast England over a 2-year period), 74 infants below the 5th centile on a thrive index were identified, compared with 86 controls; both groups were assessed with the Bayley Scales at 4 and 9 months, and their mothers were interviewed (McDougall, Drewett, Hungin, & Wright, 2009). The 6.1% of term-born infants identified as weight-faltering over the first 6–8 weeks of life had more feeding problems and showed more developmental delay at both 4 and 9 months, and their families were not significantly different from those of controls on any economic or educational measure (McDougall et al., 2009). These various findings have led clinicians and researchers to conclude that the long-term concerns and effects of FTT on cognitive development, future academic performance, and behavior remain unclear (Cole & Lanham, 2011; Jeong, 2011; Tuohy et al., 2008). There is a consensus that severe, prolonged malnutrition, which is common in developing countries, can negatively affect a child's future growth and cognitive development (Cole & Lanham, 2011; Rudolf & Logan, 2005).

A small percentage of children fail to thrive in the context of chronic neglect or abuse (Wright & Birks, 2000). Mackner, Starr, and Black (1997) demonstrated that the cognitive performance of children with both FTT and neglect was significantly below that of children with neglect only, children with FTT only, and controls with neither FTT nor neglect, suggesting a cumulative effect of neglect and FTT on cognitive functioning and poor outcomes for those children. Kerr, Black, and Krishnakumar (2000) found that children with a history of both FTT and maltreatment had more behavior problems and worse cognitive performance and school functioning than children with neither risk factor. Children with only one risk factor (either FTT or maltreatment) achieved intermediate scores. In a prospective, controlled study of family environments of children who had been hospitalized with FTT, Drotar, Pallotta, and Eckerle (1994) found that the quality of family relationships at the point of diagnosis did not predict family relationships, residence, or constellation changes on average 3.5 years later. However, mothers of children who had been hospitalized for FTT reported less adaptive relationships within the family than controls. Findings from these various studies do not help to elucidate the direction of effects.

The effectiveness of interventions addressing feeding difficulties (e.g., Batchelor, 2007; Hampton, 1996; Southall & Schwartz, 2000) and FTT (e.g., Batchelor, Gould, & Wright, 1999) has been reported. Children with FTT who are treated in multidisciplinary clinics experience a more rapid correction of FTT (Bithoney et

al., 1991) and improved cognitive testing scores (Mackner, Black, & Starr, 2003) when compared with such children within a traditional primary care setting (Atalay & McCord, 2012). Evidence is available to document the effectiveness of home visiting and parenting programs (Barrett, 2003; Kendrick et al., 2000; Wright et al., 1998) and multidisciplinary approaches (Batchelor, 2008; Hanks & Hobbs, 1993; Hobbs & Hanks, 1996).

Epidemiology

Estimates of the incidence and prevalence rates of FTT vary widely and depend on the terminology or definition used and the demographics of the population studied, with higher rates occurring in economically disadvantaged rural and urban areas (Cole & Lanham, 2011; Gahagan & Holmes, 1998; Olsen, Skovgaard, Weile, & Jørgensen, 2007; Tuohy et al., 2008). In the United States, FTT is estimated to affect from 1 to 5% of infants under age 2 admitted to hospitals, 10% of those living below the poverty level in rural and urban areas, 20% of infants born prematurely, and up to 30% of infants seen in inner-city emergency room and ambulatory care settings (Bithoney, Dubowitz, & Egan, 1992; Daniel, Kleis, & Cemeroglu, 2008; Frank & Ziesel, 1988; Powell, Low, & Speers, 1987; Schwartz, 2000). Longitudinal data for infants from birth to 2 years were analyzed for 1978 healthy, full-term infants born between 1999 and 2001, and the period prevalence of underweight was 24% (Ross et al., 2009). Male and female infants appear to be equally affected. In Britain, 1.8% of infants in the community and 3.3% of those born full-term and of appropriate weight for gestational age are affected (Skuse, Gill, Reilly, Wolke, & Lynch, 1995; Skuse, Wolke, & Reilly, 1992). In the northeast England case–control study described above, 6.1% of term-born infants were identified as weight-faltering over the first 6–8 weeks of life (McDougall et al., 2009). In Israel, 3.9% of full-term infants in the community were found to develop FTT (Wilensky et al., 1996). In a large cohort of Danish infants with varying socioeconomic status and living in a suburban environment, FTT was identified in 0.5–5.0%, depending on which of six anthropometric criteria were used to define FTT (Tuohy et al., 2008). In pediatric hospitals in developed countries, 2–25% of children suffer from malnutrition, and FTT is usually a symptom of an underlying disease (Nützenadel, 2011). In a recent study examining the links between infant feeding and stunting/underweight in children under age 24 months from 14 poor countries, the prevalence of both underweight and stunting was found to increase with age, and at least 50% of 12- to 23-month-old infants had stunted growth (Marriott, White, Hadden, Davies, & Wallingford, 2012).

Causal or contributing organic pathology should be considered in FTT (Ficicioglu & an Haack, 2009), given that 16–30% of children with FTT may have organic problems severe enough to explain their growth failure (Berwick, Levy, & Kleinerman, 1982). However, it is worth keeping in mind that a clear underlying medical condition is never identified in more than 80% of cases (Atalay & McCord, 2012; Cole & Lanham, 2011; Gahagan, 2006; Jeong, 2011; Schwartz, 2000; Stephens, Gentry, Michener, Kendall, & Gauer, 2008), and that in three separate population-based studies, an underlying organic disease was found in 6% or fewer of children with FTT (e.g., Emond, Drewett, Blair, & Emmett, 2007; Tuohy et al., 2008). Most cases of FTT involve inadequate caloric intake caused by behavioral or psychological issues (Cole & Lanham, 2011). A "mixed" etiology (i.e., one in which both organic and nonorganic factors are simultaneously present and likely to be contributing to the onset and/or perpetuation of FTT) can be found in 15–35% of infants with FTT (Singer, 1986).

Etiology

Many etiological factors, often coexisting, have been suggested and reflect the multifactorial etiology and heterogeneity of FTT. The common denominator in all cases of FTT is that an infant is not receiving enough calories to meet nutritional and caloric needs. There are many possible reasons for this, including various underlying medical problems that increase caloric/nutritional needs, such as excessive caloric expenditure due to hypermetabolic states and/or inadequate caloric absorption due to malabsorption (Bergman & Graham, 2005; Jeong, 2011; Wright, Parkinson, Shipton, & Drewett, 2007). There is increasing recognition that in many children the cause of FTT is multifactorial and can include any combination of biological, psychosocial, and environmental contributors (Batchelor, 2008; Emond et al., 2007; Jeong, 2011).

Epidemiological work by Skuse (1993), Wolke (1996), and other researchers as indicated suggests that children who may be likely to develop FTT include the following: children with small appetites and undemand-

ing or fussy eaters; children with oral–motor problems (Harris, 2010) or poor appetite regulation; those who do not communicate hunger clearly; those with hypersensitivity to certain food textures (Harris, 2004, 2010); those with a weak sucking or problems of weaning (Emond et al., 2007); those with problems related to the mechanics of eating (e.g., cleft palate); and those with developmental disorders such as autism spectrum disorder (Batchelor, 2008; Drewett, Kasese-Hara, & Wright, 2004; Field, Garland, & William, 2003). The children may also have inherited characteristics that make them more neophobic than their peers, and therefore make them more likely to refuse new foods (Harris, 2010). Skuse and colleagues (1992) concluded that there were no differences in infants' temperament between cases and comparisons (Batchelor, 2008), although infant temperament had previously been considered a contributing factor (Benoit, 2009). No genetic contributor per se has been identified as causing FTT or feeding disorders. However, some genetic disorders (e.g., inborn errors of metabolism, cystic fibrosis) have been associated with FTT.

Other possible etiological factors may include a disordered caregiver–infant relationship (see Benoit, 2009, for a review). In their community-based study, Skuse and colleagues (1992) concluded that there were no differences in infants' attachment behavior between cases and comparisons. However, clinical studies have shown insecure and/or disorganized attachment and/or insensitive caregiving as contributing factors for some children with FTT (Atalay & McCord, 2012; Batchelor, 2008; see Benoit, 2009, for a review; Iwaniec, 2004; Ward et al., 2000). Contrary to the links once made between maternal deprivation and FTT, Skuse and colleagues' (1992) prospective community-based study provided little evidence of maternal deprivation, abuse, or neglect in families of children with nonorganic FTT (Batchelor, 2008). Two community-based studies also failed to identify markers of social deprivation or neglect as an important cause (Emond et al., 2007; Wright & Birks, 2000). Nonetheless, child neglect and abuse must also be considered because children with FTT are four times more likely to be maltreated than children without FTT (Cole & Lanham, 2011; Jeong, 2011), although neglect may only account for a small proportion of all children with FTT (Batchelor, 2008; Skuse, 1985; Wright, 2005). Even among neglected children, FTT is believed to be due to inadequate calorie consumption, with the exception of a rare condition in which children with an inborn constitutional predisposition may, under stress, develop growth hormone deficiency (Batchelor, 2008). In their literature review on parenting and FTT, Boddy and Skuse (1994) concluded that there was an association between parenting behavior and poor infant growth. Research also documented an association between a mother's IQ and mother–child interactions (e.g., Wolke, 1996), with maternal IQ determining "interactional synchrony" (Batchelor, 2008). Studies have also identified a relationship between mothers' problem-solving abilities and children's FTT (Boddy et al., 2000; Robinson et al., 2001). Maternal depression is thought to be significant in some clinical settings (e.g., Atalay & McCord, 2012), but one recent community-based study (Wright et al., 2006) found that maternal depression had little influence on infants' weight gain (Batchelor, 2008). For a small number of mothers, their own attitudes to food may be significant in their children's feeding problems and/or FTT (Douglas & Bryon, 1996).

Other family factors can contribute to inadequate caloric intake at any age, including a caregiver's mental health problems, inadequate nutritional knowledge, and family financial difficulties (Atalay & McCord, 2012; Benoit, 2009; Jeong, 2011). Poverty is the greatest single risk factor for FTT in developed and developing countries (Cole & Lanham, 2011; Jeong, 2011), but it is important to keep in mind that FTT occurs across all socioeconomic groups (Wright, 2005).

Future Directions

The lack of either a universally accepted definition of FTT or a validated classification system continues to hamper research in this area. Research is needed to validate existing definitions, anthropometric measures of FTT, and classification systems (e.g., DC:0–3R, DSM-5), and to document the frequency of association between FTT and feeding disorders. Much of the existing research addressing various etiological contributors fails to address the direction of effects, and this should be carefully examined in future studies. There is a need for cohort studies with long-term follow-up into adulthood to clarify how to reliably identify normal, constitutionally small children for whom no specific intervention is required, and to clarify the effects of early FTT on growth, cognitive development, and academic performance (Tuohy et al., 2008). Future research is also needed with respect to efficacy and effectiveness of specific intervention programs.

Feeding and Eating Disorders

Description of the Disorders and Diagnostic Considerations

A knowledge and understanding of normative aspects of eating, and of normal feeding-related developmental milestones and behavior, is important in working with infants and toddlers who have feeding problems (Harris, 2010; Udall, 2007). Some researchers and clinicians define "feeding *problems*" as persistent refusal of most or all new foods, refusal of previously accepted foods, extreme emotional responses to feeding, aversion to sensory stimuli, persistent expulsion of foods, frequent vomiting during feeding, resolute avoidance of feeding, and inability to chew and/or swallow food; they define "feeding *disorders*" as occurring when feeding problems are associated with significant weight loss, insufficient growth, or developmental deficits (e.g., Aldridge, Dovey, Martin, & Meyer, 2010). However, in reality, the study of childhood feeding and eating disorders in infancy and toddlerhood is plagued by inconsistencies in use of terminology and diagnostic criteria, lack of consensus on definitions, and lack of a universally accepted classification system (Bryant-Waugh, Markham, Kreipe, & Walsh, 2010; Burklow, Phelps, Schultz, McConnell, & Rudolph, 1998; Chatoor, Conley, & Dickson, 1988; Williams, Field, & Seiverling, 2010). The feeding and eating disorders described in DSM-5 that are most relevant to infancy and toddlerhood include pica, rumination disorder, and avoidant/restrictive food intake disorder. Below, we describe these and other feeding disorders that are described in some of the classification systems of feeding disorders relevant to infancy, such as DC:0–3R and (to a lesser extent) ICD-10.

RUMINATION DISORDER

DSM-5 defines rumination disorder as the regurgitation of food (which may be rechewed, reswallowed, or spit out), repeated over 1 month or more. This regurgitation is not due to an associated gastrointestinal or other medical condition such as pyloric stenosis or gastroesophageal reflux, and it does not occur exclusively during the course of avoidant/restrictive food intake disorder (and, for older children, anorexia nervosa, bulimia nervosa, or binge-eating disorder). Another DSM-5 diagnostic criterion indicates that if the symptoms occur in connection with another mental disorder (e.g., intellectual disability or another neurodevelopmental disorder), they must be severe enough to warrant separate clinical attention. Finally, DSM-5 requires a specification of "in remission" if, after full criteria for rumination disorder were met earlier, they have not been met for a definite period of time.

Rumination disorder is not identified as a separate diagnostic entity in ICD-10, but is included as a symptom of feeding disorders of infancy and childhood. The age of onset is usually between 3 and 12 months of age. Infants with rumination disorder display a characteristic position of straining and arching the back with the head held back, making sucking movements with their tongues. Research findings suggest that in rumination disorder (see Benoit, 1993, 2009, for reviews), the regurgitation and rumination may occur in a state of relaxation, self-absorption, and pleasure, and appears to have a self-soothing or self-stimulatory function. Infants may be irritable and hungry between periods of regurgitation. Predisposing factors may include lack of stimulation, neglect, parent–child relationship problems, and other stressful life events. Rumination disorder commonly occurs in the context of intellectual disability and autism spectrum disorder. Although in infants, rumination disorder may remit spontaneously, complications of a protracted course may include severe malnutrition/FTT, dehydration, gastric problems, and a 25% mortality rate. Boys are affected five times more often than girls. Two types of rumination disorder have been described: (1) psychogenic (with a younger age of onset and associated significant disturbances or inadequacies in the caregiving environment); and (2) self-stimulation (with a later age of onset and associated intellectual disability in the affected child).

PICA

DSM-5 defines pica as persistently eating nonfood, non-nutritious substances; this eating is not appropriate to the individual's developmental level, is not an aspect of a socially normative or culturally supported practice, and occurs for at least 1 month. In addition, if pica occurs in the context of another mental disorder or medical condition, it has to be sufficiently severe to justify separate clinical attention. As it does for rumination disorder, DSM-5 also requires specification of whether pica is in remission (i.e., after full criteria for pica were previously met earlier, the criteria have not been met for a definite period of time). Examples of substances that can be ingested include clay, dirt, sand, stones, pebbles, hair, feces, and many other substances (see

Benoit, 1993, 2009, for reviews). DSM-5 and ICD-10 diagnostic criteria suggest a minimum age (chronological or mental) of 2 years for the diagnosis, indicating that pica is no longer an appropriate diagnosis in young infants. Solyon, Solyon, and Freeman (1991) reported that pica usually appears during the second year of life and often remits spontaneously during early childhood. The main comorbid presentations of pica in toddlers include intellectual disability and autism spectrum disorder (Bryant-Waugh & Piepenstock, 2008). Possible "physical" etiological factors have been identified, such as deficiencies in iron, calcium, and zinc. Other possible etiological or associated factors include poverty, child maltreatment, parental psychopathology, lack of stimulation, and family disorganization.

OTHER FEEDING BEHAVIOR DISORDERS

The DSM-5 criteria for avoidant/restrictive food intake disorder (Table 15.3) map partially onto the alternative classification system DC:0–3R (Zero to Three, 2005). Table 15.4, which includes DC:0–3R's six subtypes of feeding behavior disorder, is largely based on the important work conducted by Irene Chatoor and her colleagues over many years, including some validation work pertaining to the DC:0–3R subcategories (e.g., Chatoor, Ganiban, Hirsch, Borman-Spurrell, & Mzarek, 2000; Chatoor, Hirsch, Ganiban, Persinger, & Hamburger, 1998). Three of the six DC:0–3R feeding behavior disorders are not considered in DSM-5. These three are feeding disorder associated with concurrent medical condition (such a disturbance would not meet criteria for a mental disorder and thus is not included in DSM-5; Bryant-Waugh et al., 2010); feeding disorder of state regulation (a disturbance in infant regulation, similar to disturbances in sleep or crying); and feeding disorder of caregiver–infant reciprocity. Only two of the six DC:0–3R feeding behavior disorders (sensory food aversion, and feeding disorder associated with insults to the gastrointestinal tract) do not require the presence of "growth deficiency" or failure to gain weight or weight loss (or FTT) to make the diagnosis, and thus four of the six DC:0–3R feeding behavior disorders (and, by extension, some of the DSM-5 categories) may overlap with FTT. The DC:0–3R feeding behavior disorders are described here.

1. *Feeding disorder of state regulation* requires difficulty reaching and maintaining a calm state during feeding, starting in the newborn period.

2. *Feeding disorder of caregiver–infant reciprocity* consists of a lack of social reciprocity during feeding that is not due solely to a physical disorder or a pervasive developmental disorder.

TABLE 15.3. DSM-5 Diagnostic Criteria for Avoidant/Restrictive Food Intake Disorder

A. An eating or feeding disturbance (e.g., apparent lack of interest in eating or food; avoidance based on the sensory characteristics of food; concern about aversive consequences of eating) as manifested by persistent failure to meet appropriate nutritional and/or energy needs associated with one (or more) of the following:
   1. Significant weight loss (or failure to achieve expected weight gain or faltering growth in children).
   2. Significant nutritional deficiency.
   3. Dependence on enteral feeding or oral nutritional supplements.
   4. Marked interference with psychosocial functioning.

B. The disturbance is not better explained by lack of available food or by an associated culturally sanctioned practice.

C. The eating disturbance does not occur exclusively during the course of anorexia nervosa or bulimia nervosa, and there is no evidence of a disturbance in the way in which one's body weight or shape is experienced.

D. The eating disturbance is not attributable to a concurrent medical condition or not better explained by another mental disorder. When the eating disturbance occurs in the context of another condition or disorder, the severity of the eating disturbance exceeds that routinely associated with the condition or disorder and warrants additional clinical attention.

Specify if:

In remission: After full criteria for avoidant/restrictive food intake disorder were previously met, the criteria have not been met for a sustained period of time.

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TABLE 15.4. DC:0–3R Diagnostic Criteria for Feeding Behavior Disorder

601. *Feeding Disorder of State Regulation*. The diagnosis requires that ALL THREE of the following criteria be met:
   (1) The infant has difficulty reaching and maintaining a calm state during feeding (e.g., the infant is too sleepy, too agitated, and/or too distressed to feed).
   (2) Feeding difficulties start in the newborn period.
   (3) The infant fails to gain weight or loses weight.

602. *Feeding Disorder of Caregiver–Infant Reciprocity*. The diagnosis requires that ALL THREE of the following criteria be met:
   (1) The infant or young child does not display developmentally appropriate signs of social reciprocity (e.g., visual engagement, smiling, or babbling) with the primary caregiver during feeding.
   (2) The infant or young child shows significant growth deficiency.
   (3) The growth deficiency and lack of relatedness are not due solely to a physical disorder or a pervasive developmental disorder.

603. *Infantile Anorexia*. The diagnosis requires that ALL SIX of the following criteria be met:
   (1) The infant or young child refuses to eat adequate amounts of food for at least 1 month.
   (2) Onset of the food refusal occurs before the child is 3 years old.
   (3) The infant or young child does not communicate hunger and lacks interest in food but shows strong interest in exploration, interaction with caregiver, or both.
   (4) The child shows significant growth deficiency.
   (5) The food refusal does not follow a traumatic event.
   (6) The food refusal is not due to an underlying medical illness.

604. *Sensory Food Aversions*. The diagnosis requires that ALL FOUR of the following criteria be met:
   (1) The child consistently refuses to eat specific foods with specific tastes, textures, and/or smells.
   (2) Onset of the food refusal occurs during the introduction of a novel type of food (e.g., the child may drink one type of milk but refuse another, may eat carrots but refuse green beans, may drink milk but refuse baby food).
   (3) The child eats without difficulty when offered preferred foods.
   (4) The food refusal causes specific nutritional deficiencies or delay in oral motor development.

605. *Feeding Disorder Associated with Concurrent Medical Condition*. The diagnosis requires that ALL FOUR of the following criteria be met:
   (1) The infant or young child readily initiates feeding, but shows distress over the course of feeding and refuses to continue feeding.
   (2) The child has a concurrent medical condition that the CLINICIAN JUDGES to be the cause of the distress.
   (3) Medical management improves but does not fully alleviate the feeding problem.
   (4) The child fails to gain adequate weight or may even lose weight.

606. *Feeding Disorder Associated with Insults to the Gastrointestinal Tract*. The diagnosis requires that ALL FOUR of the following criteria be met:
   (1) Food refusal follows a major aversive event or repeated noxious insults to the oropharynx or gastrointestinal tract (e.g., choking, severe vomiting, reflux, insertion of nasogastric or endotracheal tubes, suctioning) that trigger intense distress in the infant or young child.
   (2) The infant or young child's consistent refusal to eat takes one of the following forms:
      (a) The infant or young child refuses to drink from the bottle but may accept food offered by spoon. (Although the child may consistently refuse to drink from the bottle when awake, she may drink from the bottle when sleepy or asleep.)
      (b) The infant or young child refuses solid food but may accept the bottle.
      (c) The child refuses all oral feedings.

(continued)

TABLE 15.4. *(continued)*

(3) Reminders of the traumatic event(s) cause distress, as manifested by one or more of the following:
  (a) The infant shows anticipatory distress when positioned for feeding.
  (b) The infant or young child resists intensely when a caregiver approaches with a bottle or food.
  (c) The infant or young child shows intense resistance to swallowing food placed in her mouth.

(4) The food refusal poses an acute or long-term threat to the child's nutrition.

Note. This diagnosis should not be used when a young child's feeding problem is primarily due to Disorders of Affect, Adjustment Disorder, Posttraumatic Stress Disorder, Deprivation/Maltreatment Disorder, or a Relationship Disorder.

If organic/structural problems (e.g., cleft palate, reflux) affect the child's ability to eat or digest food, the clinician should not use Feeding Behavior Disorder as a primary diagnosis. The clinician can indicate the appropriate medical diagnosis under Axis III. However, if a feeding disturbance that originated from organic or structural difficulties continues after these initial difficulties have been resolved, the diagnosis of Feeding Behavior Disorder may be appropriate.

3. *Infantile anorexia* is characterized by refusal to ingest adequate amounts of food; lack of interest in food, combined with strong interest in exploration and interaction; and apparent lack of hunger (Chatoor et al., 2000; Chatoor, Ganiban, et al., 1998; Chatoor, Ganiban, Surles, & Doussard-Roosevelt, 2004). Klein and colleagues (2012) were the first to publish data on the diet and growth in 62 children ages 1–3 years with infantile anorexia. Ammaniti, Lucarelli, Cimino, D'Olimpio, and Chatoor (2010) compared 184 mothers and infants ages 6–36 months with infantile anorexia to 187 mothers and infants without infantile anorexia; they found that the former group showed higher scores on both mother and child symptomatic characteristics and on dysfunctional interactions during feeding, compared to the latter group, and that both child and mother characteristics were significant predictors of dyadic conflict during interactions.

4. *Sensory food aversions* are characterized by persistent refusal to eat specific foods but no difficulty with preferred foods, associated with specific nutritional deficiencies or delay of oral–motor development. Sensory food aversions are among the most common feeding disorders during the first 3 years, particularly when young children start making the transition to self-feeding and when issues of autonomy and dependency need to be negotiated between caregiver and child (Chatoor, 2009). Although many children are "picky eaters," they may not suffer from sensory food aversions, which constitute a more serious feeding disorder. Feeding-related sensory processing problems may be suspected if a child does not explore by mouthing objects when developmentally appropriate; shows excessive gagging, coughing, retching, or vomiting that interferes with eating or nutrition; accepts only a severely restricted variety of foods and/or liquids; shows difficulty progressing or an inability to progress to solid foods; has feeding periods longer than 30–45 minutes (e.g., Reau, Senturia, Lebailly, & Christoffel, 1996); holds and/or stores food in cheeks or under tongue, interfering with food intake; and shows prolonged dependence on pureed foods (Thompson, Bruns, & Rains, 2010). Thompson and colleagues (2010) have described sensory modulation strategies to address feeding-related sensory processing problems.

5. *Feeding disorder associated with concurrent medical condition* consists of initial acceptance of feeding, followed by progressive distress and then refusal over the course of feeding. These symptoms are caused by a concurrent medical condition and are associated with improvement (but not complete alleviation) after medical management of the medical condition.

6. *Feeding disorder associated with insults to the gastrointestinal tract* requires that the food refusal be persistent and follow a major aversive event or repeated noxious insults to the oropharynx or gastrointestinal tract, and that distress be present at exposure to reminders of the traumatic event(s). This feeding disorder has also been termed "posttraumatic feeding disorder" and was first described by Chatoor and colleagues (1988) in children of latency age. The incidence and prevalence rates of this feeding disorder are unknown, but it could be on the increase because of advances in medical technology that now contribute to the survival of infants

with complex medical problems, whose survival is often contingent upon prolonged periods of tube feeding. Several reports suggest that infants who are tube-fed are at risk for developing severe feeding difficulties (e.g., extreme food selectivity, conditioned avoidance, or "food phobia") when oral feedings are introduced (Blackman & Nelson, 1985, 1987; Geertsma, Hyams, Pelletier, & Reiter, 1985; Levy, Winters, & Heird, 1980; Linscheid, Tarnowski, Rasnake, & Brams, 1987). The traumatic oral experiences related to medical treatment (e.g., suctioning, repeated insertion of nasogastric or endotracheal tubes) that many of these children experience, or episodes of choking and gagging on food or medicine, may lead to pervasive problems with refusal of solids and fluids. Because many of these infants are tube-fed, they may not suffer from FTT even though they often have a severe feeding disorder.

Etiology of Feeding and Eating Disorders

The etiology of feeding and eating disorders is multifactorial, with anatomical or physiological factors (e.g., sensory-perceptual abnormalities; oral–motor dysfunction; health problems; temperamental and regulation characteristics) and/or behavioral and ecological factors (traumatic experiences; mealtime behaviors; and characteristics of the caregiver, caregiver–infant relationship, family, and social environment) interacting (Aldridge et al., 2010; Benoit, 2009; Benoit, Wang, & Zlotkin, 2000; Chatoor et al., 1997, 2000; Cooper, Whelan, Woolgar, Morrell, & Murray, 2004; Kerwin, 1999; Piazza, 2008; Williams, Field, & Seiverling, 2010). Whelan and Cooper (2000) found the odds ratio of a maternal eating disorder for 4-year-old children with feeding problems to be 11:1. The recognition of multifactorial contributors to the onset and perpetuation of feeding problems and disorders has led clinicians and researchers to emphasize that multifactorial and multidisciplinary team approaches, as well as the use of individually and developmentally appropriate techniques, are necessary to address the numerous challenges faced by young children with feeding disorders (e.g., Ammaniti et al., 2010; Batchelor, 2008; Bruns & Thompson, 2010; Cole & Lanham, 2011; Jeong, 2011; Owen et al., 2012; Tuohy et al., 2008; Udall, 2007).

Developmental Course and Prognosis

Marchi and Cohen (1990) followed a sample of over 800 children over a 10-year period (from early–middle childhood to late childhood–adolescence). They found that feeding problems in young children were stable over time. Maladaptive eating behavior and pica in early childhood were significant risk factors for bulimia nervosa in 9- to 18-year-old children and young adolescents, whereas picky eating and "digestive problems" were risk factors for later anorexia nervosa. Findings from this study suggest that eating problems in infancy and early childhood may persist into later childhood and adolescence.

One study (retrospective reports of childhood sleep and eating problems derived from parent reports) of 164 offspring who had at least one parent with major depressive disorder, and were assessed at three times over 20 years by evaluators who were unaware of the parents' status and used a structured diagnostic interview, suggests that eating and sleep problems during early childhood may be risk factors for mood and anxiety disorders later in life (Ong, Wickramaratne, Tang, & Weissman, 2006). Irregularities in eating and sleeping schedules in childhood (described as low rhythmicity) were associated with adolescent-onset major depression and anxiety disorders, as well as childhood-onset anxiety disorders. Eating irregularities were not associated with adult-onset psychopathology (Ong et al., 2006).

In a study conducted 6 years after 230 families of children who had early feeding and/or sleeping problems were first assessed clinically, these children continued to have more sleep and feeding problems than reference children did (Ostberg & Hagelin, 2011). In the same study, mothers in the clinical group reported more health problems, were less content with their social support, and had more psychosocial problems and stressful life events, compared to mothers in the comparison group. Children in the clinical group had more internalizing problems than comparison children, while recent feeding and sleeping problems were connected to more externalizing and internalizing problems.

There is also some evidence suggesting that behavioral feeding disorders may be associated with suboptimal development, which relates to conflict between parent and child rather than to the adequacy of food intake per se (Chatoor, Surles, et al., 2004; Kerzner, 2009).

Several treatment components characterize the management of feeding problems and food refusal. In her review of the literature on treatments for severe feeding problems in children (some of which have

been used with toddlers), Kerwin (1999) noted that contingency management treatment—including both positive reinforcement of appropriate feeding responses (e.g., accepting rather than removing the spoon during food refusal training and swallow induction) and ignoring or guiding of inappropriate responses—were effective interventions. Williams and colleagues (2010) reviewed 38 intervention studies of food refusal in children, published from 1979 to 2008. Of the 218 participants who received treatment, 212 had some form of medical issue. Positive reinforcement was the most common component described in these intervention studies, and 21 of the 38 intervention studies specifically mentioned purposefully ignoring a child's inappropriate mealtime behavior and other behavioral strategies. These other strategies included escape prevention (a proven procedure to increase acceptance of food) with either physical guidance or nonremoval of the spoon; representation (which involves replacing food that has been expelled back into the child's mouth); texture fading; and appetite manipulation. There has been only one randomized controlled study to compare the efficacy of some of these techniques (Benoit et al., 2000).

Epidemiology

Accurate incidence and prevalence rates of feeding problems and feeding disorders are difficult to determine, in part due to the previously mentioned lack of consensus pertaining to definitions and classifications. Incidence rates of feeding and eating problems vary based on the source of information, specific population studied, or definition used. For example, incidence rates based on parent report range from approximately 20 to 60% (Bernard-Bonnin, 2006; Carruth, Ziegler, Gordon, & Barr, 2004; Jacobi, Agras, Bryson, & Hammer, 2003; Kerzner, 2009; Reau et al., 1996). Severe and persistent feeding problems tend to worsen over time and have been reported as more prevalent in children with physical disabilities (26–90%), intellectual disabilities (23–43%), and chronic medical illness, prematurity, or low birth weight (10–49%) (Bernard-Bonnin, 2006; Burklow et al., 1998; Dahl & Sundelin, 1986; Kerwin, 1999; Palmer & Horn, 1978). Feeding disorders are rarer than feeding problems, with reported incidence rates ranging from 1–2% (Aldridge et al., 2010) to 3–10% (Kerwin, 1999) to 6–35% (Jenkins, Bax, & Hart, 1980; Palmer & Horn, 1978; Richman, 1981).

Future Directions

As with other clinical problems of infancy and early childhood, the lack of standard definitions or accepted diagnostic criteria for feeding disorders has hampered research in the field. The lack of distinction between FTT and feeding disorders has been another complication. Future research should address issues of definition, etiology, pathophysiology, prevention, and treatment. Such research should carefully tease out the relative contribution of multiple factors in the development and/or perpetuation of feeding disorders (e.g., infant characteristics, caregiver characteristics; caregiving and environment characteristics), and should determine how these factors should be best targeted in intervention. Future research needs to address the questions of for whom, when, and which empirically supported treatments of feeding problems are appropriate. As with FTT, there is a need for large-scale studies with long-term follow-up into adulthood to clarify the effects of early feeding problems and feeding disorders on children's developmental, social, and emotional outcomes, as well as the impact of interventions on feeding disorders and outcomes. Finally, more research is needed to determine whether eating problems in infancy and early childhood are also risk factors for eating disorders in adolescence and adulthood.

Sleep–Wake Disorders

Description of the Disorders and Diagnostic Considerations

Familiarity with normal sleep–wake development and sleep physiology (e.g., normal sleep states, diurnal organization or sleep–wake cycle, and ultradian organization—the cycle of rapid-eye-movement [REM] and non-rapid-eye-movement [NREM] sleep) is important for an understanding of sleep disorders occurring during infancy and early childhood (Anders, Carskadon, & Dement, 1980; Anders, Goodlin-Jones, & Sadeh, 2000; Chamness, 2008; Iglowstein, Jenni, Molinari, & Largo, 2003; Owens & Burnham, 2009; Sadeh & Anders, 1993; Touchette, Petit, Tremblay, & Montplaisir, 2009). Sleep problems represent one of the most common pediatric problems during the first 3 years of life. Although there is no universally accepted definition of sleep problems in infancy and toddlerhood (Owens & Burnham, 2009) some classification systems of sleep disorders have some utility—for instance, the *International Classification of Sleep Disorders*, second

edition (ICSD-2; American Academy of Sleep Disorders, 2005), DSM-5 (APA, 2013), and DC:0–3R (Zero to Three, 2005; see Table 15.5). Table 15.6 provides a list of the various sleep–wake disorders described in DSM-5, although many do not apply to infants and toddlers. Only sleep–wake disorders that apply to infants and toddlers are described below. Objective measures of sleep include actigraphy, video, and polysomnography at home and in the sleep laboratory (Touchette et al., 2009).

Using some of the aforementioned classification systems, clinicians can classify sleep disorders as dyssomnias (difficulties in initiating or maintaining sleep or sleep fragmentation), parasomnias, or symptoms of underlying disorders (Owens et al., 2002; Pearl, 2002). Dyssomnias are further divided into intrinsic (those with a primarily or purely biological cause) and extrinsic (those caused by influences outside the body, such as parental discipline style and medication use). Examples of intrinsic dyssomnias include narcolepsy, sleep apnea syndrome, and periodic limb movement disorder (Pearl, 2002). DSM-5 defines narcolepsy as recurring periods of an overwhelming need to sleep, lapses into sleep, or napping occurring within the same day, and at least three times per week over the previous 3 months. DSM-5 also requires the presence of at least one of the following: (1) episodes of cataplexy at least a few times per month, consisting of either (a) brief (seconds to minutes) episodes of sudden bilateral loss of muscle tone with maintained consciousness, brought on by laughter or joking, in individuals with long-standing disease; or (b) spontaneous grimaces or jaw-opening episodes with global hypotonia or thrusting of the tongue, in children or individuals within 6 months of onset; (2) hypocretin deficiency; and (3) a nocturnal sleep polysomnograph showing REM sleep latency of 15 minutes or less, or a multiple sleep latency test showing mean sleep latency of 8 minutes or less and at least two sleep-onset REM periods. Narcolepsy in infants and toddlers is extremely rare and difficult to diagnose, due to its atypical features, the impossibility for infants and toddlers to report symptoms verbally, and the lack of polysomnographic criteria validated for infants and toddlers (Nevsimalova, 2009). However, narcolepsy has been reported in a 2-week-old infant (Hood & Harbord, 2002) and in a handful of infants whose narcolepsy began in the first or second year of life (see Nevsimalova, 2009, for a review).

Examples of extrinsic dyssomnias in infants and toddlers include inadequate sleep hygiene; sleep-onset association disorder (or trouble falling asleep), defined as a sleep latency of more than 30 minutes (Gaylor, Goodlin-Jones, & Anders, 2001; Ottaviano, Giannotti, Cortesi, Bruni, & Ottaviano, 1996); insufficient sleep disorder; and limit-setting sleep disorder (Pearl, 2002). Dyssomnias are influenced by a combination of biological (maturation of the central nervous system, child's characteristics, genetics) and environmental factors (Jenni & O'Connor, 2005; Sadeh & Anders, 1993; Touchette et al., 2009). The most common sleep disturbances in infancy and toddlerhood are excessive night waking (in infants) and settling difficulties or trouble

TABLE 15.5. DC:0–3R Diagnostic Criteria for Sleep Behavior Disorder

510. *Sleep-Onset Disorder (Sleep-Onset Protodyssomnia)*

Sleep-onset problems are reflected in the time it takes a child to fall asleep, the child's need for the parent to stay in the room until she falls asleep, and/or the child's need for reunions with the parent (i.e., the parent leaves the room and comes back in response to bids from the child).

The diagnosis of Sleep-Onset Disorder requires that there be significant difficulty falling asleep for AT LEAST 4 WEEKS, with five to seven episodes per week.

The child must be 12 months of age or older.

520. *Night-Waking Disorder (Night-Waking Protodyssomnia)*

Night-waking problems are reflected in awakenings that require parental intervention and/or removal to the parental bed.

A diagnosis of Night-Waking Disorder requires that significant difficulty in nighttime awakenings be present for AT LEAST 4 WEEKS and involve five to seven episodes per week.

The child must be 12 months of age or older.

TABLE 15.6. DSM-5 Sleep–Wake Disorders

Insomnia disorder
Hypersomnolence disorder
Narcolepsy
Breathing-related sleep disorders
Obstructive sleep apnea hypopnea
Central sleep apnea
Sleep-related hypoventilation
Circadian rhythm sleep–wake disorders
Delayed sleep phase type
Advanced sleep phase type
Irregular sleep–wake type
Non-24-hour sleep–wake type
Shift work type
Parasomnias
Non-rapid eye movement sleep arousal disorders
Nightmare disorder
Rapid eye movement sleep behavior disorder
Restless legs syndrome
Substance/medication-induced sleep disorder
Other specified insomnia disorder
Unspecified insomnia disorder
Other specified hypersomnolence disorder
Unspecified hypersomnolence disorder
Other specified sleep–wake disorder
Unspecified sleep–wake disorder

falling asleep (in toddlers) (Mindell, 1993; Owens & Burnham, 2009).

Parasomnias (or disturbances of NREM sleep or sleep state dissociation) are the most common sleep problems in preschool and school-age children, but are relatively uncommon during the first 18–24 months of life; the period from birth to 18 months in particular has little overt expression of parasomnias (Kotagal, 2009). Parasomnias include arousal disorders (confusional arousals, somnambulism, night terrors); sleep–wake transition disorders (rhythmic movement disorder); REM-associated parasomnias (e.g., nightmares); other parasomnias (nocturnal enuresis, sleep bruxism, infantile sleep apnea, sudden infant death syndrome, benign neonatal sleep myoclonus, congenital central hypoventilation syndrome); and sleep disorders associated with medical/psychiatric disorders (Pearl, 2002). Possible triggers for parasomnia events include fever, stress, anxiety, extreme fatigue, noise, full bladder, periodic limb movements, and sleep-disordered breathing (Chamness, 2008).

Confusional arousal is the most common parasomnia in infancy and toddlerhood (Kotagal, 2009). The onset of symptoms is typically within 2–3 hours of sleep onset (at the time of transition from slow-wave sleep to a lighter state of sleep). A child typically sits up in bed, whimpers, cries or moans, may utter words like "no" or "go away," appears distressed, and remains inconsolable regardless of parental efforts (Kotagal, 2009). The episodes can last 10–30 minutes and vary in frequency from nightly to two to three per month (Kotagal, 2009).

Sleep terrors occur between ages 3 and 10 years, typically in the first third of the night sleep, with a usual frequency of two to three times per month or per week (Kotagal, 2009). During a sleep terror episode, the child awakens abruptly from sleep with a blood-curdling scream, appears agitated, is flushed over the face with sweating, has tachycardia, may jump out of bed as if running away from an unseen threat, and may remain unresponsive to parental efforts at calming (Kotagal, 2009). Mild episodes of sleepwalking may occur during toddlerhood—for example, when a toddler sits up and crawls around the crib, or when a child walking quietly in sleep comes and stands by the parental bed (Kotagal, 2009). Separation anxiety may be a predisposing factor for both sleep terrors and sleepwalking (Petit, Touchette, Tremblay, Boivin, & Montplaisir, 2007).

Although sleep-disordered breathing, a parasomnia, is most common in preschoolers, it can occur in infants and toddlers. It includes conditions such as primary snoring and obstructive sleep apnea (the two extremes of the spectrum) and the upper airway resistance syndrome (Spicuzza, Leonardi, & La Rosa, 2009). Symptoms of sleep-disordered breathing in 3- to 36-month-old infants include snoring, witnessed apnea episodes, frequent arousals, mouth breathing/dry mouth, nocturnal sweating, FTT, nasal congestion, hyperextended neck, recurrent otitis media and/or upper respiratory infections, and noisy breathing (Sinha & Guilleminault, 2010). Other symptoms of sleep-disordered breathing specific to infants ages 3–12 months include poor suck, apparent life-threatening event, poor day–night cycle, stridor, and breath-holding spells. Additional symptoms of sleep-disordered breathing that appear to be specific to toddlers (1–3 years old) include sleep terrors, confusion arousal, irritability, daytime sleepiness, and restless sleep (Sinha & Guilleminault, 2010).

Young children who are sleep-deprived do not typically complain of daytime sleepiness. Instead, they

may be easily frustrated, agitated, irritable, aggressive, moody, emotionally labile, or impulsive, and/or may show increased activity, behavior problems, and (later) neurocognitive deficits and school/learning problems (Chamness, 2008; Fallone et al., 2002). Because of their apparent inattention and hyperactivity, they may be diagnosed with ADHD, especially during preschool or later (Corkum, Tannock, Moldofsky, Hogg-Johnson, & Humphries, 2001).

Rhythmic movement disorder, another parasomnia, is a sleep–wake transition disorder that comprises a group of stereotyped, repetitive movements involving large muscles (usually of the head and neck), such as side-to-side head rolling, head banging, or body rocking (Kotagal, 2009; Kuhn & Elliott, 2003). It is important to keep in mind that rhythmic movements in infants and toddlers at the time of drifting off from wakefulness to sleep are physiologically normative, and generally resolve by the age of 3–4 years (Kotagal, 2009). Rhythmic movement *disorder* is identified when the movements lead to significant consequences such as self-injury (Kotagal, 2009). The rhythmic movements that occur around sleep–wake transitions should be distinguished from those seen in autism spectrum disorder, which tend to persist also into wakefulness (Kotagal, 2009).

Developmental Course and Prognosis

Anders and colleagues (2000) have pointed out that nearly half of infants with sleep problems continue to have sleep problems in later years; this suggests that the myth about children outgrowing their sleep problems is refuted by research findings. Without treatment, pediatric sleep disturbances may persist for years (Anders et al., 2000; Kataria, Swanson, & Travathan, 1987; Owens et al., 2002). This is concerning, given the accumulating evidence that sleep deprivation and fragmentation may impair psychological, cognitive, and social functioning (Dahl, 1996; Lewin, England, & Rosen, 1996; Mindell, Owens & Carskadon, 1999; Owens et al., 2002; Randazzo, Muehlbach, Schweitzer, & Walsh, 1998; Touchette et al., 2009).

Touchette and colleagues (2007, 2009) emphasize the serious potential consequences of a modest but chronic loss of sleep in childhood. In their longitudinal study, children with short nocturnal sleep duration before age 3.5 years showed increased risk (2.5 times) for high hyperactivity–impulsivity scores and low cognitive performance at 6 years, compared to children who slept 11 hours per night, after the investigators controlled for potentially confounding variables (Touchette et al., 2007, 2009). Moreover, persistent short sleep duration in early infancy increased by almost three times the risk for overweight or obesity at 6 years of age, again after adjustments for potentially confounding variables (Touchette et al., 2007, 2009; Touchette, Petit, Tremblay, Boivin, & Montplaisir, 2008). Another longitudinal study (Reilly et al., 2005) also documents that short sleep duration increases the risk for obesity in school-age children. Touchette and colleagues (2009) stress the importance of allowing a child to sleep at least 10 hours per night in early childhood for optimal child development, in accordance with recommendations from the National Sleep Foundation Poll (Mindell, 2004).

The treatments of choice of many dyssomnias appear to be behavioral interventions that involve the parents (Kuhn & Elliott, 2003; Kuhn & Weidinger, 2000; Mindell, 1999; Owens, Palermo, & Rosen, 2002; Richman, Douglas, Hunt, Lansdown, & Levere, 1985; Sadeh, 2005). A detailed description of behavioral interventions and the associated empirical evidence supporting their use is beyond the scope of this chapter. Several authors summarize various behavioral interventions and the empirical evidence supporting their use to treat sleep-onset disorder or "behavioral insomnia of childhood, limit-setting type" (to use ICSD-2 terminology) seen in infancy; they provide descriptions of behavioral interventions such as extinction, graduated extinction, scheduled waking, positive bedtime routines, bedtime fading, response cost, and positive reinforcement, as well as parent education, advice, and support (Kuhn & Elliott, 2003; Mindell, 1999; Owens & Burnham, 2009; Owens, France, & Wiggs, 1999; Owens et al., 2002; Ramchandani, Wiggs, Webb, & Stores, 2000; Sadeh, 2005). Factors influencing the outcome of behavioral interventions include characteristics of the caregiver (compliance; exhaustion due to sleep deprivation; depression or other mental illness; unwillingness/inability to devote time and energy to implementing the behavioral intervention; lack of acceptance of the treatment plan; and lack of understanding of aspects of the treatment plan) and characteristics of the home environment (e.g., living arrangements; presence of extended family or siblings; family financial difficulties) (Owens et al., 2002; Owens & Burnham, 2009).

Since 2002, the American Academy of Pediatrics has had a Clinical Practice Guideline recommending that all children be screened for snoring (Chamness, 2008; Section on Pediatric Pulmonology and Sub-

committee on Obstructive Sleep Apnea Syndrome, American Academy of Pediatrics, 2002). The gold standard for diagnosing sleep disordered breathing is laboratory polysomnography (Sinha & Guilleminault, 2010). Once sleep-disordered breathing is diagnosed, the accepted first-line treatments in children are tonsillectomy and adenoidectomy, although other treatments are available; these include rapid maxillary expansion, radiofrequency ablation of the nasal turbinates, continuous positive airway pressure, and weight loss if children are overweight or obese (Sinha & Guilleminault, 2010). Untreated sleep-disordered breathing in young children, especially obstructive sleep apnea, may be associated with neurocognitive and learning deficits (particularly in short-term memory and concentration ability) and poor school performance (Chervin et al., 2006; Curcio, Ferrara, & De Gennaro, 2006; Giordani et al., 2008; Gottlieb et al., 2004; Gozal, 1998; Mitchell & Kelly, 2007), behavioral and mood and anxiety disorders (Dahl, 1996; Ong et al., 2006; Touchette et al., 2007). It may also be linked to physical health problems, such as pulmonary hypertension, systemic hypertension, and possible cardiovascular and metabolic disorders (particularly if the disordered breathing is associated with obesity; Spicuzza et al., 2009). It is not clear whether the cardiovascular and neurocognitive impairment is reversible (Spicuzza et al., 2009). However, findings from these studies have typically related to older children and adolescents, and it is not clear whether they also apply to infants (Owens & Burnham, 2009). In infants, significant disturbances of growth such as FTT have been associated with obstructive sleep apnea (Bonuck, Parikh, & Bassila, 2006; Chamness, 2008; Sinha & Guilleminault, 2010; Spicuzza et al., 2009). For example, Freezer, Bucens, and Robertson (1995) showed that 52% of infants under age 18 months referred for adenotonsillectomy with clinical symptoms of sleep apnea had FTT, and similar data were obtained by Williams and colleagues (1991) in a population of children ages 6–36 months (see also Spicuzza et al., 2009).

There is no specific treatment for narcolepsy in infants (see Nevsimalova, 2009, for a review), and no satisfactory treatment for rhythmic movement disorder (Kotagal, 2009; Kuhn & Elliott, 2003). Infrequently occurring (once or twice a month) confusional arousals, sleep terrors, and sleepwalking may not need to be treated (Kotagal, 2009). There is limited research on behavioral interventions for parasomnias, and only one intervention for sleep terrors and sleepwalking (scheduled awakenings) has sufficient empirical support to be considered promising (Kuhn & Elliott, 2003), although its use with infants is unclear. With the exception of bedtime refusal and night waking, there are surprisingly few empirically supported interventions for pediatric sleep problems (Kuhn & Elliott, 2003). The use of medications is not generally accepted to manage sleep problems in infancy and toddlerhood (Owens, 2011). Owens and colleagues (Owens, 2011; Owens, Rosen, Mindell, & Kirchner, 2010) suggest that exogenous melatonin has considerable promise as a therapeutic intervention for children with circadian rhythm disturbances and chronic insomnia, although there is no convincing evidence that its use should be recommended for children under age 36 months (Owens, 2011).

Epidemiology

Prevalence rates of sleep disorders in infants and toddlers vary from study to study, depending in part on definitions, types of sleep problems, children's ages, and populations studied. For example, some studies estimate that 15–30% of children suffer from sleep problems during the first 3 years of life (Adair, Bauchner, Philipp, Levenson, & Zuckerman, 1991; Armstrong, Quinn, & Dadds, 1994; Johnson, 1991; Lozoff, Wolf, & Davis, 1985; Richman, 1981; Sadeh, 2005); others report that up to 50% of infants experience difficulty settling and frequent night wakings (Chamness, 2008; Mindell & Owens, 2003), with approximately 10% of young children having concurrent difficulty settling and frequent night wakings (Anders & Keener, 1985; Keener, Zeanah, & Anders, 1988). Approximately 25–50% of preschoolers experience sleep disturbances such as bedtime resistance, delayed sleep onset, and disruptive night wakings (Owens et al., 2002). Beltramini and Hertzig (1983) report that infants younger than 2 years suffer more from frequent nocturnal awakening than older toddlers and preschoolers, who suffer more often from sleep-onset difficulties, increasing in prevalence across the first 4 years: from 6% at 1 year to 12% at 2 years, 24% at 3 years, 49% at 4 years, and 33% at 5 years. A high prevalence rate for sleep problems has been reported in children with neurodevelopmental disorders, with estimates ranging from 13 to 85% (Owens & Burnham, 2009). No gender differences have been identified with respect to night waking (Paret, 1983).

Although the prevalence of sleep-disordered breathing has been estimated at between 1 and 4%, it is some-

what difficult to ascertain, as definitions vary and the condition has only recently been recognized in children (Sinha & Guilleminault, 2010). Sleep-disordered breathing can occur at any age, but seems to present most commonly in 2- to 5-year-olds (Hoban & Chervin, 2005; Sinha & Guilleminault, 2010). Spicuzza and colleagues (2009) suggest that primary snoring and obstructive sleep apnea are common sleep disorders in the pediatric age group, accounting for more than three-quarters of all sleep disorders.

No known socioeconomic factors are associated with sleep problems in infancy and early childhood. There are cultural variations and individual family differences in sleeping habits and routines (e.g., some families and cultures have adults and children sleeping in close proximity, whereas others isolate children from adults during sleep), and these should be considered in determining whether a young child has a sleep problem or disorder (Owens & Burnham, 2009).

Etiology

Transient sleep disturbances (also called "adjustment sleep disorders") may be associated with a stressful life event, a physical illness (e.g., ear infection, cold), or a disruption in usual routines (e.g., jet lag, trip).

Medical conditions that increase the risk of developing sleep-disordered breathing compared to the general population include overweight/obesity (including Prader–Willi syndrome), syndromes with midface hypoplasia (e.g., Pierre Robin sequence, Crouzon syndrome), large tongue (e.g., trisomy 21), and neuromuscular disorders (e.g., cerebral palsy and myotonic dystrophy) (Mitchell, 2009; Sinha & Guilleminault, 2010). The etiology of the sleep-disordered breathing spectrum is multifactorial, consisting of a complex interplay between anatomic and neuromuscular factors and an underlying genetic predisposition toward the disease (Spicuzza et al., 2009). Adenotonsillar hypertrophy remains the most common cause of obstructive sleep apnea in preschool children and infants (Spicuzza et al., 2009).

Little is known about the genetic/molecular basis of normal sleep (Nunes & Bruni, 2008). Genetic studies have been mostly restricted to narcolepsy, restless legs syndrome, and obstructive sleep apnea (Nunes & Bruni, 2008). One of the current pathophysiological models for narcolepsy–cataplexy involves an autoimmune-mediated destruction of some neurons (Nevsimalova, 2009). For two sleep circadian disorders (delayed sleep phase syndrome and advanced sleep phase syndrome), associated genes have been recently discovered (Nunes & Bruni, 2008). Parasomnias for which a genetic basis has been reported include sleepwalking, confusional arousals, night terrors, and nocturnal enuresis (Nunes & Bruni, 2008). Using animal models of sleep deprivation, researchers have identified a gene, Homer1a, whose expression reflects susceptibility to sleep loss (Nunes & Bruni, 2008).

Stress, maturational factors, and temperament have repeatedly been related to sleep state organization and sleep problems (Keener et al., 1988; Sadeh & Anders, 1993; Touchette et al., 2005). Other factors, such as allergies, cosleeping, nutritional factors, and states of physical discomfort, may also be contributing, but findings are contradictory (see Anders et al., 2000, for a review). In a prospective longitudinal study (Savino et al., 2005), sleep disorders were more frequent for infants with colic, but another study did not find persistent sleep problems in infants with colic (Wake et al., 2006). As discussed earlier, some clinicians and researchers view sleep disorders as manifestations of an underlying regulation disorder (Greenspan & Wieder, 1993). Factors such as prematurity and use of a transitional object do not seem to be strongly associated with consolidated sleep, in a way that is independent of parental behaviors (Touchette et al., 2009).

The role of prenatal and perinatal problems in sleep disturbances in children is unclear (Goodlin-Jones, Eiben, & Anders, 1997; Oberklaid, Prior, & Sanson, 1986; Touchette et al., 2009; Wolke, Söhne, Riegel, Ohrt, & Osterlund, 1998; Zuckerman, Stevenson, & Bailey, 1987). For gender, there are also mixed results, but in general it does not seem to have a major impact on the development of sleep consolidation (Beltramini & Hertzig, 1983; Gaylor et al., 2001). Health-related factors (e.g., ear infections, cold, gastroesophageal reflux, milk allergy, neurological impairments, medication effects, pain from teething) are also linked to sleep problems. Children with neurodevelopmental disorders, such as autism spectrum disorder, ADHD, Tourette's disorder, and genetic syndromes associated with intellectual disability, are also known to be prone to sleep disorders.

One of the most consistent research findings is the association between sleep problems and parent–child interactions at bedtime (Touchette et al., 2009). Excessive interventions to induce sleep (e.g., rocking, holding, patting, nursing, bottle feeding, pacifier use, and

car rides) have been linked to sleep-onset association disorder, and excessive nighttime feeding and poor limit setting have been linked to sleeplessness in infants and toddlers (Owens & Burnham, 2009; Pearl, 2002). Parental characteristics such as maternal age and education have little influence on sleep problems. Findings from research show conflicting results as to the role of a mother's immigrant status, depression, overprotectiveness, or feeling of efficacy in the onset and perpetuation of sleep problems (e.g., Touchette et al., 2005, 2009). Breast feeding versus bottle feeding was found to be highly associated with poor sleep consolidation in early childhood (Carey, 1974; Paret, 1983; Touchette et al., 2005), although other studies did not document such an association (e.g., Adair et al., 1991; Kahn, Mozin, Rebuffat, Sottiaux, & Muller, 1989). Cosleeping or sharing a room with another family member was also associated with poor sleep consolidation in early childhood (Touchette et al., 2005), although cosleeping in response to nocturnal awakenings increased the occurrence of sleep problems, whereas regular cosleeping was not detrimental to sleep quality (Lozoff, Askew, & Wolf, 1996). In fact, there is no reported association between cosleeping and sleep problems in non-Western cultures (Morelli, Rogoff, Oppenheim, & Goldsmith, 1992). Parental psychopathology has been associated with increased prevalence of childhood sleep problems (Gelman & King, 2001; Hiscock & Wake, 2001; Van Tassel, 1985; Zuckerman et al., 1987).

Environmental factors (e.g., fear or anxiety in abusive, neglectful, or dysfunctional families; parental conflict; maternal psychopathology; maternal insensitivity in reading and responding to infant cues; family stress; parent–child relationship disturbances) have been identified as contributing to the onset and/or perpetuation of sleep problems in infancy and toddlerhood (e.g., Benoit, Zeanah, Boucher, & Minde, 1992; Bernal, 1973; Paret, 1983; Pearl, 2002). There are significant discrepancies in research findings on the impact of familial and cultural factors on infant sleep consolidation, summarized in Touchette and colleagues (2009).

Future Directions

More longitudinal data are needed to examine the developmental course of sleep disorders from infancy into adulthood, as well as factors within the sleep-disordered infant and the caregiving environment that might contribute to the onset and perpetuation of sleep problems. The long-term systemic consequences of primary snoring in infants and toddlers, and the risk of such children's progressing to adult sleep apnea, should also be investigated; this would underline the need to find treatment options and solutions for early-onset snoring (Spicuzza et al., 2009). More research is needed to investigate mediated associations between dyssomnias and various risk factors such as temperament (including the objective comparison of physiological sensory thresholds in good and poor sleepers), as well as the contribution of genetics to childhood dyssomnias and problematic parasomnias, since these are clustered in families (Kotagal, 2009; Touchette et al., 2009). More longitudinal studies should examine whether the consequences of short sleep duration are independent of each other, or to what extent they interact to produce a more complex predicament. Given the reported associations between feeding and sleep problems, experimental studies are needed to further explore the relationship between sleep and appetite/feeding problems (with or without FTT). More rigorous research designs and large-scale prospective studies are required to firmly establish the efficacy of behavioral interventions for both dyssomnias and parasomnias, to delineate the situations in which each is best applied, and to assess the impact of treating sleep disorders in early childhood (Kotagal, 2009; Owens et al., 2002; Sadeh, 2005; Touchette et al., 2009). Finally, research on prevention and outcome of sleep problems during infancy is also necessary.

Posttraumatic Stress Disorder

Description of the Disorder

According to DSM-5, PTSD includes symptom clusters of reexperiencing the traumatic event, avoiding reminders of the event, negative alterations in mood or cognition, and increased arousal as central features (APA, 2013; see also Nader & Fletcher, Chapter 10, this volume). These types of symptoms have been noted in both children and adults, and research during the past 20 years has documented that they also occur in young children who experience severe trauma (Scheeringa, Zeanah, & Cohen, 2011). Systematic research has shown that although young children demonstrate the same clusters of symptoms of PTSD following traumatic events, the same diagnostic algorithms do not apply.

Diagnostic Considerations

It has been reported for many years that young children can experience symptoms associated with PTSD (see Gaensbauer, Chatoor, Drell, Siegel, & Zeanah, 1995; Zeanah & Burk, 1984). Beginning in the mid-1990s, however, Scheeringa, Zeanah, and Cohen (2011) conducted systematic research demonstrating that the DSM-IV (APA, 1994) algorithm for PTSD was not applicable for young children, and that a different algorithm was more valid (see Scheeringa, 2009, for a review). They studied and validated an alternative set of criteria, or alternative algorithm (PTSD-AA), which was more developmentally sensitive than the DSM-IV criteria.

The initial studies indicated that traumatized young children were far more likely to be diagnosed as having PTSD when the alternative algorithm (PTSD-AA) was used than when the DSM-IV algorithm was used (Scheeringa, Zeanah, Drell, & Larrieu, 1995). Eight subsequent studies of traumatized young children have confirmed that using PTSD-AA leads to significantly higher rates of diagnosed PTSD than using the DSM-IV algorithm does (Egger et al., 2006; Levendosky, Huth-Bocks, Semel, & Shapiro, 2002; Meiser-Stedman et al., 2008; Ohmi et al., 2002; Scheeringa, Peebles, Cook, & Zeanah, 2001; Scheeringa, Zeanah, Myers, & Putnam, 2003, 2005; Scheeringa, Myers, Putnam, & Zeanah, 2012). Frequency alone is not sufficient reason to favor the alternative algorithm, however, and other studies have examined the validity of these alternative criteria.

First, many young children who were traumatized and highly symptomatic did not meet DSM-IV criteria for PTSD. Two studies of criterion validity of the DSM-IV algorithm and PTSD-AA in severely traumatized preschool children demonstrated the better fit of PTSD-AA (Scheeringa et al., 2001, 2003). When best-estimate diagnosis of DSM-IV PTSD was used as a reference, children who met criteria for that diagnosis had the most symptoms when PTSD-AA was used, whereas traumatized young children who had subthreshold PTSD symptomatology had intermediate levels of symptoms, and nontraumatized children had the lowest levels of symptoms. If the DSM-IV symptom counts were used, however, a dimensional correlation was not evident in either study.

Second, in these two studies the mean number of signs/symptoms in the children diagnosed with PTSD-AA was significantly higher than the number of signs/symptoms in the children who were traumatized but not diagnosed with PTSD-AA, whereas this was not true when the DSM-IV criteria were used. The fact that traumatized and highly symptomatic children did not achieve the diagnostic threshold with the DSM-IV criteria but did with PTSD-AA is another indication of stronger criterion validity.

Because of these data, DSM-5 created a preschool subtype, derived from the work on PTSD-AA (see Table 10.2 in Nader & Fletcher, Chapter 10, this volume, for DSM-5 PTSD criteria for children 6 years and younger). Scheeringa and colleagues (2012) showed that the DSM-5 algorithm and PTSD-AA were essentially comparable, and that both identified more cases of PTSD in young children than did the DSM-IV algorithm. The subtype of PTSD for children age 6 years and younger is the first developmental subtype in the DSM to define early childhood manifestations of a lifespan disorder.

Developmental Course and Prognosis

Evidence that PTSD signs/symptoms are more than transient in young children comes from three studies. Two studies have followed children prospectively after exposure to trauma, using PTSD-AA. Meiser-Stedman and colleagues (2008) studied 62 preschool children 2–4 weeks after they had experienced a motor vehicle accident, and then again 6 months later. Of the exposed children, 6.5% met PTSD-AA criteria at 2–4 weeks after the trauma and 10% at 6 months following the trauma. The diagnosis was moderately stable from 3 weeks to 6 months, whereas diagnosis of DSM-IV acute stress disorder (ASD) at 2–4 weeks was not related to DSM-IV PTSD at 6 months after the trauma. In this study, no cases of ASD diagnosed at 2–4 weeks were diagnosed with DSM-IV PTSD at 6 months after the trauma. Thus the PTSD-AA criteria demonstrated greater predictive validity than did the DSM-IV criteria.

Scheeringa and colleagues (2005) studied 62 children who had experienced a variety of traumas at three time points: initially an average of 4 months after the trauma, and then 16 and 28 months later. They found significant stability of PTSD-AA symptoms over the 2 years. There was no decline in symptomatology over 2 years either in those children who met criteria for PTSD-AA, or in those who were symptomatic but subthreshold for the diagnosis.

It was striking that the number of symptoms did not diminish by even one symptom over a 2-year period for either group. PTSD-AA diagnosis at Time 1 also significantly predicted degree of functional impairment 1 and 2 years later, and predicted PTSD-AA diagnosis 2 years later. Ohmi and colleagues (2002) studied preschool children in Japan following a gas explosion in a nursery school. They did not track stability of the diagnosis of PTSD-AA, but they did show stability of PTSD-AA signs/symptoms over 1 year in the children who attended the school.

Thus the available evidence indicates that PTSD symptomatology in young children is stable. This is especially important, given that more than one-quarter of the children in the Scheeringa and colleagues (2005) sample received treatment in the community during the longitudinal investigation and yet had no remission in symptomatology. Since three randomized controlled trials have now demonstrated that effective treatments for PTSD in young children exist (Cohen & Mannarino, 1996; Lieberman, Van Horn, & Ghosh Ippen, 2005; Scheeringa et al., 2012), it seems clear that without effective treatment, symptomatology does not remit in the short or intermediate term.

Long-term outcome data about prognosis are not available, but several studies have addressed factors responsible for severity of symptomatology. In a study of young traumatized children, Scheeringa and Zeanah (1995) examined a number of possible child- and trauma-related factors that might relate to severity of traumatic symptomatology: gender, age at trauma, chronic versus acute trauma, witnessed versus experienced, injured or not, and caregiver threatened or not. The single best predictor of severity of posttraumatic symptomatology in young children was whether or not their caregivers had been threatened by the traumatic events. This finding was replicated in a subsequent sample of children traumatized by injury (Scheeringa, Wright, Hunt, & Zeanah, 2006).

There are two possible mechanisms for the link between caregiver threat and a young child's posttraumatic symptomatology. First, in a direct effect, young children may appreciate the threat to themselves posed by a threat to their primary caregivers, leading to an intensification of their own symptoms. Second, in an indirect effect, a caregiver may be traumatized by the same event that traumatizes a child. This may result in the caregiver's being less able to respond empathically to the child, leading to an intensification of the child's posttraumatic symptoms. Either way, it is clear that the caregiver–child relationship is related in important ways to the child's symptomatology.

Physically and sexually abused young children have been noted to develop posttraumatic symptoms, although in many of these cases the trauma is not a single, discrete event, but rather a series of traumatic events or even an enduring circumstance. In examining the effects of acute versus chronic trauma, Scheeringa and Zeanah (1995) found that young children who had suffered acute trauma were more severely affected overall and had more symptoms of reexperiencing the traumatic event than infants who had experienced chronic trauma. This should not suggest that acute traumatic events are more injurious than chronic trauma, but only that the symptom picture differs in the two instances. Some have suggested, for example, that the effects of chronic trauma may be more apparent in long-term effects on personality or other developmental domains than in acute symptomatology.

In fact, it has been known for some time that very adverse early experiences are associated with many subsequent problems beyond PTSD (Cicchetti & Toth, 1995). Because of this, van der Kolk (2005) has proposed "developmental trauma disorder" as a new disorder intended to describe the varied sequelae in children who experience serious adversity. The challenges for such a diagnosis are (1) whether a single disorder can encompass the heterogeneity of problems following serious chronic trauma, and (2) whether the course and correlates of this putative entity are internally consistent and distinct. To date, no research on the disorder has appeared.

Future Directions

An important question about vulnerability to PTSD in young children is why only a minority of exposed children develop sustained signs and symptoms. Age appears to be one factor because only toward the end of the first year of life do young children have the requisite cognitive abilities to manifest signs of the reexperiencing cluster (Scheeringa, 2009). One study has implicated the influence of genetic variation in the dopamine transporter (DAT) 3' untranslated region variable number tandem repeat allele on the development of PTSD in preschool children exposed to Hurricane Katrina (Drury, Theal, Keats, & Scheeringa, 2009). In a recent study of children who survived the great

east Japan earthquake, investigators conducted structural MRI before and after the event (Sekiguchi et al., 2013). They found that children with smaller gray matter volume in the right ventral anterior cingulate cortex before the earthquake, and those with smaller gray matter volume in the left orbitofrontal cortex after the earthquake, were more likely to have PTSD symptoms. Because both regions are known to be involved in processing of fear and anxiety, these results demonstrate vulnerability for PTSD symptoms. More research on vulnerability is clearly needed.

An important area for future exploration concerns the neurobiology of trauma in young children. There is a large and ever-growing literature on the neurobiology of trauma in adults and older children. Our knowledge of the importance of brain development in the first few years of life (Sheridan & Nelson, 2009), and preliminary evidence about the effects of trauma not just on brain functioning but also on brain structure, make this an important area to explore.

An active and promising line of investigation concerns the effects of trauma on subcellular processes including gene expression. Much of this work is being undertaken in studies of "epigenetics"—that is, the processes by which environmental conditions in early life structurally alter DNA, providing a biological basis for the influence of the environment on an individual's phenotype. This work has ranged from studies of methylation involved in regulating gene expression (for reviews, see Bick et al. 2012; Szyf, 2012) to assessing telomere length as an index of cellular aging (Drury et al., 2011). Understanding these processes promises to illuminate biological mechanisms by which exposure to trauma, including both discrete events and enduring circumstances, may lead to symptomatology and maladaptation.

Reactive Attachment Disorder and Disinhibited Social Engagement Disorder

Description of the Disorders

Despite concerns about serious disturbances of attachment in the scientific literature dating back to the beginning of the 20th century, reactive attachment disorder (RAD) first appeared in official psychiatric nomenclatures only in 1980, with the publication of DSM-III (APA, 1980). Criteria describing this disorder were revised in subsequent DSM editions, but the changes in DSM-5 (APA, 2013) separated these two types—the inhibited and disinhibited—into distinct disorders, although ICD-10 (WHO, 1992) had taken a similar approach two decades earlier.

In DSM-5, RAD describes young children who exhibit limited or absent initiation or response to social interactions with caregivers and aberrant social behaviors (see Table 15.7). In particular, when distressed, the child fails to seek or respond consistently to comfort from caregivers and exhibits emotion dysregulation. In disinihibited social engagement disorder (DSED), children exhibit lack of social reticence with unfamiliar adults, failure to check back with caregivers in unfamiliar settings, and a willingness to go off with strangers (see Table 15.8). Somewhat older children exhibit intrusive and overly familiar behavior with strangers, including asking overly personal questions, violating personal space, or initiating physical contact without hesitation. Recent reviews have concluded that although the two patterns do arise in similar conditions of extreme caregiving risk, they are best conceptualized as two distinct disorders rather than as two subtypes of a single disorder because of differences in the phenomenology, correlates, and responses to intervention of RAD and DSED (Rutter, Kreppner, & Sonuga-Barke, 2009; Zeanah & Gleason, 2010).

RAD is essentially the absence of a preferred attachment to anyone. For example, in studies of young children living in institutions, absence of a preferred caregiver and unclassifiable attachment in the Strange Situation procedure (because of the paucity or absence of attachment behaviors) were found in the same children who were diagnosed with RAD (Smyke, Dumitrescu, & Zeanah, 2002; Zeanah, Smyke, Koga, Carlson, & the BEIPCore Group, 2005). This disorder, characterized by emotional constriction and social unresponsiveness, is more closely linked to internalizing disorders and converges modestly with depression (Gleason et al., 2011), whereas DSED is more closely linked to ADHD and disruptive behavior disorders and converges modestly with them (Gleason et al., 2011). Furthermore, it is not necessarily that attachment behaviors to caregivers are disinhibited in DSED, but rather that social engagement behaviors are expressed nonselectively. Children adopted internationally may turn selectively to their adoptive parents for comfort, support, nurturance, and protection, and still show lack of reticence around strangers and struggle to conform with social boundary norms. The two disorders are phenomenologically distinct, and they have different relationships to attachment behaviors. RAD is es-

TABLE 15.7. DSM-5 Diagnostic Criteria for Reactive Attachment Disorder of Infancy

A. A consistent pattern of inhibited, emotionally withdrawn behavior toward adult caregivers, manifested by both of the following:
   1. The child rarely or minimally seeks comfort when distressed.
   2. The child rarely or minimally responds to comfort when distressed.

B. A persistent social and emotional disturbance characterized by at least two of the following:
   1. Minimal social and emotional responsiveness to others.
   2. Limited positive affect.
   3. Episodes of unexplained irritability, sadness, or fearfulness that are evident even during nonthreatening interactions with adult caregivers.

C. The child has experienced a pattern of extremes of insufficient care as evidenced by at least one of the following:
   1. Social neglect or deprivation in the form of persistent lack of having basic emotional needs for comfort, stimulation, and affection met by caregiving adults.
   2. Repeated changes of primary caregivers that limit opportunities to form stable attachments (e.g., frequent changes in foster care).
   3. Rearing in unusual settings that severely limit opportunities to form selective attachments (e.g., institutions with high child-to-caregiver ratios).

D. The care in Criterion C is presumed to be responsible for the disturbed behavior in Criterion A (e.g., the disturbances in Criterion A began following the lack of adequate care in Criterion C).

E. The criteria are not met for autism spectrum disorder.

F. The disturbance is evident before age 5 years.

G. The child has a developmental age of at least 9 months.

Specify if:

Persistent: The disorder has been present more than 12 months.

Specify current severity:

Reactive attachment disorder is specified as **severe** when a child exhibits all symptoms of the disorder, with each symptom manifesting at relatively high levels.

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sentially equivalent to lack of or incompletely formed preferred attachments (Zeanah et al., 2005), whereas DSED occurs in children who lack attachments to one or more primary caregivers, in children who display clear selective attachment behavior, and even in children whose attachment behavior is classified as secure (Chisholm, 1998; Gleason et al., 2011; O'Connor, Heron, Golding, & Glover, 2003; Zeanah, Smyke, & Dumitrescu, 2002, O'Connor, Marvin, Rutter, Olrick, & Britner, 2003). DSM-5's separation of the two phenotypes into distinct disorders—one that is thought to reflect a lack of attachment, and the other more clearly describing disinhibited social engagement—better reflects contemporary research, and it is hoped that this division will encourage further research delineating their unique correlates.

Diagnostic Considerations

RAD and DSED have been reliably identified by structured interviews with caregivers (Smyke et al., 2002; Zeanah et al., 2005), by observational procedures (Gleason et al., 2011; Lyons-Ruth, Bureau, Riley, & Atlas-Corbett, 2009), or by both (Boris et al., 2004; Gleason et al., 2011; O'Connor, Marvin, et al., 2003). Furthermore, studies demonstrating reasonably good convergence among different approaches suggests that the same phenomena are being studied by diverse methods (Gleason et al., 2011; Zeanah et al., 2002, 2005). Studies have further confirmed that signs of RAD and DSED are rare to nonexistent in low-risk samples, and remain rare in higher-risk samples, but are readily identifiable in maltreated and institutionalized samples (reviewed in Zeanah & Smyke, 2009).

TABLE 15.8. DSM-5 Diagnostic Criteria for Disinhibited Social Engagement Disorder

A. A pattern of behavior in which a child actively approaches and interacts with unfamiliar adults and exhibits at least two of the following:
   1. Reduced or absent reticence in approaching and interacting with unfamiliar adults.
   2. Overly familiar verbal or physical behavior (that is not consistent with culturally sanctioned and with age-appropriate social boundaries).
   3. Diminished or absent checking back with adult caregiver after venturing away, even in unfamiliar settings.
   4. Willingness to go off with an unfamiliar adult with minimal or no hesitation.

B. The behaviors in Criterion A are not limited to impulsivity (as in attention-deficit/hyperactivity disorder) but include socially disinhibited behavior.

C. The child has experienced a pattern of extremes of insufficient care as evidenced by at least one of the following:
   1. Social neglect or deprivation in the form of persistent lack of having basic emotional needs for comfort, stimulation, and affection met by caregiving adults.
   2. Repeated changes of primary caregivers that limit opportunities to form stable attachments (e.g., frequent changes in foster care).
   3. Rearing in unusual settings that severely limit opportunities to form selective attachments (e.g., institutions with high child-to-caregiver ratios).

D. The care in Criterion C is presumed to be responsible for the disturbed behavior in Criterion A (e.g., the disturbances in Criterion A began following the pathogenic care in Criterion C).

E. The child has a developmental age of at least 9 months.

Specify if:

Persistent: The disorder has been present for more than 12 months.

Specify current severity:

Disinhibited social engagement disorder is specified as **severe** when the child exhibits all symptoms of the disorder, with each symptom manifesting at relatively high levels.

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Developmental Course and Prognosis

The courses of RAD and DSED have been documented to differ substantially. For example, signs of DSED are readily identified in children adopted following institutional rearing, whereas signs of RAD have not been reported in these samples (Chisholm, 1998; O'Connor, Marvin, et al., 2003). However, studies of children living in institutions identify elevated rates of both RAD and DSED among these children (Tizard & Rees, 1975; Zeanah et al., 2005). Therefore, signs of RAD seem to disappear after children are placed in adequate family settings, whereas signs of DSED often persist. This has been documented in the only randomized clinical trial of foster care as an alternative to institutional care, in which signs of RAD declined rapidly after children were removed from institutions and placed in families, whereas the declines were less marked for DSED (Smyke et al., 2012).

An important remaining question is about the degree of recovery of young children who were diagnosed with RAD or DSED early in life, but in whom signs of the disorder have diminished or disappeared following placement into better caregiving environments. In other words, once signs of the disorder have disappeared, are children able to develop healthy and secure attachments to their new caregivers, or do they experience continuing difficulties with interpersonal relationships? Data to address these questions are limited, but what we have invite caution about assuming full recovery. For example, signs of RAD and DSED in the second year of life are predictive of subsequent psychiatric impairment in the preschool years, even if signs of these disorders have subsequently diminished or disappeared (Gleason et al., 2011). In addition, signs of DSED have been shown to persist into adolescence and to be associated with peer relational difficulties,

even when children have been adopted into nurturing homes (Hodges & Tizard, 1989; Rutter et al., 2007). Increased risks for atypical patterns of attachment to new caregivers are also seen among adopted, formerly institutionalized children (Chisholm, 1998; O'Connor, Marvin, et al., 2003; Marcovitch et al., 1997).

Future Directions

Advances in the study of disordered attachment in general, and of RAD and DSED in particular, have been notable since the first two editions of this volume appeared. In fact, almost all we know about these disorders comes from studies conducted in the past decade. There is a great deal more we need to know, however.

One vexing question for investigators is why such distinctly different phenotypes arise in similar conditions of risk. Within the heterogeneous conditions that we label "neglect" or "deprivation," are there differences in individual experiences that might account for the phenotypic differences? Alternatively, are there biological differences in vulnerability that might account for the phenotypic differences (see, e.g., Drury et al., 2012)? Much remains to be done to delineate the origins of these disorders more clearly.

Critical questions about the long-term course and sequelae of the disorders remain largely unanswered. The data to date suggest that signs of RAD disappear after children are placed in an adequate caregiving environment. However, we do not know whether these children remain at risk for subsequent interpersonal or behavioral difficulties. Improved data on developmental sequelae could critically inform the design of interventions. Similarly, we know that signs of DSED may persist even after caregiving environments improve. This raises the question of what additional interventions should be provided to children to address the social-cognitive abnormalities associated with DSED, which may underlie the difficulties with social boundaries and peer relationships that in some cases are evident years later.

Advances in understanding the forms of attachment disorders seen among children in institutional care have come in part from clarifying the complex relations between RAD and DSED and the secure, insecure, and disorganized attachment patterns that are more prevalent among children not exposed to institutional care, though much remains to be learned (see Zeanah, Berlin, & Boris, 2011). The next section of the chapter reviews in more detail the individual and contextual risk factors for the disorganized attachment patterns that are more common among at-risk infants and toddlers reared in family settings.

RISK FOR LATER DISORDER: LONGITUDINAL STUDIES, PARENTING CONTEXTS, AND BRAIN–BEHAVIOR RELATIONS

The Developmental Context of Disorder

The Child in the Family Context

Because of the unique location of infancy at the beginning of the developmental process, clinicians and researchers who focus on infants have a special charge to maintain an orientation toward prevention of mental disorder, as well as treatment of existing conditions. DSM-5 (APA, 2013) defines a mental disorder as "a syndrome characterized by clinically significant disturbance in an individual's cognition, emotion regulation, or behavior that reflects a dysfunction in the psychological, biological, or developmental processes underlying mental functioning" (p. 20). As longitudinal research increasingly makes clear, family factors that substantially increase the risk of a child's manifesting clinically significant disturbance in cognition, emotion regulation, or behavior are beginning to be traced back to the infancy or prebirth periods, before the child him- or herself may be symptomatic. Because of the rapidity of developmental changes characteristic of the early years, family factors may also be more stable predictors of later child maladaptation than particular infant symptoms may be (Belsky & Fearon, 2002; Lyons-Ruth, Bureau, Holmes, Easterbrooks, & Brooks, 2013), although this remains an important question for research.

Child factors are also important correlates of a wide range of psychiatric disorders, as documented by chapters in the current volume. Child factors correlated with or predictive of disorder have included inhibited temperament, specific genetic markers, and nonspecific genetic contributions identified by behavioral genetic studies. Family factors may also be shaped by genetic inheritance, including both passive and evocative gene–environment correlations for children. The relatively recent application of sophisticated longitudinal research methods to the study of child psychopathology now offers the potential to delineate predictable relations in how family and environmental influences interact with child genetics and temperament to produce identifiable developmental trajectories over time.

Furthermore, with the recent unparalleled advances in the neurosciences—including neurobiology, structural and functional magnetic resonance imaging (MRI) studies, molecular genetics, and epigenetics—developmental studies are beginning to link experience-related behavioral changes to associated physiological and neurobiological changes at both the animal and human levels (e.g., Andersen et al., 2008; Cohen et al., 2006; Dannlowski et al., 2012; Meaney & Szyf, 2005). This research has the potential to extend previous biobehavioral models of risk (which typically focused on autonomic and hypothalamic–pituitary–adrenocortical [HPA] stress response systems) to include neural structure and function as possible mediators of environmental effects on psychological disorder and risk for disorder.

One important point to keep in mind in the following review is that while neurobiological processes are often framed as the "underlying mechanisms" or causal factors linking environmental risks to behavioral changes, we must be aware of the increasingly prevalent "neural as causal" fallacy. Associations between neurobiological processes and behavioral or relational processes do not establish etiological priority for either level of mechanism. Instead, as we know from many randomized animal models, changes in the infant's behavioral interactions with the caregiving environment causally drive many neurobiological adaptations (e.g. Francis, Diorio, Liu, & Meaney, 1999). Therefore, while neurobiological processes may "underlie" behavioral processes in the sense of being less visible to the naked eye, they do not necessarily "underlie" behavioral/environmental processes in the sense of acting as causal mechanisms. Causal mechanisms need to be established by a confluence of careful studies using randomized assignment, prospective longitudinal designs, and sophisticated modeling of mediating and moderating factors across these levels of analysis. Thus we need to be cautious about using the term "underlying mechanisms" as applying only to neurobiological processes. Changes in a child's behavior in response to changes in the environment, and particularly the relational environment to which humans are exquisitely biologically and psychologically attuned, are just as likely to constitute the "underlying mechanisms" in the sense of being etiologically causal to a particular developmental outcome, as well as to the neurobiological processes associated with those outcomes. For example, current human studies relate early maternal depression to poor-quality care, as well as to increased stress responding (Brennan et al., 2008) and amygdala volume (Lupien et al., 2011) in the child. Randomized animal studies establish that reduced care is one causal mechanism associated with both neurobiological outcomes (Francis et al., 1999; Vyas, Jadhav, & Chattarji, 2006). For a full understanding of how early risk factors may produce developmental trajectories toward later disorder, we must keep in mind both potential directions of effect between neurobiology and behavior.

Developmental Timing: The Prenatal Period and Infancy as Sensitive Periods in Development

Both animal and human studies provide clear evidence for the developmental influence of prenatal experiences on enduring brain structure and function (Del Cerro et al., 2010), as well as on long-term behavioral and cognitive outcomes in children (Beydoun & Saftlas, 2008; Buss, Davis, Muftuler, Head, & Sandman, 2009; Van den Bergh, Mulder, Mennes, & Glover, 2005). For example, in studies of nonhuman primates, experimentally induced prenatal stress in mothers has been associated in offspring with reduced hippocampal volume (Coe et al., 2003) and altered size of the corpus callosum (Coe, Lulbach, & Schneider, 2002). Human research has also found decreased gray matter (based on MRI studies) in multiple brain regions among children whose mothers experienced high levels of prenatal anxiety (Buss et al., 2009). Research on developmental psychopathology also identifies associations between elevated prenatal stress and increased risk of anxiety disorders (O'Connor, Heron, et al., 2003; Van Den Bergh & Marcoen, 2004), ADHD (O'Connor, Heron, et al., 2003), conduct disorder (Barker & Maughan, 2009; O'Connor, Heron, et al., 2003), and atypical stress response indexed by HPA activity (Glover, O'Connor, & O'Donnell, 2009; Gutteling, de Weerth, & Buitelaar, 2005). Similarly, prenatal exposure to nicotine, alcohol, and illicit substances has been associated with nonoptimal developmental outcomes, such as higher levels of child irritability and attachment insecurity (O'Connor, Sigman, & Kasari, 1992; Rodning, Beckwith, & Howard, 1991) and externalizing behavior (Buschgens et al., 2009). Although a fetal programming hypothesis has been proposed to explain how changes in the fetal environment can cause long-lasting changes in brain structure and function, as well as in biobehavioral development in children (Barker, 1998, 2003; Rutter & O'Connor, 2004), recent research suggests that subsequent post-

natal experiences can attenuate potential prenatal effects. For example, O'Connor and colleagues reported that maternal emotional support attenuated the association between prenatal alcohol exposure and attachment insecurity, and Bergman and colleagues reported that the associations between elevated prenatal stress and high child fearfulness, as well as between elevated cortisol and poorer child cognitive development, were each only observed among children with insecure infant–mother attachments (Bergman, Sarkar, Glover, & O'Connor, 2008, 2010).

The moderating effects of early family environment and infant–parent attachment quality are not surprising. It is a widely accepted tenet of developmental science that early caregiving exerts a profound and long-term influence on multiple domains of child development. Evidence for the effects of early caregiving can be traced from early rodent studies of postnatal handling (Denenberg, 1964) to contemporary epigenetic research using rodent models (Meaney & Szyf, 2005), as well as the thoughtful studies of gene–environment interplay involving molecular genetics and out-fostering conditions of nonhuman primates (Bennett et al., 2002; Suomi, 2006). Recent research on the effects of small-group foster care on previously institutionalized children has also pointed to the likelihood of a sensitive period for normal social attachment among human infants (Nelson et al., 2007; Windsor, Glaze, Koga, & the BEIP Core Group, 2007). Thus existing human and animal research strongly suggests that the infant and early toddler years represent a sensitive or critical period during which an individual's early experiences with a caregiver may scaffold the development of key biological and psychological processes.

Comparative neuroscience supports the notion of unique postnatal developmental periods during which brain activity may be highly sensitive to early caregiving effects—ranging from 21 postnatal days for rodents to 180 days for macaque monkeys, and through the third year of life for humans (Fox, Levitt, & Nelson, 2010). During this time, environmental experiences can potentiate or inhibit neural connectivity (Knudsen, 2004), thus shaping the structural and functional maturation of the brain. Cameron, Coleman, Dahl, Kupfer, and Ryan (1999) found that different timing of mother–infant separation experiences among infant macaques had very different effects on the offspring's long-term social behavior. Infants who were separated after making an attachment bond with their mothers (at 1 month of age) showed extreme initial withdrawal and lack of interaction with others, followed by "adopting" another animal and staying in very close contact with the adopted caregiver. In the long term, these monkeys showed increased anxious behavior and sought more contact with other animals than did controls without early separation. In contrast, monkeys separated before establishing an attachment relationship (at 1 week of age) showed no initial withdrawal. However, they did not develop normal social contacts with the other monkeys in the group and exhibited extremely atypical social behavior for the rest of their development, freezing when approached and engaging in more self-directed comforting behavior. Thus the timing of caregiving deviations in infancy may result in very different organizations of subsequent social and symptomatic behavior.

Similar profound effects of early experience, as evidenced in studies of children institutionalized from birth, suggest that positive changes in early caregiving environments before the age of 2 years are associated with higher IQ (Nelson et al., 2007), greater language ability (Windsor et al., 2007), and more positive attachment quality (Smyke, Zeanah, Fox, Nelson, & Guthrie, 2010). More recently, Pollak and colleagues (2010) reported differences in neurodevelopmental functioning in middle childhood between postinstitutionalized children adopted early (before 8 months of age) and those adopted late (after 12 months of age). The late adoptees scored lower on memory and attention tasks than did either early adoptees or matched nonadopted controls (the latter groups performed comparably across tasks), further suggesting that the first year of life is a highly sensitive period to environmental experience. Assessing such interactions between developmental phase and type of stressor will be critical to further progress in early identification and intervention in pathways toward child and adult psychopathology.

Phenotypic Discontinuity: The Importance of Longitudinal Studies

Because of the dramatic cognitive and behavioral reorganizations that take place during the first 4 years of life, early behavioral maladaptation at either the child or family level may have little surface similarity to forms of individual or family psychopathology exhibited later in development. Because of this phenotypic discontinuity over developmental epochs, particular early behaviors or family relational patterns may not be recognized initially as important precursors, pro-

dromes, or disorders of infancy. Therefore, prospective longitudinal studies from the early years of life constitute a particularly powerful methodology for exploring whether there are identifiable environmental or biological markers, risk conditions, or early precursor forms of child behavior that contribute to the development of a deviant trajectory over time. For example, odd behaviors in the presence of the parent in infancy, such as those considered criteria for disorganized attachments (see below), or unusual friendliness to strangers, as seen in DSED, may only gain significance as indicators of infant disorder if they are shown to be systematically related to later serious psychopathology. Thus studies of infant diagnostic groupings need to proceed in concert with more broadly based longitudinal studies of high-risk groups if the full range of early signs of disorder is to be identified.

The Regulatory Role of Early Relationships

Because these sensitive-period effects have all been a function of the quality of the caregiving relationship, a focus on understanding the role and patterning of early relationships is critical to a complete understanding of early human biobehavioral development and its relation to later emotional disorder (Lyons-Ruth & Jacobvitz, 2008). The past several decades of infancy research have also been distinctive in maintaining a concentrated focus on how to conceptualize and assess parent–infant relationships at both a behavioral and a representational level. However, the study of family relationships has been relatively neglected in recent psychopathology research because of the methodological and conceptual challenges inherent in directly observing relational behavior. This lack needs to be redressed in light of the strong body of animal studies indicating that parental nurturing behaviors are critical for establishing enduring parameters of a child's neurophysiology and subsequent behavior. With the recent unparalleled advances in the neurosciences, current studies in developmental psychopathology are increasingly focused on how child behavior, stress physiology, and neural structure and function are associated with both typical and atypical developmental trajectories.

Disrupted Parenting, Child–Parent Attachment, and Risk for Psychopathology

Although there has been a relative dearth of systematic research on diagnostically defined disorders of infancy, a sophisticated research literature exists delineating family contextual features evident before or during infancy that are associated with later child maladaptation. In this section, three particularly active areas of infant-oriented longitudinal work relevant to exploring the early developmental trajectories leading to childhood psychopathology are reviewed. These include research on intergenerational transmission of relational behavior; research on the context and correlates of disorganized/disoriented infant attachment behaviors; and research on early predictors of later psychiatric symptomatology.

Caregiving Received in Parents' Childhoods and Subsequent Parenting

Researchers from a variety of traditions have demonstrated that caregiving patterns established in relation to an infant not only have a degree of stability over time, but have roots in the adaptation of the parent *prior* to the birth of the child. One clear implication of this literature is that parental developmental history and psychological structure, in addition to parental genetic transmission, make contributions to the shaping of the child's relational behavior and biology; therefore, these need to be understood in their own right if the complex interplay between environmental and genetic contributions to deviant pathways is to be understood.

A number of studies have documented prediction from parents' childhood experiences (e.g., abuse) and aspects of later parental and marital relationships (Belsky & Pensky, 1988). Recent studies are now using multimethod, prospective longitudinal designs to search for mediating processes that might explain how prenatal adaptation and/or parents' childhood experiences influence the early parent–child relationship (Bailey, DeOliveira, Wolfe, Evans, & Hartwick, 2012; Kim, Trickett, & Putnam, 2010). For example, Cox and colleagues (1985) found that prebirth maternal characteristics predicted 41% of the variance in positive quality of mother–infant interaction at 3 months of age. In this study, the maternal prebirth assessments included measures of prenatal marital competence (assessed both through interview and observational measures) and individual psychological health based on 10 standardized measures. In addition, this study included a measure of the quality of parenting received in a parent's family of origin. Unexpectedly, the family-of-origin reports were much stronger predictors of mothers' parenting than the marital and psychological health variables, and the

marital and psychological health variables accounted for no further variance after family-of-origin variables were entered. The mothers' reports of their own parents' hostility and intrusiveness were particularly strong predictors of their own parenting. Additional analyses of these data also revealed that mothers' prenatal reports of histories of profound role reversal with their caregivers during childhood predicted their role reversal behaviors (as observed by researchers) when interacting with their children 2 years later (Macfie, McElwain, Houts, & Cox, 2005).

The power of family-of-origin interview assessments has been repeatedly replicated in other longitudinal multivariate studies. For example, Belsky, Hertzog, and Rovine (1986) gathered data on the contributions of prebirth maternal personality and marital adjustment, quality of care in family of origin, maternal social network contact assessed at 3 and 9 months, and infant temperament assessed at 3 and 9 months. Again, they found direct and unmediated effects of a mother's developmental history on current mother–child interaction quality, and the family-of-origin assessment made the greatest overall contribution of any variable to the prediction of parenting. Similarly, Lyons-Ruth and colleagues (Lyons-Ruth, 1992; Lyons-Ruth, Zoll, Connell, & Grunebaum, 1989), studying an impoverished, socially at-risk sample, expected that influences of childhood history on parenting would be mediated through influences on a mother's current depressive symptoms, marital status, number of children, and age at first childbearing. However, these mediated effects of childhood history were overshadowed by the large *direct effects* of a mother's childhood experiences on her parenting behavior, with the childhood experience measure accounting for more overall variance in parenting (27%) than all other risk factors. In response to these accumulated findings, Lyons-Ruth (1992) concluded that implicit representations of strategies of interaction in intimate relationships may be developed in early family relationships and reaccessed directly as parents establish relationships with their infants.

The most impressive demonstration of intergenerational continuity in parenting has come from Elder and colleagues' longitudinal study using the Berkeley Guidance Study Archives (Elder, Caspi, & Downey, 1986; Elder, King, & Conger, 1996). Although not focused on infancy per se, this longitudinal study (begun in 1928) has included four generations, encompassing grandparents, parents, children, and grandchildren; thus measures of childhood experience were obtained *prospectively,* rather than by retrospective report as in the studies described above. Elder and colleagues found that personality measures, marital conflict, and parenting styles tended to be correlated within families across generations, and that these correlated parental qualities were in turn related to child behavior. Parents who displayed conflicted, unstable personalities also experienced marital tension and displayed irritable, explosive behavior toward their children. Their children, in turn, displayed irritable, explosive behavior both in childhood and adulthood. However, if unstable personality and marital conflict did not find expression in punitive parental behavior toward children, intergenerational transmission did not occur.

These intergenerational continuities are undoubtedly a complex product of learned relational behavior and of both genetic and environmental effects on physiological functioning (see below). The next generation of research on intergenerational continuity and discontinuity needs to incorporate experimental manipulations (such as randomized interventions), in concert with genetic analyses, close observations of early interactions, and assessments of parent and infant physiological responses, in order to begin to tease apart these correlated etiological factors. Given that randomized interventions consistently improve parenting and child outcomes (e.g., Cicchetti, Rogosch, & Toth, 2006; Dozier, Peloso, Lewis, Laurenceau, & Levine, 2008; Fisher, Gunnar, Chamberlain, & Reid, 2000; Toth, Rogosch, Manly, & Cicchetti, 2006; Webster-Stratton & Hammond, 1997), these continuities are unlikely to reflect genetic transmission alone. It is important to note that measures of maternal psychological symptoms were included in all these studies and did account for significant variance in parenting, but their effects were smaller than the effects associated with childhood experiences of parenting received in the family of origin.

Parental Attachment Strategies, Parenting Behavior, and Subsequent Infant Attachment Strategies

Research guided by attachment theory has also underscored the power of assessments that explore parents' childhood experiences by demonstrating the strong associations between prenatal scores on the Adult Attachment Interview (AAI; George et al., 1985) and infant attachment behavior assessed at 1 year of age (see below). The AAI was developed to explore the implicit mental representations or "internal working models" that parents have formed of their own early attachment-

related experiences. The scoring of the AAI has been revolutionary, however, in enabling investigators to go beyond a focus on the objective content of early experience and beyond a reliance on the adult's conscious reporting to a focus on the underlying forms of discourse and cognition through which those experiences are presented (Main & Goldwyn, 1998). A summary description of the AAI and its coding procedures can be found in Bakermans-Kranenburg and van IJzendoorn (2009).

In several prospective studies, parental attachment classification assessed before the birth of the first child was found to predict the infant's attachment classification 1 year later. In a meta-analysis of 18 studies, including both prospective and concurrent designs, van IJzendoorn (1995) confirmed a 75% correspondence rate between secure versus insecure mother and child attachment classifications, with an overall effect size of 0.47 (see next section for descriptions of secure and insecure attachment patterns). Prediction from fathers to infants has been somewhat lower (Fonagy, Steele, & Steele, 1991; Steele & Steele, 1994; Suess, Grossmann, & Sroufe, 1992).

van IJzendoorn (1995) also evaluated the relationship between parental AAI classification and parental sensitive responsiveness toward the infant because sensitive parental behavior is hypothesized to mediate the relationship between parent and infant attachment classifications. For 10 studies, the effect size was 0.34 in the expected direction. As van IJzendoorn points out, this effect size is robust—but it also indicates that parental interactive behavior (as currently assessed) is not accounting for all the correspondence between parent and infant attachment classification, so that other factors such as genetic resemblance may also play a role in the obtained correspondences.

However, no strong evidence for a direct genetic or temperamental effect on child attachment quality has emerged, despite numerous studies. Evidence for the effect of an environmental contribution to infant attachment security includes the following sets of findings: (1) The attachment pattern with one parent is not strongly associated with the attachment pattern shown to the other parent (Fox, Kimmerly, & Schafer, 1991; Grossmann, Grossmann, Huber, & Wartner, 1981; Main & Weston, 1981); (2) infant attachment to the primary caregiver is predictable from the caregiver's state of mind with regard to attachment issues assessed before the birth of the infant; (3) child attachment strategy displayed toward the primary caregiver is more predictive of later child social adaptation than attachment strategies shown toward the nonprimary caregiver (Main, Kaplan, & Cassidy, 1985; Main & Weston, 1981; Suess et al., 1992), *even when the primary caregiver is not biologically related* (Oppenheim, Sagi, & Lamb, 1988); and (4) infant temperament has predicted distress at separation, but has not predicted whether the distressed or nondistressed behavior pattern is classified as secure or insecure (Belsky & Rovine, 1987; Kochanska, 1998; Vaughn, Lefever, Seifer, & Barglow, 1989).

Finally, neither behavioral genetic studies nor molecular genetic studies evaluating specific genes have produced consistent evidence of a genetic contribution to infant security of attachment. In a behavioral genetic study of 138 pairs of 1-year-old twins (Bokhorst et al., 2003), only shared and nonshared environmental factors accounted for the variance in twin concordances in secure, insecure, and disorganized patterns of attachment behavior. In a second behavioral genetic study of 110 twin pairs age 3.5 years (O'Connor & Croft, 2001), only shared and nonshared environmental effects on attachment classification were significant. Due to the small sample size, however, O'Connor and Croft (2001) did not separately test genetic influences on disorganized/controlling attachment (as also in a study by Finkel & Matheny, 2000).

These studies examined genetic effects by statistically comparing monozygotic and dizygotic twin correlations. However, a good deal of power is needed to detect significant differences between correlations, making large sample sizes necessary. With only one modestly sized twin study reporting on disorganized forms of attachment, no firm conclusions on heritability estimates for infant disorganization can yet be drawn.

With the recent advent of molecular genetic techniques, it is easier to detect small effects of particular genes with modest sample sizes. In a low-risk Hungarian sample, the risk for disorganized attachment was increased 4-fold among infants carrying the exon III 7-repeat polymorphism of the dopamine D4 receptor (DRD4) gene (Lakatos et al., 2000), and this association was increased to 10-fold in the presence of a -521 C/T single-nucleotide polymorphism of the same DRD4 allele (Lakatos et al., 2002). However, a Dutch study failed to replicate the main effect of D4.7 on disorganization in a small low-risk twin sample (Bakermans-Kranenburg & van IJzendoorn, 2004). Spangler and Zimmermann (2007) also found no overall main effect of the D4.7 allele on attachment disorganization. In addition, Cicchetti, Rogosch, and

Toth (2011) reported mixed results when examining direct associations between candidate genes and child disorganized attachment, with and without associated maltreatment. For maltreated children, there was a correlation between attachment disorganization and the *absence* of the DRD4 7-repeat allele, but only at 1 year of age prior to the intervention; no genetic differences in attachment disorganization for maltreated children were observed following the intervention at 2 years of age. There were, however, significant associations between serotonergic and dopaminergic genes and attachment disorganization within a nonmaltreatment control group. At 2 years of age, *nonmaltreated* children with the DRD4 7-repeat allele were more likely to be classified as disorganized than children without the allele, replicating the Lakatos and colleagues (2000) data. Also at 2 years of age, children with the s/s or s/l alleles in the serotonin transporter (5-HTT) linked promoter region (5-HTTLPR), which have been associated with increased negative emotional response (Canli & Lesch, 2007), were more likely to be classified as disorganized than children with the l/l allele; furthermore children classified as disorganized at both 1 and 2 years of age were more likely to have the s/s–s/l as compared to the l/l genotype. Although this study provided limited replication of the Lakatos and colleagues findings, a recent report using two birth cohort studies (the Generation R study from the Netherlands, and the NICHD Study of Early Child Care and Youth Development) failed to replicate a simple association between attachment disorganization and either the DRD4 or the 5-HTT genes. They did report, however, that children with the Val-Met genotype had higher levels of disorganization scores than children without it, although this finding is somewhat difficult to interpret (Luijk et al., 2011).

There is also growing evidence for genetic moderation of environmental effects on the formation of disorganized patterns of attachment. Gervai and colleagues (2007) reported that in the presence of the more prevalent nonrisk DRD4 short allele, the quality of infant attachment was related to the quality of mother–infant interaction, as has been repeatedly shown in meta-analyses (e.g., Madigan, Moran, Schuengel, Pederson, & Otten, 2007; van IJzendoorn, Schuengel, & Bakermans-Kranenburg, 1999). However, among infants with the long DRD4 7-repeat risk allele, the expected relation between the quality of caregiving and the quality of infant attachment security did not hold. This interaction effect between maternal behavior and the DRD4 polymorphism on infant attachment disorganization was replicated in the study by Luijk and colleagues (2011), using the two large data sets of the National Institute of Child Health and Human Development (NICHD) Study of Early Child Care and Youth Development in the United States and the Generation R study in the Netherlands. The interaction effect was replicated in the NICHD data, but not in the Generation R data. However, the Generation R study was flawed as a vehicle for evaluation of such a gene–environment interaction because in this sample maternal sensitivity was not related to infant attachment outcomes, as it should have been based on previous meta-analyses (Madigan et al., 2007; van IJzendoorn et al., 1999). Thus the Generation R sample is not appropriate for testing an interaction between genetic factors and maternal sensitivity in predicting infant attachment behavior because the expected effect of maternal sensitivity on infant attachment was not obtained. If maternal sensitivity is not coupled with infant behavior in the sample in the first place, then the sample cannot provide an adequate test of whether genetic factors uncouple that relation. Thus, in the only two studies that have satisfied the prior expectation that maternal behavior be related to infant attachment behavior, the DRD4 risk allele (7-repeat) has been found to confer *less* sensitivity to maternal behavior, while the DRD4 normal variant (4-repeat) produces the expected coupling of infant attachment behavior to the quality of maternal care (Gervai et al., 2007; Luijk et al., 2011).

Because the coupling of infant and maternal behavior has been such an overwhelmingly supported finding, this result is consistent with the expectation that a widely dispersed "normal" gene variant would be supporting this coupling, while a less widely dispersed "risk" allele would be involved in the uncoupling of the relation between infant attachment behavior and quality of care. However, a related report by van IJzendoorn and Bakermans-Kranenburg (2006) assessing maternal state of mind on the AAI interview found that maternal unresolved state of mind predicted infant attachment disorganization with a significantly higher probability among infants who carried the long "risk" allele versus the "normative" short polymorphic variant of the DRD4 allele. Thus further work is needed to explore the effects of aspects of dopamine function on infants' responses to their mothers.

Another polymorphism involving variations in the 5-HTTLPR gene has been implicated in a similar interaction but in a much smaller sample. Spangler,

Bovenschen, Globisch, Krippl, and Ast-Scheitenberger (2009) reported that children homozygous for the short "risk" allele of this gene who were reared with insensitive mothers were more likely to be classified as disorganized than children with either the homozygous long or heterozygous long/short version of the gene. In summary, a large body of evidence supports the hypothesis that qualities of the caregiving environment influence the development of infant attachment behavior, while research on genetic influence on attachment security is still new and findings remain inconclusive.

Disorganized/Disoriented Attachment Patterns and Infant Risk

These findings on the intergenerational transmission of relational patterns have increased interest in understanding how the infant organizes patterns of relational behavior within particular caregiving contexts. One influential research tradition that has explored the interface between normative and disturbed behavior in infancy is that of attachment studies. This literature has described the organization of infant attachment behavior in both normal and socially at-risk samples, and has repeatedly documented increased rates of disorganized/disoriented forms of infant behavior in disturbed family contexts. The accumulated data on the context and correlates of disorganized/disoriented infant behavior indicates clearly that these behaviors are risk factors for later clinical disorders. There is also a persuasive argument that disorganized attachment relationships in infancy should be considered as a current relational disorder of infancy, given the associations between early disorganization and both current and subsequent impairments in functioning. In this section, we review what is known about the infant context of disorganized attachment behaviors; in the section that follows, we link this literature to longitudinal studies of the psychiatric sequelae of those infant behaviors.

THE ATTACHMENT BEHAVIORAL SYSTEM

As defined initially by John Bowlby (1969), the attachment behavioral system includes those infant behaviors that are activated by stress and that have as a goal the reinstating of a sense of security, usually best achieved in infancy by close physical contact or proximity with a familiar caregiver. The attachment system can be thought of as the psychological version of the immune system, in that the attachment system is the preadapted behavioral system for combating and reducing fearful arousal, just as the immune system is the biological system for combating physical disease. Under normal conditions, an adequately functioning attachment relationship will serve to buffer the infant (and adult) against elevated levels of fearful arousal. Although the attachment system is viewed as only a single circumscribed motivational system among other systems, it is also regarded as preemptive when aroused because it mobilizes responses to fear or threat. In that sense, the quality of regulation of fearful affect is foundational to the developing child's freedom to turn attention away from issues of threat toward other developmental achievements, such as exploration, learning, and play.

From 1970 to 1985, investigators focused on replicating and extending the original discovery of Ainsworth, Blehar, Waters, and Wall (1978) that three organized patterns of infant behavior toward the caregiver were identifiable at 1 year of age in response to mild stress. These behavioral profiles were termed "secure," "avoidant," and "ambivalent" attachment patterns, and their characteristics are summarized in Table 15.9. Main (1990) describes secure infants as maintaining a stance or strategy of open communication of both positive and negative effect. Infants in the ambivalent group are viewed as maintaining a strategy of heightening signals of anger and distress with the goal of eliciting a response from a less responsive caregiver. Main characterizes the strategy of avoidant in-

TABLE 15.9. Organized Patterns of Attachment Behavior during Infancy

Secure strategy	Avoidant strategy	Ambivalent strategy
Open communication of affect	Restricted communication of affect	Heightened communication of affect
May or may not be distressed at separation	Little display of distress	Heightened distress
Positive greeting or contact seeking	Avoidance of contact	Anger and contact seeking combined
Soothing effective if distressed	Displacement of attention	Failure of soothing

fants as one of restricting the communication of anger and distress by displacing attention onto the inanimate environment, away from cues that might intensify the desire to seek comfort from a parent who rejects attachment behavior. Secure, avoidant, and ambivalent patterns of infant behavior were empirically related to both current and prior differences in maternal caregiving behavior observed at home, with mothers of infants classified as secure rated as more sensitive and responsive than mothers of infants in the other two groups (Ainsworth et al., 1978). A series of subsequent studies demonstrated that infants displaying secure patterns of attachment behavior also exhibited more positive social behaviors toward both parents and peers throughout the preschool years (for reviews, see Cassidy & Shaver, 2008).

DISORGANIZED/DISORIENTED ATTACHMENT BEHAVIOR

From 1985 to the present, as attachment researchers increasingly began to study high-risk families and clinical samples, it became apparent that the behaviors of some infants did not fit any of the three behavioral patterns common among low-risk cohorts. Main and Solomon (1990) then developed coding criteria for a fourth infant attachment category, labeled "disorganized/disoriented" (D) attachment behavior. Disorganized/disoriented infant attachment behaviors are now gaining empirical support as precursors or prodromal forms of a variety of child and adult psychiatric symptoms (see below). The term "disorganized/disoriented" refers to the apparent lack of a consistent strategy for organizing responses to the need for comfort and security when an individual is under stress. The term does *not* refer to mental disorganization or to behavioral disorganization more generally, although other infant correlates of disorganized attachment behavior are only beginning to be explored. Approximately 15% of infants in two-parent, middle-class families display disorganized attachment behavior. The rates of disorganized behavior increase under attachment-relevant family risk conditions such as child maltreatment, maternal alcohol consumption, maternal depression, adolescent parenthood, or multiproblem family status, with estimates ranging from 24% among infants of middle-income depressed parents to a high of 82% among low-socioeconomic-status maltreated infants (see van IJzendoorn et al., 1999, for a meta-analytic review).

Infants who show disorganized behavior do not consistently manage distress and approach tendencies by avoidance and displacement, as in the avoidant attachment pattern; nor do they consistently voice their distress at separation and actively seek contact when their mothers return, as usually occurs in the secure or ambivalent patterns. The particular forms and combinations of disorganized behaviors tend to be fairly idiosyncratic from child to child, but they include apprehensive, helpless, or depressed behaviors; unexpected alternations of approach and avoidance toward the attachment figure; or other conflict behaviors such as prolonged freezing or stilling, or slowed "underwater" movements, as summarized in Table 15.10 (see Main & Solomon, 1990, for a full description of the coding system). Often the outlines of a "best-fitting" or "forced" secure, avoidant, or ambivalent strategy can also be discerned in the context of an infant's disorganized attachment behavior. Therefore, all disorganized infants are also assigned a secondary organized strategy, yielding final classifications as "disorganized–secure," "disorganized–avoidant," or "disorganized–ambivalent." Given the array of odd or contradictory behaviors contributing to the disorganized category, further work is needed to identify distinct subgroups that might share a particular etiology and/or a subsequent developmental pathway. It is not yet clear whether the forced or secondary classifications now assigned are the most empirically useful subgroupings (but see

TABLE 15.10. Indices of Disorganization/Disorientation in Presence of Parent

1. Sequential display of contradictory behavior patterns, such as strong attachment behavior followed by avoidance or disorientation.
2. Simultaneous display of contradictory behavior patterns, such as strong avoidance with strong contact seeking, distress, or anger.
3. Undirected, misdirected, incomplete, and interrupted movements and expressions.
4. Stereotypies, asymmetrical movements, mistimed movements, and anomalous postures.
5. Freezing, stilling, or "slow-motion" movements and expressions.
6. Direct indices of apprehension regarding the parent.
7. Direct indices of disorganization or disorientation in presence of parent, such as disoriented wandering, confused or dazed expressions, or multiple, rapid changes of affect.

Note. See Main and Solomon (1990) for complete descriptions.

Lyons-Ruth et al., 2013, concerning differential pathways related to these subgroups).

Physiological Correlates. In support of the view that infant disorganized attachment behavior constitutes the least adaptive behavior pattern, Spangler and Grossmann (1993) demonstrated that disorganized infants exhibited significantly greater heart rate elevation during the Strange Situation assessment than secure or avoidant infants (ambivalent infants were not studied), even though overt distress was similar among disorganized and secure infants. In addition, cortisol levels assessed 30 minutes after the assessment remained significantly elevated among infants with disorganized strategies compared to infants with secure strategies, whereas cortisol levels of avoidant infants were intermediate in value. Similar findings reporting greater cortisol reactivity in response to the Strange Situation among children with disorganized attachments have been reported by Hertsgaard, Gunnar, Erickson, and Nachmias (1995) and Bernard and Dozier (2010). Spangler and Grossmann interpreted their data as consistent with animal data indicating that the adrenocortical system is only activated when adequate behavioral strategies for finding comfort are not effective. Beyond atypical patterns of cortisol reactivity, infant attachment disorganization has also been associated with atypical patterns of diurnal cortisol. Whereas typical patterns of daytime cortisol levels decrease during the course of the day, Luijk and colleagues (2010) reported that infants classified as disorganized at 14 months of age displayed a more flattened rate of change across the day at 2 years of age than that of nondisorganized children. This pattern of lower waking cortisol and less decrease over the day has also been observed among maltreated children in foster care (Bruce, Fisher, Pears, & Levine, 2009; Fisher et al., 2000, Gunnar & Vazquez, 2001). Taken together, these studies suggest that the inability of a parent and child to organize a consistent attachment relationship may substantially increase the risk for aberrant functioning of the child's stress response systems.

Cognitive Correlates. There is less evidence that infant attachment is related to cognitive outcomes. Lyons-Ruth, Repacholi, McLeod, and Silva (1991) reported that disorganized infant attachment behavior accounted for variance in infant mental development scores at 18 months, independent of variance related to maternal behavior and maternal IQ. This link between disorganized attachment strategies and less effective cognitive functioning has also been demonstrated in an Icelandic cohort followed from ages 7 to 17 years (Jacobsen, Edelstein, & Hoffman, 1994) and a Belgian cohort followed from approximately 4 to 7 years of age (Stievenart, Roskam, Meunier, & van de Moortele, 2011). Given the well-established link between chronically elevated cortisol levels and structural changes in the hippocampus (Liu et al., 2001), further work is needed on the interrelations among disorganization of attachment strategies, HPA activity, and cognitive development.

Developmental Reorganization. As disorganized infants and toddlers make the transition into the preschool years, a developmental reorganization occurs for many of these children, with the signs of conflict, apprehension, or helplessness characteristic of disorganized attachment strategies in infancy becoming augmented or replaced by various forms of controlling behaviors toward the parent, including caregiving behavior or punitive behavior by age 3 (Cassidy, Marvin, & the MacArthur Working Group on Attachment, 1992; Main & Cassidy, 1988; NICHD Early Child Care Research Network, 2001). Controlling children "actively attempt to control or direct the parent's attention and behavior, and [they] assume a role, which is usually considered more appropriate for a parent with reference to a child" (Main & Cassidy, 1988, pp. 418–419). Two forms of controlling behavior are observed. "Controlling–caregiving" behavior is characterized by organizing and guiding the parent or providing support and encouragement (e.g., the child asks the mother if she is all right). "Controlling–punitive" behavior is characterized by episodes of hostility toward the parent that are marked by a challenging, humiliating, cruel, or defying quality (e.g., a child gives orders to the parent; the child tells the parent that the parent is terrible at doing the task). However, some disorganized infants remain disorganized over the preschool period and do not adopt controlling strategies. Moss, Cyr, Bureau, Tarabulsy, and Dubois-Comtois (2005) found that 25% of young children who were disorganized at age 3 remained disorganized at age 6. Bureau, Easterbrooks, and Lyons-Ruth (2009) extended this age range by finding that behavioral disorganization, as well as controlling forms of behavior, continued to be evident at age 8.

The size of the association between disorganized behavior in infancy and disorganized or controlling behavior *after* infancy has varied, however, with stability estimates ranging from 20% (NICHD Early Child Care Research Network, 2001) to 80% (van IJzendoorn et al., 1999). However, the NICHD Early Child Care Research Network (2001) only assessed attachment behavior up to age 3, so the lower stability seen in that study may reflect turbulence over the transition period of toddlerhood; the higher figure was derived from studies assessing stability from infancy to later in the preschool and early school-age periods. Finally, it should be noted that a sizable number of children who do *not* appear disorganized in infancy begin to display controlling behaviors over the preschool years (Bureau et al., 2009; Main & Cassidy, 1988; NICHD Early Child Care Research Network, 2001; Wartner, Grossmann, Fremmer-Bombik, & Suess, 1994).

Controlling behaviors at age 3 and beyond are also markers of risk. Disorganized or controlling dyads display lower-quality parent–child communication and reciprocity than secure and insecure organized dyads (e.g., Moss, Cyr, & Dubois-Comtois, 2004; NICHD Early Child Care Research Network, 2001), and children in such dyads exhibit the highest levels of teacher-reported disruptive and internalizing symptoms (Fearon et al., 2010; Moss et al., 2004; O'Connor, Bureau, McCartney, & Lyons-Ruth, 2011). Notably, none of the above-cited studies have found consistent gender differences in the rates of controlling or disorganized attachment behavior.

Additional longitudinal studies investigating the timing of this shift in behavioral organization are needed, however, particularly among high-risk or clinically referred infants. Cicchetti and Barnett (1991) found that among maltreated children, the disorganized behaviors seen in infancy were still more prominent than controlling patterns from 30 to 48 months of age.

Parental Correlates. During the AAI, parents of infants exhibiting disorganized attachment behavior have been found to display lapses of monitoring of reasoning or discourse in discussing childhood experiences of loss or trauma (see van IJzendoorn, 1995), leading Main and Goldwyn (1998) to classify them as "unresolved" with respect to those experiences. van IJzendoorn (1995), in his meta-analysis, reported an overall association of .31 between the unresolved classification of a mother's AAI and an infant's disorganized attachment behavior. However, the relation between the parent's unresolved status on the AAI and disorganized infant attachment status has been explored primarily in nonclinical samples. Recent studies indicate that AAI protocols of adults in clinical samples are often placed in rare and less well-described AAI coding categories (e.g., "cannot classify" or "overwhelmed by trauma"), in addition to or in place of categorization in the unresolved group (Bakermans-Kranenburg & van IJzendoorn, 2009; Holtzworth-Munroe, Stuart, & Hutchinson, 1997; Patrick, Hobson, Castle, Howard, & Maughn, 1994). The infant behaviors correlated with these forms of parental attachment organization have not been identified. Therefore, description of parental states of mind beyond unresolved status may be important in capturing the organization of parental attachment representations in clinical samples.

Work by Lyons-Ruth and colleagues (Lyons-Ruth, Melnick, Patrick, & Hobson, 2007; Lyons-Ruth, Yellin, Melnick, & Atwood, 2005) has identified additional "hostile–helpless" features of a mother's attachment representations on the AAI that account for additional variance in infant disorganization, beyond variance accounted for by the unresolved, cannot classify, or overwhelmed by trauma classifications. Thus the hostile-helpless codes appear to delineate new ways in which contradictory and pervasively unintegrated affective evaluations of attachment relationships may be displayed on the AAI and contribute to disrupted parenting and infant disorganization.

All of these more distal correlates of disorganized or controlling behaviors, such as parental unresolved attachment classifications or parental psychosocial risk factors, point to a contribution of parent–infant interaction to the genesis of infant disorganization (see Lyons-Ruth & Jacobvitz, 1999; van IJzendoorn et al., 1999). However, studies using Ainsworth's sensitivity scale in particular have generated only a small association, albeit a reliable one, between parental behavior and infant disorganization (van IJzendoorn et al., 1999). Thus it appears that parental behaviors other than those captured by the sensitivity coding must be investigated.

Main and Hesse (1990) have hypothesized that disorganization of infant attachment strategies results from parental unresolved fear, which is then transmitted to the infant through behavior that is either "frightened or frightening" (FR) to the infant. Lyons-Ruth, Bronfman, and Parsons (1999) explored a broader fear-related hypothesis that differed from the Main and Hesse hypoth-

esis slightly in viewing infant fearful arousal as stemming not only from FR behaviors of the parent, but also from an absence of adequate parental regulatory responses to infant fearful arousal related to *other aspects* of the environment. In this view, parental withdrawing behaviors, disoriented behaviors, or role-confused behaviors that leave the infant without adequate parental regulation of fearful affect would also be disorganizing, regardless of whether the parent's behaviors were directly FR to the infant. To examine this possibility, Lyons-Ruth and colleagues used an atypical maternal behavior inventory (AMBIANCE) that indexed the frequency of maternal withdrawing, negative–intrusive, role-confused, disoriented, and contradictory behaviors in response to infant cues, as well as the FR behaviors included on the Main and Hesse (1992) coding inventory. The frequency of atypical caregiving behaviors was significantly related to the infant's display of disorganized attachment behaviors, even after Lyons-Ruth and colleagues controlled for maternal behaviors that were directly FR. This suggests that infant disorganization occurs in a broader context of dysregulated and atypical communication between mother and infant. A meta-analysis has confirmed the links between maternal atypical behavior and both infant disorganization and maternal unresolved status on the AAI across a wide range of socioeconomic groups (Madigan et al., 2006).

In summary, disorganized infant attachment behaviors are emerging as potential indices of a relational disorder of infancy, since they are often characterized by signs of conflict and dysphoria, by increased infant distress, and by increased physiological markers of unmodulated infant stress. As currently described, however, these behaviors are subtle, need considerable training to identify reliably, and include a wide range of infant presentations. The diversity of behavioral presentations also raises the possibility that a number of subgroups may exist within the overall category, with different implications for current disorder or later prognosis. However, the established reliability and concurrent validity of these infant behaviors mandate continued research to distill the most powerfully predictive and clinically usable indicators of disorganized attachment status and integrate them into current diagnostic thinking. New data on the longitudinal prediction of psychiatric symptomatology from early assessments of disorganized attachment status and family context, which are reviewed below, further underscore this conclusion.

FATHER–INFANT ATTACHMENT

Most studies in the attachment field have concentrated on mother–infant attachment. In the much smaller literature on father–infant attachment, the relations between sensitivity in father–infant interaction and infants' attachment to fathers have been more variable (see Grossmann, Grossmann, Kindler, & Zimmermann, 2008). Based on data from a 20-year longitudinal study, Grossmann and colleagues (2008) concluded that father–child and mother–child attachment relationships are based on different kinds of interactions and have different long-term effects on child adaptation. They suggested that fathers are more attuned to their children's motivation to explore, and that the father–infant relationship is more likely to predict "security in exploration." Additional studies are needed to examine whether mothers' and fathers' attachment relationships are similar and additive (i.e., whether two secure relationships are better) or whether fathers' relationships are distinct and complementary (for reviews, see Newland, Freeman, & Coyl, 2011; Grossmann et al., 2008).

Infant Attachment and Later Psychiatric Symptomatology

AGGRESSIVE BEHAVIOR DISORDERS

The research literatures on conduct disorder and antisocial personality disorder have long pointed to the early onset of aggressive behavior disorders among a substantial subgroup of cases identified in adolescence or adulthood (see, e.g., Kimonis, Frick, & McMahon, Chapter 3, this volume). In addition, families of conduct-disordered children have particularly elevated scores on measures of family adversity (Blanz, Schmidt, & Esser, 1991), as well as higher rates of diagnosable disorder, including antisocial personality, major depression, and substance abuse (Biederman, Munir, & Knee, 1987; Lahey, Russo, Walker, & Piacentini, 1989). Even more well documented is the relationship between harsh and ineffective parental discipline and aggressive behavior problems—a relationship now documented as early as 2 and 3 years of age (e.g., Campbell, 1991).

Work by Dodge and others has further established that both aggressive boys and their mothers tend to attribute hostile intentions to others in ambiguous situations, with mothers of aggressive children attributing child misbehavior more to negative personality dimensions and endorsing more forceful disciplinary

responses, and children of mothers who make hostile attributions displaying more aggression (Dix & Lochman, 1990; Dodge, Pettit, McClaskey, & Brown, 1986; Pettit, Dodge, & Brown, 1988).

Infant research is now indicating that all of these correlates of disorder may be evident and predictive of later aggression during the first 18 months of life, before the onset of coercive cycles of interaction. Egeland and colleagues (1993), studying a large low-income cohort before the discovery of the disorganized form of infant attachment behavior, demonstrated that maternal intrusive control observed when children were 6 months old predicted the following: insecure infant attachment behavior at 12 months of age; negative, noncompliant, and hyperactive behavior at age 3½ years; and elevated teacher ratings of both internalizing and externalizing problems in first grade. When assessed in infancy, intrusive mothers reported more anxiety and suspiciousness, displayed less appreciation of the need for reciprocity with their children, and were unlikely to be living with a partner. In a later follow-up, both insecure attachment in infancy and maternal hostility at age 3½ years predicted first- through third-grade teacher-rated aggression.

Lyons-Ruth, Alpern, and Repacholi (1993), following a cohort of 64 low-income families from infancy, found that maternal psychosocial problems (particularly chronic depressive symptoms) and disorganized infant attachment behavior made additive contributions to the prediction of child hostile–aggressive behavior in kindergarten. If a mother had psychosocial problems *and* the mother–child attachment relationship was disorganized, a majority of infants (56%) exhibited highly hostile behavior in kindergarten, compared to 5% of low-income children with neither risk factor. In addition, the predictive effect of maternal psychosocial problems was mediated through the increased hostile–intrusive behavior shown by such mothers in interaction with their infants at home at 18 months of age. By second grade, Lyons-Ruth, Easterbrooks, and Cibelli (1997) found that a deviant level of externalizing behavior at age 7 was correctly predicted in 87% of cases from the infancy assessments of disorganized attachment and mental development. Kochanska, Barry, Stellern, and O'Bleness (2009) found that coercive patterns of parent–child interaction observed in middle childhood were only observed among children who were classified as insecure in infancy, and were absent among children with secure attachments. A similar pattern of findings was obtained in a study that used DSM-III-R criteria for defining oppositional defiant disorder (Speltz, Greenberg, & DeKlyen, 1990). Although a number of studies in both low- and middle-income samples have now confirmed this link between disorganized attachment and later externalizing problems (for a meta-analysis, see van IJzendoorn et al., 1999), it remains possible that parenting factors underlying infant attachment quality may be more stable predictors of later developmental outcomes than infant attachment patterns per se. For example, Shi and colleagues (2012) reported that maternal withdrawal in infancy better predicted antisocial personality disorder features 20 years later than infant attachment disorganization did.

This body of infant studies considerably broadens and deepens our view of the developmental pathways leading to conduct problems by demonstrating that a child's coercive behavior is likely to be preceded by serious disturbances in the security of the attachment relationship in infancy. In addition, the literature suggests substantial phenotypic discontinuity in the presentation of to-be-aggressive children from infancy to school age, with the disorganization in infancy characterized by indicators of conflict, apprehension, helplessness, and distress rather than by coercive behavior per se. Attachment theory would interpret these behaviors as responses to dysfunction in the infant's primary attachment relationships—dysfunction that leaves the infant unable to develop an organized relational strategy for regulating arousal.

DISSOCIATIVE SYMPTOMS, DEPRESSIVE SYMPTOMS, ANXIETY DISORDERS, AND OVERALL PSYCHOPATHOLOGY

As already noted, a number of studies have found that disorganized or controlling attachment strategies predict elevations in *both* internalizing and externalizing behavior problems. What is less clear is whether disorganized attachment primarily predicts internalizing symptoms that are comorbid with externalizing disorders, or whether purely internalizing disorders are also related to early attachment disorganization. Lyons-Ruth and colleagues (1997) reported that purely internalizing symptoms were predicted by early organized avoidant attachments, while comorbid internalizing and externalizing symptoms were predicted by attachment behaviors that were both avoidant and disorganized. Hubbs-Tait, Osofsky, Hann, and Culp (1994) and Goldberg, Gotowiec, and Simmons (1995) have also found that internalizing symptoms were more strongly related to avoidant attachment behavior. Subsequent

meta-analytic evidence has confirmed that attachment disorganization, in infancy at least, is predictive of externalizing problems (Fearon et al., 2010) but not internalizing problems (e.g., Groh et al., 2012; Madigan, Atkinson, Laurin, & Benoit, 2013), whereas avoidant attachment is more strongly related to internalizing symptoms. However, additional studies are needed that differentiate between comorbid and noncomorbid internalizing symptoms.

Dissociative symptomology in adolescence is one type of internalizing symptom that has been related to early disorganized attachment strategies both theoretically and empirically. Liotti (1992) has pointed out the phenotypic similarity between the contradictory and unintegrated quality of disorganized behaviors in infancy and the contradictory and unintegrated nature of dissociated mental states in adulthood. He speculated that disorganized behaviors represent a developmental "anlagen" or precursor state for later dissociative symptoms. Ogawa, Sroufe, Weinfield, Carlson, and Egeland (1997) tested this hypothesis in a study from infancy to adolescence of 126 children from low-income families. From a wide array of potential predictors from infancy, preschool, and middle childhood, the two independent predictors of symptoms on the Dissociative Experiences Scale at age 19 were disorganized attachment at 12–18 months and a mother's psychological unavailability from 0 to 24 months. Surprisingly, the variance in dissociative symptoms related to sexual or physical abuse was not predictive once the quality of the early caregiving relationship was controlled for.

This pattern of findings was replicated in a second study of dissociative symptoms among 56 young adults followed prospectively from infancy (Dutra, Bureau, Holmes, Lyubchik, & Lyons-Ruth, 2009). Specifically, indices of the mother's emotional unavailability in the first 18 months of life accounted for half of the variance (50%) in later dissociation. These variables included a mother's level of disrupted communication in the lab, the mother's lack of positive affective involvement at home, and the mother's flatness of affect at home. Infant disorganization in itself was not significantly related to later dissociation. Extent of emotional abuse, but not physical or sexual abuse or witnessed violence, added to the prediction of dissociation once quality of early care was considered. Notably, maternal dissociation and depression were not significant correlates of adolescent dissociation, weighing against the alternative possibility that maternal symptomatology would be a stronger predictor of adolescent dissociation than would quality of early care. Similar to the Ogawa and colleagues (1997) study, then, quality of parent–infant interaction before 24 months of age was the strongest predictor of dissociative symptoms at age 20.

These findings are also beginning to suggest that patterns of early maternal withdrawal and emotional unavailability are associated with different forms of child and adolescent psychopathology than the forms of maternal hostile affect and intrusive behavior. Whereas the latter has been associated with early-onset conduct problems and externalizing behaviors, the quieter, more withdrawn maternal behaviors appear to be associated with internalizing disorders that are not identified until adolescence, including dissociation, borderline personality features, and suicidality (see below). Perhaps the most surprising aspect of these findings is that the prediction from infancy to adolescence was direct and unmediated by a number of other well-chosen variables. These intervening variables, such as maternal symptoms, occurrence of abuse, or childhood behavior problems, would be expected to "carry forward" or mediate the variance in adaptation initially associated with quality of care in infancy. Instead, the early caregiving relationship appears to create a broader vulnerability to late adolescent psychiatric symptoms than is captured by our current assessments of preschool and school-age symptoms and risk factors, or by our assessment of maternal symptomatology.

Two other papers from the same study sample have explored infancy, preschool, and school-age predictors of adolescent depressive or anxiety disorders, although for unclear reasons disorganized attachment status was not included as a variable for analysis in either study. In relation to depressive symptoms, Duggal, Carlson, Sroufe, and Egeland (2001) examined only maternal contributors to both childhood (first–third grades) and adolescent (16–17½ years) depression among 168 families. Predictors examined included maternal depressive symptoms (7 years), early maternal stress (12–64 months), later maternal stress (6–17 years), support for parenting (12–64 months), early maternal supportive care to child (12–42 months), later maternal supportive care (13 years), and maternal abuse to child (0–64 months). Significant associations occurred between all variables and depressive symptoms in childhood, but only the extent of maternal abuse and the degree of early maternal stress made unique contributions in a multiple-regression analysis. In contrast, depression in adolescence across gender was related most strongly to lack of supportive early care. This was particularly true

of boys, whereas for girls the primary predictor was maternal depressive symptoms at age 7 (the earliest age at which maternal depression was assessed). Other variables did not add to the variance accounted for by these two predictors. Bureau and colleagues (2009) also examined prospective predictors from infancy to depressive symptoms in late adolescence. Mothers' depressive symptoms in infancy, but not in childhood or young adulthood, predicted young adult depression, but infant attachment did not add to the model.

Warren, Huston, Egeland, and Sroufe (1997) assessed whether variables coded during the first year of life were related to anxiety disorders at 17.5 years in the same sample. The factors examined included nurse-rated and examiner-rated neonatal temperament, maternal trait anxiety, and anxious/resistant attachment as assessed at 12 months of age. The relation between the range of state scores on the Neonatal Behavior Assessment Scale and anxiety disorders was significant, but in the opposite direction than predicted. Anxious/resistant (i.e., ambivalent) attachment in infancy was also a significant predictor, but accounted for only 4% of the variance. Other variables related to quality of early maternal care were not examined, so it remains unclear whether anxious/resistant attachment indexes a unique aspect of the early parent–child relationship.

Other work examining the concept of behavioral inhibition and using Kagan, Reznick, Clarke, Snidman, and Garcia-Coll's (1984) criteria has shown a relation between behavioral inhibition at 21 months of age and anxiety disorders in childhood, as well as between parental anxiety disorder and offspring behavioral inhibition at 2–7 years of age (Biederman et al., 1993; Kagan, Snidman, Zentner, & Peterson, 1999). However, complex transactional effects seem to characterize the relations between attachment security and behavioral inhibition. In other work from Kagan's lab, Arcus, Gardner, and Anderson (1992) found that maternal directive caregiving style interacted with infant temperament, reducing the tendency for infants with "high reactive" temperament at 4 months to become behaviorally inhibited by 14 months. Calkins and Fox (1992), examining 33 measures of both difficult and inhibited temperament across the first year, found that only 1 of 33 measures predicted anxious/resistant attachment at 14 months, but that anxious/resistant attachment at 14 months did predict behavioral inhibition at 24 months. Mills-Koonce, Propper, and Barnett (2012) also reported that child negative affect during a maternal soothing episode following a laboratory stressor differentiated children with the ambivalent type of insecure attachment from secure and other insecure children, and that ambivalent attachment quality mediated the association between child negativity and later affective problems. Similarly, Kochanska (1998) found that behavioral inhibition did not predict whether an infant was classified as secure or insecure, but did predict type of insecurity (inhibited insecure children were classified as ambivalent rather than avoidant).

In one of the few studies that has examined security of attachment among anxiety-disordered *mothers* and their young children (ages 18–59 months), Manassis, Bradley, Goldberg, Hood, and Swinson (1994) found that 78% of anxiety-disordered mothers were classified as unresolved with respect to loss or trauma on the AAI, and that 65% of the children of anxiety-disordered mothers ($N = 20$) were classified as disorganized in their attachment strategies. Behavioral inhibition was also assessed, and 65% of offspring were classified as behaviorally inhibited (Manassis, Bradley, Goldberg, Hood, & Swinson, 1995). There was no statistical relation between behavioral inhibition and insecure attachment, however, with three of the four secure children classed as inhibited. Of the three children with DSM-III-R anxiety disorders, all were insecurely attached, but only one was behaviorally inhibited. In sum, studies to date indicate that both infant temperament and the quality of early caregiving and attachment contribute to the development of anxiety disorders, but there is disagreement across studies as to how these two classes of variables relate to one another.

Two prospective studies to date have evaluated the contribution of disorganized or controlling behaviors in early childhood to features of borderline personality disorder in young adulthood (Carlson, Egeland, & Sroufe, 2009; Lyons-Ruth et al., 2013). Both studies found prediction from the quality of the mother–child attachment relationship in early childhood to these personality features in young adulthood. Lyons-Ruth and colleagues (2013) further demonstrated that neither quality of later parent–child interaction nor severity of later abuse could account for the prediction from early maternal withdrawal. In a separate set of longitudinal analyses, Obsuth, Hennighausen, Brumariu, and Lyons-Ruth (in press) also found that disorganized infant attachment behaviors predicted the disoriented forms of interaction observed with parents at 20 years, which were in turn related to elevated rates of borderline features and suicidality. In addition, disorientation in interaction with the parent was the only type of inter-

action significantly related to unresolved states of mind regarding attachment experiences on the AAI in young adulthood (Obsuth et al., in press). It was also notable that suicidality/self-injury alone had somewhat different developmental predictors from those associated with overall borderline features. Recurrent suicidality/self-injury in late adolescence was more likely to have been preceded by clear (albeit disorganized) approach behavior toward the mother when under stress in infancy, and was less likely to be associated with childhood abuse experiences than were borderline features overall.

Finally, when longitudinal findings are considered—data from the high-risk Harvard and Minnesota studies, as well as the very large but lower-risk NICHD Study of Early Child Care and Youth Development—all converge on the conclusion that although infant attachment behavior is an important predictor of some outcomes, more substantial and consistent prediction is obtained from the quality of maternal interaction with the child, both in infancy and during later developmental periods (Belsky & Fearon, 2002; Dutra, Bureau, Holmes, Lyubchik, & Lyons-Ruth, 2009; Lyons-Ruth et al., 2013; NICHD Early Child Care Research Network, 2001; Sroufe, 2005).

Randomized Controlled Trials: Interventions to Reduce Attachment Disorganization in Infancy

Intervention programs aimed at promoting infant attachment security have proliferated over the last decade. A meta-analysis with 842 participants across 15 preventive interventions revealed a range of effectiveness across studies in reducing attachment disorganization, but the overall effect size was not significant ($d = 0.05$) (Bakermans-Kranenburg, IJzendoorn, & Juffer, 2005). Two studies included in the meta-analysis successfully reduced the occurrence of infant attachment disorganization in randomized controlled trials (Heinicke et al., 1999; Juffer, Bakermans-Kranenburg, & van IJzendoorn, 2005). However, only one of the interventions included in the meta-analysis focused specifically on preventing disorganization, and most studies had very few disorganized infants.

Since this meta-analysis was published, however, new and more intensive randomized controlled trials have been reported in samples with sizable groups of disorganized infants. These studies also included a normal community comparison group, in additional to the randomized control group(s) (Cicchetti et al., 2006; Toth et al., 2006). Cicchetti and colleagues (2006) recruited 137 children at age 12 months from maltreating low-income families, and randomly assigned mother–infant dyads to one of three groups: (1) a group receiving mother–infant psychodynamic psychotherapy (Fraiberg, Adelson, & Shapiro, 1987; Lieberman, Weston, & Pawl, 1991), involving weekly visits with each mother and infant for 1 year, focused on helping the mother gain insight into herself and how she related to her child; (2) a psychoeducational parenting intervention based on the work of Olds and Kitzman (1990), involving weekly home visits with the mother to provide her with education regarding infant physical and psychological development, encouragement to seek further education, and enhancement of the mother's social supports; or (3) a community standard control group. In addition, 52 infants from low-income, nonmaltreating families were also assessed. As expected, there were significantly more disorganized infants in the maltreatment sample (89.9%) than in the community standard control group (43%).

Postintervention results revealed significantly higher rates of attachment disorganization in the community standard control group than in the two intervention groups, indicating that both the infant–parent psychotherapy program and the psychoeducational parenting intervention were effective in reducing the incidence of attachment disorganization. Therapists were provided with extensive training prior to implementing the interventions and had considerable experience working with low-income families. In addition, caseloads were lower than those found in typical mental health outpatient settings.

In a second study, Toth and colleagues (2006) randomly assigned depressed mothers to an intervention or control group ($N = 163$). They also recruited a nondepressed comparison group. The intervention was derived from the work of Fraiberg and colleagues (1975) and Lieberman and colleagues (1991): The therapist assisted each mother to recognize how she perceived her infant and herself. Through a corrective emotional experience with the therapist, the mother was helped to alter distorted perceptions of her child so that she could respond more sensitively to him or her. Mothers and toddlers participated in an average of 45 sessions. At preintervention, mothers who were depressed had disorganized infants more often than those who were not depressed. At postintervention, depressed mothers in the intervention group had fewer disorganized infants than depressed mothers in the control group, and no

longer differed from the nondepressed mothers in the comparison group.

The Attachment and Behavioral Catch-Up (ABC) program, developed to reduce frightening behavior and enhance sensitive behavior among mothers at risk for maltreatment (Dozier, Lindheim, & Ackerman, 2005), has also been evaluated in a randomized clinical trial with mothers and infants. Among 120 children of mothers at high risk for child maltreatment, children in the ABC program were observed to have a lower rate of disorganized attachment and a higher rate of secure attachment, compared to children whose parents received a control educational intervention (Bernard et al., 2012).

These intervention trials provide strong experimental evidence that disorganized attachment processes are amenable to change. Among both depressed middle-income mothers and low-income maltreating mothers, thoughtful and sustained interventions (>40 sessions) were associated with significant reductions in disorganized attachments relative to randomized untreated controls. Contrary to expectations, however, intervention models expected to produce change at a representational level were not more effective than those aimed at improving parent–child interactions directly, suggesting that a relatively broad array of more intensive intervention formats may be effective. Despite the success of these models, however, the mechanisms contributing to the changes—such as changes in caregiver attributions or behavior—were not identified. Although the results from these intervention studies are promising, further work with randomized controls is needed both to replicate these findings and to advance our understanding of the relational and child processes involved in their short- and long-term efficacy.

Parental Caregiving, Parent–Child Relationships, and Infant Stress-Related Neurophysiology

Stressful life experiences in childhood and adolescence explain 32% of adult psychiatric disorders and 44% of childhood disorders, but many of these disorders do not emerge until long after the period of stress has occurred (Pechtel & Pizzagalli, 2013; Teicher, Samson, Polcari, & Anderson, 2009). Why, then, is early life stress such a potent risk factor for many forms of psychopathology?

Recent neuroscience research using randomized rearing conditions with both rats and rhesus macaques are demonstrating that both infant neurotransmitter systems and the infant stress response system mediated by the amygdala and the HPA axis are open systems at birth that depend on the patterning of caregiver behavior to set enduring parameters of their functioning across the lifespan (Champagne et al., 2008; Coplan et al., 1996; Liu, Diorio, Day, Francis, & Meaney, 2000; Nemeroff, 1996). Specifically, the amygdala is a major neuroanatomical center associated with emotional processing and is particularly relevant to stressors encountered during the early years of life because it appears to be essentially mature at birth. For example, Amaral and his associates studied monkeys ages 2, 4, and 12 weeks and found that all the connections between the neocortex and the amygdala seen in older animals had been established by 2 weeks of age. They argued that in monkeys "the entire complement of adult corticoamygdala and amygdalocortical connections" is established very early in postnatal life (Nelson et al., 2002, p. 512). Whether this will apply to human infants remains to be explored.

The animal literature further demonstrates that early stress is associated with amygdala hypertrophy, which in turn produces greater reactivity to negative stimuli and a more anxious phenotype (Vyas et al., 2006). Anxious children and adults have been found to have a larger and more reactive amygdala, as well as a greater processing bias for negative information (De Bellis et al., 2000; MacMillan et al., 2003; Thomas et al., 2001). Data from animal models also suggest that changes in amygdala morphology are resistant to recovery over time, whereas changes in hippocampal volume secondary to stress are reversible over time (Vyas, Pillai, & Chatterji, 2004). Tottenham and colleagues (2010) have extended these results to human infants, finding that the older the age of adoption out of institutional care, the greater the volume of the amygdala years after adoption. Larger amygdala volume in turn was associated with higher ratings of anxiety and more internalizing behavior among previously institutionalized children. These findings further emphasize the long-term relevance of quality of early care for later psychopathology, as well as the potential for building models of likely neurobiological and behavioral mechanisms mediating such effects.

Evidence for parenting influences on the HPA axis in early childhood has been provided by Blair and colleagues (Blair et al., 2008; Blair, Granger, et al., 2011; Blair, Raver, et al., 2011) and Mills-Koonce and colleagues (2011), using data from a large epidemiological study of children and families living in poor rural

communities in the United States. In this study, sensitive maternal parenting was associated with more optimal levels of HPA functioning, including baseline, reactivity, and regulation levels to a developmentally appropriate child stressor in infants ages 7, 15, and 24 months. Using the same sample, Mills-Koonce and colleagues reported that fathers' harsh parenting (after adjustments for mothers' parenting) at 6 months was associated with higher levels of child cortisol at both 6 months and 24 months of age. These findings suggest unique effects of maternal and paternal caregiving behaviors in shaping early infant psychophysiological responses to stress. Parenting and parent–child attachment associations with physiological responses to stress have also been observed in other stress response systems, including sympathetic and parasympathetic branches of the autonomic system (Haley & Stansbury, 2003; Hill-Soderlund et al., 2008; Moore et al., 2009). Furthermore, longitudinal analyses of parasympathetic functioning during the first year of life suggests that maternal sensitivity can moderate early genetic influences on child vagal tone, an index of neural regulation of cardiac activity (Propper et al., 2008). Although emotional and stress reactivity in early childhood have a foundation in central and peripheral nervous system physiology, the development of this physiology and its relation to behavior appear to be shaped in part by early experience, particularly maternal behavior (Crockenberg & Leerkes, 2006; Gunnar & Quevedo, 2007).

Caregiving Effects on Infant Neurophysiology: Gene–Environment Interaction or Epigenetic Mechanism?

From a traditional genetic perspective, genetic architecture and expression affecting neural function is a constant from birth, with certain genetic variants intrinsically conferring greater vulnerability to particular environmental stressors than others. However, there are also gene–environment interactions in which the *gene itself* is structurally altered through histone modifications induced by the environment. These are termed "epigenetic" effects, as noted earlier, and they need to be carefully distinguished conceptually from gene–environment interactions in which biological structure remains unchanged.

What do we mean by epigenetic changes? At the heart of gene expression lies the process of gene transcription, through which the gene influences the production of particular proteins. Underlying gene transcription is a class of proteins referred to as "transcription factors." These transcription factors are proteins that have the ability to bind to the regulatory regions of the gene. Altering rates of binding of transcription factors to regulatory gene regions is one potent mechanism through which the environment can alter the rate at which a particular genetic site contributes to protein production.

The access of transcription factors to the regulatory sites of the gene is mediated in part by how tightly the DNA is wrapped around a region of histone proteins. For transcription to occur, chemical modification is needed to lessen the positive charge of the histone proteins that are bound to the DNA, so that the closed configuration becomes more open to the binding of the transcription factors (e.g., Grunstein, 1997). This occurs through acetylation, or the addition of an acetyl group to the histone proteins in the tail region of the nucleosome. Conversely, there are other modifications to the histone tails, such as methylation, which *increases* the binding of the histones to DNA, and thereby reduces the access of transcription factors to the DNA and reduces transcription activity. We refer the reader to Meaney (2010) for a much more detailed treatment of the biology underlying gene transcription.

Through the work of several investigators, we have a clear evidence trail in rodent and primate studies that links controlled environmental variations (e.g., randomized assignment to more or less nurturing mothers) to changes in gene expression mediated through histone modifications as early as the first week of life (e.g., Weaver et al., 2004, 2005). The evidence is most complete for the activity of serotonin on glucocortocoid receptor gene transcription in hippocampal neurons (Mitchell, Rowe, Boksa, & Meaney, 1990; Weaver et al., 2007). The consequence of this process of environmental regulation of gene transcription is that we have a clearly identified mechanism through which the expression of the DNA structure itself is altered. Only if the genomic variation (e.g., the short allele of the 5-HTTLPR gene, discussed earlier) is being actively expressed will it contribute to the pathways of biochemical activity that ultimately affect behavior. If input from the environment either increases the expression of a gene that contributes to risk (e.g., the short 5-HTTLPR allele) or decreases the expression of a gene that buffers risk (e.g., the long 5-HTTLPR alleles), the impact of a particular genetic inheritance will be altered.

This ability of environmental inputs to change the histone structures regulating gene expression radically

alters our understanding of the relations between genes and environment. We are only at the beginning of developing methods of analysis that can be applied to human studies (e.g., McGowan et al., 2009). However, epigenetic effects have been primarily demonstrated in relation to aspects of maternal care, in both rodent and nonhuman primate studies. Thus environmental regulation of gene expression is likely to be particularly relevant to the infancy period, when environmental regulation can have the most pervasive effects on developing neural structures, and hence can exert the most influence in adapting the infant to the environmental conditions that have shaped its mother's behavior.

Currently, for most reported gene–environment interactions, we do not know whether the environmental mechanism underlying the interaction is epigenetic or not. That is, is the environmental effect occurring at the level of altering the expression of the gene itself, or is the genetic expression stable but interacting nonlinearly with particular environments (as has been the conventional interpretation)? For example, it may be that a high level of nurturance biochemically up-regulates acetylation and hence increases the transcription of the short 5-HTTLPR variant to negate the usual effect of carrying a short allele. Alternatively, it may be that a fixed lower level of serotonin transcription does not result in negative outcomes under conditions of strong environmental protection and regulation, but results in greatly increased nonlinear effects on negative outcomes (e.g., depression and anxiety) when a nurturing environment is not available to provide additional external regulation.

Second, we do not know which developmental systems are more open to epigenetic alterations and which are less open. For example, limb development would seem to be relatively more resistant to small variations in environmental input, while variations in aspects of neurotransmitter function seem designed to be more open to environmental influences.

Third, we do not know whether neurobiological systems are only open to epigenetic alterations at particular sensitive developmental periods, or whether such alterations are equally likely at any time in development. Whether stress and trauma later in life can cause similar genetic reprogramming is not clear from animal models. In relation to human studies in particular, existing studies do not allow us to clearly disentangle effects of maltreatment later in childhood from preexisting inadequacies in care during infancy, which are likely to precede and accompany later maltreatment.

Finally, we do not yet know how reversible such epigenetic effects are over the course of development. Do changes in gene expression early in the developmental process affect later developments in a way that "locks in" aspects of cellular and neurobiological structure over the long term? Or are these effects designed to be more temporary, to allow a continuing process of adjustment and adaptation to the environment? To date, a number of changes in genetic expression related to stress response in rats and primates have been shown to be enduring into adulthood, while later changes in maternal care have not yet been shown to cause such genetic reprogramming.

CONCLUDING COMMENTS

The body of infant research reviewed here has implications for our conceptions of childhood disorder more generally. First, this literature points up the need for a longitudinal–developmental conception of childhood psychopathology, since late emerging internalizing and externalizing disorders appear to be more strongly related to early precursors or risk factors than was previously thought. Second, this literature converges with the broader clinical literature in pointing to the importance of the biological and social regulation available in the family context as one mediator of childhood psychopathology. Longitudinal research from infancy has constituted particularly fertile ground for the development of sophisticated theoretical and research approaches to the assessment of relational processes between parents and children, including both the biological concomitants and the representational processes associated with patterns of family interaction. As noted earlier, case–control studies of infant disorders, such as feeding disorders, sleep disorders, and regulation disorders, have implicated both current parent–child interactional problems and problematic parental attachment histories as correlates of child disorder. This literature presses us to extend more sophisticated relational assessments to the study of psychopathology, including a more comprehensive view of parental affect and behavior toward the child; increased information about parental relationship histories and implicit representational models for guiding caregiving behavior; and increased study of the intergenerational transmission of particular patterns of relating. These relational methods in turn need to be integrated into genetic and intervention designs with the potential to evaluate multiple interacting causal influences.

Finally, the combined findings from the infancy literature and the larger developmental and clinical research literatures are pressing us to reexamine our tradition of individually oriented diagnostic criteria and assessment practices, and to move toward more systematic assessment of family context and relational behavior. Current diagnostic criteria are inconsistent in emphasizing relational behavior as intrinsic to some disorders (e.g., externalizing disorders and character disorders) but not others (e.g., most internalizing disorders). Infant research is urging us toward a more systematic and developmental view of implicit representation, affect, stress responsivity, and relational behavior as inextricably linked expressions of interpersonal relational systems with intergenerational trajectories. These accumulated insights into family relational systems will need to be integrated with work in genetics, neurobiology, child temperament, and psychophysiology, to give us a better understanding of how genetic diathesis and temperamental or regulatory qualities of the individual interact with the quality of biopsychological regulation provided in the family system to produce developmental trajectories culminating in psychological disorder.

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CHAPTER 16

Child Maltreatment

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Child maltreatment is a tragedy of human error and human circumstances. At its most basic level, child maltreatment denotes parenting failure—a failure to protect the child from harm, and a failure to provide the positive aspects of a parent–child relationship that can foster development. The responsibility for this failure is shared not only by the individual parents for not adequately providing for their child, but also by society, for not adequately providing families with supports and safety nets. Furthermore, the health care community fails in its mandatory reporting requirements for suspicion of child abuse and neglect, with missed opportunities for early intervention and protection of at-risk children (Wekerle, 2011, 2013). The lack of concerted effort in evidence-based child maltreatment assessment and training remain an unnecessary impediment to protecting children and adolescents who present to primary care and emergency rooms, as well as specialty services (such as mental health, addictions, and disability programs). The cost burden of not effectively preventing maltreatment and related impairment is high: an estimated $124 billion in annual cost to the United States alone (Fang, Brown, Florence, & Mercy, 2012). Child maltreatment deaths are the result of preventable adult actions; the U.S. child abuse fatalities number is about three times greater than the number of casualties from the combined U.S. military deaths from the Iraq and Afghanistan conflicts (Every Child Matters, 2012). In the United States, more than 3 million reports of child maltreatment are made to child protective services (CPS) each year, which is about 6 referrals every minute (U.S. Department of Health and Human Services (USDHHS), 2012), confirming the scope and urgency of concern for children's safety and well-being. With this concern comes a keener sense of responsibility for research-based assessment, prevention, and treatment efforts directed toward children and their families.

Most maltreating parents do not have psychotic or other serious mental illness, and some show no apparent psychological or personality dysfunction (Wolfe, 1999). However, many have problems in related areas of depression, anxiety, posttraumatic stress disorder (PTSD), domestic violence, substance abuse (alcohol, other drug, or polysubstance abuse), personality disturbances, social isolation, and poverty, with several of these problems overlapping in both community and clinical samples (Wekerle & Wall, 2002a, 2002b). For instance, first-degree relatives of depressed, abused children have a ninefold greater likelihood of a lifetime depression than controls (Kaufman et al., 1998). Indeed, the presence of adult partner violence appears to multiply the impact of other caregiver vulnerabili-

ties (socioeconomic disadvantage, substance use, mental health, social isolation) on substantiation findings for child abuse and neglect investigations (Wekerle, Wall, Leung, & Trocmé, 2007). Such caregiver vulnerabilities are the primary predictors of eventual out-of-home placement among investigated families (Horwitz, Hurlburt, Cohen, Zhang, & Landsverk, 2011). Family risk factors elevate the chronic stress environments for children. Indeed, neglect, emotional abuse, and abusive discipline are better regarded as constituting a family style, and such homes can be regarded as maltreating homes, with expectable risks to physical and mental health (Repetti, Taylor, & Seeman, 2002). Although some of the co-occurring disorders are treatable, appropriate treatment is often lacking, due to numerous obstacles. Even if maltreatment is detected by formal systems, the focus of professional attention is on child protection and risk assessment, with fewer resources available for treating adult disorders or circumstances. This narrow response may fail to protect against further abuse by overlooking significant risk factors, such as substance abuse or childrearing disorders (English, Marshall, Brummel, & Orme, 1999).

While children present behavioral challenges to parenting (Wolfe, 1999), a child is never responsible for being abused or neglected. Child abuse is an adult act, and without this adult behavioral choice, the child would have fewer developmental problems and disorders. Moreover, maltreatment-induced psychopathology is impairing in both the short and long term, as maltreated children are challenged to maintain resilience across their lifespan. Given its association with health risk behavior, medical illness, and greater rates of psychiatric and medical needs, child maltreatment may be the single most preventable and intervenable contributor to child and adult mental illness (Norman et al., 2012). Once a child has been maltreated, there is often a long and winding road ahead to support a transition from victim to survivor, and from surviving to living.

Despite difficulties, most childhood victims achieve a level of successful adaptation in one or more life domains, as is suggested by the developing literature on resilience (Afifi & MacMillan, 2011; Luthar, 2006). Compared to matched controls, only one in five maltreated children achieve a level of functioning that corresponds to resilient adaptation by adulthood, defined as no period of homelessness, consistent employment, no juvenile or adult arrests, and other factors (Cicchetti, 2013; McGloin & Widom, 2001). Mechanisms of resilience are beginning to attract increased interest, and research is starting to focus on understanding cases when the context of adversity of maltreatment is better traversed by youth. Work to date indicates promising avenues in the areas of self-compassion (Tanaka, Wekerle, Schmuck, Paglia-Boak, & MAP Research Team, 2011; Vettese, Dyer, Li, & Wekerle, 2011), school connectedness (Hamilton, Wekerle, Paglia-Boak, & Mann, 2012), attachment style (Weiss, MacMullin, Waechter, Wekerle, & MAP Research Team, 2011), and service use satisfaction (Ungar, Liebenberg, Dudding, Armstrong, & van de Vijver, 2013). It is clear that many victims of childhood maltreatment find creative options to develop their signature strengths, obtain positive mentoring, and benefit from available community-level investments.

Children's dependency sets the stage for their greater vulnerability to a wide range of victimization experiences, including maltreatment (Finkelhor & Dziuba-Leatherman, 1994). As we discuss in more detail below, "child maltreatment" refers to four primary acts: physical abuse, neglect, sexual abuse, and psychological/emotional abuse. Although neglect is the most prevalent and chronic form of maltreatment (USDHHS, 2010), it remains the least understood (Hildyard & Wolfe, 2002). Psychological abuse is also of concern, due to its co-occurrence with most other forms of maltreatment and its assumed contribution to maladjustment (Wolfe & McIsaac, 2011); the American Academy of Pediatrics has recently released a position statement that, along with physical and sexual abuse and neglect, psychological maltreatment needs to be part of clinical assessment, given the substantial evidence on its deleterious and long-standing impact (Hibbard et al., 2012). Because these types of child maltreatment usually co-occur to some degree, research studies typically focus on the common developmental issues shared by all forms, noting differences by abuse characteristics (type, severity, age of onset, etc.) where appropriate.

Importantly, child maltreatment occurs in a relational context and may be viewed as "relational psychopathology" resulting from a poor fit of the parent, child, and environment (Cicchetti & Olsen, 1990). Insecure child attachment to the parent and poor parental bonding may set the stage for maltreatment by fostering role reversal, rejection, fear of closeness, low emotional investment, and unresolved conflict (Alexander, 1992, 1993). This relational context provides significant emotional weight to the abuse experience. The co-occurrence of violence and other forms of child

maltreatment (e.g., physical injury during sexual abuse) creates a situation of trauma within a relational context (Terr, 1991). Thus a posttraumatic stress response is one important conceptualization of how child maltreatment affects the individual's developmental course, as discussed later in this chapter.

This chapter is oriented toward the importance of the parent–child relational context and the developmental traumatology model of child maltreatment. Thus the chapter departs somewhat from the traditional taxonomic approach to abnormal child psychology, and considers how disturbed childrearing environments or unsafe communities play an important role in abnormal development during childhood and adolescence. First, we present the historical context, definitions, and epidemiology of maltreatment. Next, each type of child maltreatment is discussed in terms of its influence on domains in child development (physical, cognitive, socioemotional). Salient themes that cut across maltreatment types (e.g., dissociation, self-blame) are presented, along with relevant empirical findings. Theoretical perspectives, including a greater discussion of developmental traumatology theory and PTSD, are highlighted. Finally, etiology and future directions are discussed.

HISTORICAL CONTEXT

Maltreatment of children rarely raised concern before the middle of the 20th century because societies viewed harsh forms of discipline and corporal punishment as inconsequential and as parents' right and responsibility. Abusive acts have, in all likelihood, been commonplace throughout history (Radbill, 1987). Children who saw violence between their parents remained silent witnesses, as wives were considered property of their husbands, and violence against them and their children was accepted. For centuries, maltreatment continued undaunted by any countermovement to seek more humane treatment for children.

The medical establishment created momentum with clinical descriptions of the "battered child syndrome" in the early 1960s (Kempe, Silverman, Steele, Droegenmueller, & Silver, 1962), providing impetus for the drafting of model child abuse legislation and mandatory reporting laws. Such laws required, for the first time, that all adults who come into contact with children as part of their professional responsibilities (e.g., teachers, doctors, school bus drivers) must report any suspicion of child abuse to official child protection authorities or police. The "child protection movement," which began in the 1930s and 1940s primarily in response to the need for alternative care for orphans and unwanted children, responded to growing public awareness to seek alternative care for children deemed to be at risk of harm. Not until the passage of the first Child Abuse and Neglect Treatment Act in 1974, however, were funds earmarked for research on its causes and effects. Fortunately, counterefforts to value the rights and needs of children, and to recognize their exploitation and abuse, began to take root during the latter part of the 20th century in many developed countries, spurred by the Convention on the Rights of the Child (United Nations [UN] General Assembly, 1989).

Although still in its infancy, the growing recognition of child maltreatment has brought worldwide interest in documenting and reducing its occurrence. Today, 42 countries have an official government policy regarding child abuse and neglect, and about one-third of the world's population is included in countries that conduct an annual count of child abuse and neglect cases (International Society for Prevention of Child Abuse and Neglect, 2010). Such efforts provide the critical first steps to identifying the scope of the problem, and they justify the implementation of important societal, community, and cultural changes to combat child abuse.

TYPES OF CHILD MALTREATMENT

"Child maltreatment" is a generic term referring to four primary acts: physical abuse, emotional abuse, sexual abuse, and neglect. Determining when a parental act represents maltreatment is complicated by many factors. These include sociodemographic factors related to safety (e.g., quality of the home environment in the context of poverty and community violence) and risk (e.g., parental substance misuse and how it affects parenting); physical or medical evidence of injury severity; and systemic factors (e.g., local norms for monitoring maltreatment reports).

A widely used definition of child maltreatment established by the U.S. Child Abuse Prevention and Treatment Act refers to any recent act or failure to act on the part of a parent or caretaker, which results in death, serious physical or emotional harm, sexual abuse, or exploitation, or an act or failure to act which presents an imminent risk of serious harm (Child Welfare Information Gateway, 2011). A common element of all

definitions is that maltreatment includes not only acts of aggression and exploitation, but also acts of omission (such as abandonment or failure to provide), within the context of a power-abusive relationship. The following definitions of specific acts of child maltreatment are based on a consensus meeting by the World Health Organization (WHO; 1999, pp. 15–16), and largely remain in use today.

Physical Abuse

WHO defines *physical abuse* of a child as acts that result in actual or potential physical harm, stemming from an interaction (or lack of an interaction) that is reasonably within the control of a parent or person in a position of responsibility, power, or trust. There may be single or repeated incidents. Some of the more prominent, acute physical signs for children who have been physically abused include external signs of physical injury, such as bruises, lacerations, scars, abrasions, burns, sprains, and broken bones. Internal injuries may be present, such as head injury (intracerebral and ocular hemorrage from violent shaking or contact with a hard object), and intra-abdominal injuries (e.g., ruptured liver or spleen). Other physical indications may arise from harsh physical blows, such as missing teeth.

Physically abused children exhibit more mild neurological impairments and more serious and minor physical injuries than their nonabused counterparts do (Kolko, 2002). They are at risk of central nervous system changes from direct head injury, as well as brain changes secondary to chronic stress responses (Prasad, Kramer, & Ewing-Cobbs, 2005). So-called "shaken baby syndrome" is considered a main cause of severe traumatic brain injury among infants, and is the most common cause of mortality and morbidity in the neonatal population (American Academy of Pediatrics Committee on Child Abuse and Neglect, 2001). When it is not fatal, nonaccidental head injury or abusive head trauma often causes subdural hematoma, resulting in significant cognitive, neurological, and visual impairments (Barlow, Thompson, Johnson, & Minns, 2005).

Neglect

WHO (1999) describes child *neglect* as the failure to provide for a child in all spheres—physical and mental health, education, nutrition, shelter, and safe living conditions—in the context of resources reasonably available to the family or caregivers. Neglect causes or has a high probability of causing harm to the child's health or physical, mental, spiritual, moral, or social development. This includes the failure to supervise and protect the child properly from physical harm and to provide emotional security. Neglecting behavior encompasses educational, supervisory, medical, physical, and emotional domains. In severely neglecting families, there are typically no routines for eating, sleeping, bathing, and household cleaning. Living areas may be littered with decaying materials. Food may only be available on a random basis. There may be a failure to immunize or otherwise provide proper medical care for children. Children may be left unsupervised for hours or abandoned for days.

Because child neglect is an act of omission rather than commission, there are usually fewer physical signs. With infants, these signs may include severe diaper rash, dehydration, diseases related to malnutrition, and delayed psychomotor skills. In older children, signs may include dental decay; fatigue and listlessness; recurrent ear infections; poor physical care indicators (e.g., accumulated ear wax, foul body odor, unclean clothes, frequent lice infestations); and inadequate physical development.

Child exploitation is sometimes considered a form of neglect in terms of failing to allow normal childhood activities (e.g., play, education, proper nutrition, and safety). WHO describes exploitation of a child as the use of the child in work or other activities for the benefit of others. This includes (but is not limited to) child labor and child prostitution, the latter being considered sexual abuse as well. Countless children worldwide are pressed into dangerous work for long hours, putting them at risk for death. Globally, as many as 10 million children may be victims of child prostitution, the sex industry, sex tourism, and pornography, although accurate statistics are not available (UN Secretary-General's Study, 2006).

Similar to physically abused children, neglected children tend to differ from nonabused children on measures of language ability and intelligence (Hildyard & Wolfe, 2002). Given the low level of parental support in the primary care environment of physically and/or emotionally neglected children, their cognitive and academic achievement levels are often below those of other maltreated groups. Neglected children also lag behind in language, learning, and executive functioning (such as planning and problem solving). This association persists even after researchers control for IQ, which suggests that these children not only face issues

with school-based learning, but are also at increased risk for further developmental challenges (De Bellis, Hooper, Spratt, & Woolley, 2009).

Emotional Abuse

WHO defines "emotional abuse" as the failure to provide a developmentally appropriate, supportive environment, including the availability of a primary attachment figure, so that a child can establish a stable and full range of emotional and social competencies commensurate with his or her personal potential, in the context of the society in which the child lives. There may also be acts toward the child that cause or have a high probability of causing harm to the child's health or physical, mental, spiritual, moral, or social development. These acts must be reasonably within the control of a parent or person in a position of responsibility, power, or trust. Acts include restriction of movement (e.g., tying, confinement), as well as patterns of belittling, denigrating, scapegoating, threatening, scaring, discriminating, ridiculing, or other nonphysical forms of hostile or rejecting treatment (Wolfe & McIsaac, 2011).

Some countries, such as the United States and Canada, include children's exposure to domestic violence as a form of emotional abuse or neglect (Trocmé & Wolfe, 2001). This is in recognition that it is emotionally harming to a child to witness injury to a loved parent with whom the child identifies and on whom he or she relies for care. Furthermore, research shows that witnessing has a pronounced effect on children's adjustment, and that domestic violence often overlaps with physical abuse of the child (Jaffe, Wolfe, & Campbell, 2011). Despite considerable agreement that emotional abuse is harmful and widespread, efforts to document its occurrence have not as yet overcome the difficult challenges posed by this broad definition.

Nonorganic failure to thrive (FTT) is often considered as a form of neglect, as it stems from disturbed feeding of an infant by a caregiver (English, 1998). Neglect and FTT are identified as separate issues, but the two often overlap (Sonuga-Barke et al., 2008). They both individually put children at risk for cognitive deficits, but cumulatively result in worse outcomes. Children with histories of both FTT and maltreatment perform worse on standardized testing and have less adaptive functioning at school, compared to their age-matched, nonmaltreated, non-neglected peers (Kerr, Black, & Krishnakumar, 2000).

Sexual Abuse

WHO (1999) defines *sexual abuse* as the involvement of a child or youth in sexual activity (1) that the young person does not fully comprehend, (2) that he or she is unable to give informed consent to, (3) that he or she is not developmentally prepared for and cannot give consent to, or (4) that violates the laws or social taboos of society. The perpetrator is an adult or another child who, by development or age (typically considered 5 or more years older), is in a relationship of responsibility, trust, or power, and the sexual activity is intended to gratify or satisfy the needs of the perpetrator. This may include (but is not limited to) the inducement or coercion of a child to engage in any unlawful sexual activity (e.g., fondling, exposure, intercourse), child prostitution, and the use of children in pornography.

Childhood sexual abuse entails a violation of safety and boundaries, which may start early in life and endure for years (Trickett, Noll, Reifman, & Putnam, 2001). Sexual abuse probably causes a chronic stress response, which subsequently has a negative impact on cognition. Longitudinal studies of girls who were sexually abused in childhood or early adolescence reveal deleterious effects across a host of biopsychosocial domains; the impact on boys has not been well established to date (Trickett, Noll, & Putnam, 2011).

EPIDEMIOLOGY

Child maltreatment cuts across all lines of gender, national origin, language, religion, age, ethnicity, disability, and sexual orientation. Most industrialized countries will look to child welfare official statistics for rates of reporting, investigating, and substantiating child maltreatment cases, and to fatalities to gauge the scope of the problem of child maltreatment. Child maltreatment cases are seen in the community (day care, schools, family physicians or general pediatricians, emergency room presentations, hospital-based specialty teams); upon presentation to CPS and police services; and in the coroner's office.

Certain subpopulations are at higher risk for maltreatment, such as the area of pediatric disabilities. For example, the fourth U.S. National Incidence Study (NIS-4) estimated that 4.7 per 1,000 children with confirmed disabilities experienced emotional neglect, compared with 2.3 per 1,000 children without disabilities (Sedlak et al., 2010a). A recent review commissioned

by WHO included data from over 18,000 children with disabilities living in high-income countries (Finland, France, Israel, Spain, Sweden, the United Kingdom, and the United States). It found that children with disabilities were 3.7 times more likely than nondisabled children to be the victims of any sort of violence; 3.6 times more likely to suffer physical violence; and 2.9 times more likely to suffer sexual violence (Jones et al., 2012).

To illustrate the portrait and parameter of child maltreatment, various databases attached to the routes of case identification are described below. Cross-national studies are described to assist in understanding the policy–resource–support systems connections. If we are to understand the scope of the problem of child maltreatment, the sum of all sources of data will prove most informative to illustrating the daily living perils in which children and adolescents find themselves.

Before we provide an overview of maltreatment statistics, we must consider the caveats and cautions in appreciating the maltreatment rate estimates. In 2011, the U.S. Government Accountability Office (GAO) released a report describing the challenges faced in attempts to use state data to accurately estimate fatalities from child maltreatment on a national level. First, the GAO pointed out that official state rates of maltreatment-related deaths are almost certainly low: not all children who suffer maltreatment, or even those who die from it, are known to CPS (the agencies responsible for providing the raw data from which most estimated rates are developed) (GAO, 2011; USDHHS, 2011a, 2011b). Second, the GAO noted that different states often use different definitions of maltreatment and its subtypes, and that even when states have attempted to standardize definitions, there are inconsistencies in interpretations, so estimating the national rate of maltreatment from state data leads to substantial uncertainty. Third, states have different standards of proof for adjudicating claims of maltreatment, so national estimates of *substantiated* maltreatment will have similar errors. Finally, the GAO noted that states are inconsistent in their degree of participation with efforts to develop national data sets, leading to gaps in the national data that must be left unfilled, or are estimated. Taken together, these observations underscore the difficulties in estimating maltreatment at any level, and the further difficulties encountered in efforts to form a national picture from state data (GAO, 2011).

The epidemiology of maltreatment at the global level is clouded by the same challenges. Global maltreatment estimates are based on national rates that may lack precise or consistent definitions and reporting. Those rates must then be harmonized, despite the different maltreatment definitions and substantiation requirements the contributor nations have used. Finally, we must contend with countries that are unable to provide comprehensive data, or do not have established CPS agencies, or do not engage in birth registration and death certification. For example, approximately 51 million children born in 2007 are estimated to be unregistered; one in four developing countries with available data has a birth registration rate that is below 50% (United Nations Children's Fund [UNICEF], 2009). Children whose births have not been registered are effectively invisible in the eyes of the state, therefore putting them beyond the reach of CPS and other services (UNICEF, 2009).

This chapter is written in light of such challenges. We make use of the National Child Abuse and Neglect Data System (NCANDS) and the NIS in the United States, the Canadian Incidence Study of Reported Child Abuse and Neglect (CIS), and several WHO and UN reports to illustrate the efforts that have been made to overcome them (see the summary of these data sources in Table 16.1).

In the United States, there are two primary sources that release regular comprehensive reports estimating national child maltreatment: an annual report entitled *Child Maltreatment* released from the USDHHS and based on the NCANDS data set, and the NIS. The *Child Maltreatment* reports represent reporting on CPS by the U.S. federal government throughout a fiscal year. In addition to including data from CPS investigations, the NIS utilizes information collected over a 3-month reference period from "sentinels" (i.e., community professionals who have contact with children and families). The NIS therefore bases estimates of child maltreatment not only on CPS-involved cases, but also on those that come to the attention of community professionals and are either reported to and investigated by CPS, reported to and not investigated by CPS, or are not reported to CPS at all (Sedlak et al., 2010b). The USDHHS NCANDS-based reports and the NIS are both valuable resources for data on the overall picture of child maltreatment in the United States.

U.S. Official Reporting

A recent NCANDS-based report, *Child Maltreatment 2010*, found that more than 3.6 million children (a rate

TABLE 16.1. Available Resources on Child Maltreatment

Source	Key features	Web access
World Health Organization (WHO)	International data and data analysis on child maltreatment	*www.who.int/topics/child_abuse/en*
United Nations Children's Fund (UNICEF)	International data and data analysis on child maltreatment	*www.unicef.org/protection/index.html*
International Society for Prevention of Child Abuse and Neglect (ISPCAN)	International organization focused on child maltreatment	*www.ispcan.org*
National Child Abuse and Neglect Data System (NCANDS) and National Incidence Study (NIS)	National data sets, analyses, and publications on child maltreatment in the United States	*www.ndacan.cornell.edu* *www.acf.hhs.gov/programs/cb/pubs/cm10*
Canadian Incidence Study of Reported Child Abuse and Neglect (CIS)	Nationwide study to examine child maltreatment in Canada	*www.cecw-cepb.ca/overview*

of 44.7 per 1,000 children) in the United States were subjects of at least one CPS *report* between October 2009 and September 2010 (GAO, 2011; USDHHS, 2011b). Although over half of the reports to CPS during 2010 were received from professionals (16.5% education personnel, 11.5% social services personnel, and 8.2% medical personnel), representing a slightly increasing proportion each year since 2006, there remains a prominent role for reporting by community and family members (41.4%), with parents in particular accounting for 6.8% of reports (USDHHS, 2011b). Nearly 1 million CPS reports were *substantiated* (i.e., the weight of the evidence indicated that abuse or neglect had occurred), resulting in a rate of 10.1 substantiated cases of maltreatment per 1,000 children in the population (USDHHS, 2011b). Three-quarters of the victims had no history of maltreatment in the 4 years prior to 2010, resulting in a rate of first-time victimization of 6.9 per 1,000 children in the population (USDHHS, 2011b). However, this is not to say that the families of these children had no prior CPS involvement for maltreatment-related reports, investigations, or services.

Substantiated cases of maltreatment most commonly involved a young child as the victim and a parent as the perpetrator (USDHHS, 2011b). Of those who were involved in substantiated cases of maltreatment, four-fifths (81%) were maltreated by a parent acting either alone or with someone else; mother acting alone was determined more often than father acting alone (37.2% compared with 19.1%, respectively); and one-fifth of cases (18.5%) involved both parents. Thirteen percent of cases of maltreatment involved a perpetrator who was not a parent of the child; nearly half of these (6.1%) were relatives other than parents, and one-third were unmarried partners of the parents (4.4%) (USDHHS, 2011b).

From the NIS-4, children living with their biological parents had the lowest rate of overall maltreatment (6.8 per 1,000 children). In contrast, those living with a single parent who had a cohabiting, unmarried partner in the household had the highest rate in all maltreatment categories (and an overall rate of 57.2 per 1,000 children) (Sedlak et al., 2010a). Although biological parents were the most closely related perpetrators for 72% of children who were physical abused and for 73% of those who were emotionally abused, these rates were not consistent in cases of sexual abuse. Only 36% of these cases involved a biological parent, and 42% involved a perpetrator who was not a biological parent or a parent's partner (Sedlak et al., 2010b). In contrast with males, female perpetrators were more often responsible for child maltreatment in the form of neglect (36% vs. 86%, respectively), while male perpetrators were much more likely to be responsible for sexual abuse (87% vs. 11%).

Thus it remains the case that infants, preschoolers, school-age children, and adolescents are predominantly maltreated by their parents and parent figures, and the family environment that is the primary site for nurturance can also be the primary site for aggression and failure to provide and protect. Sexual abuse by nonparents is substantial (but not in the majority), and needs to be considered within a broader context of neglect by

parents. Parental neglect reflects a lack of monitoring of persons and places to whom a child is directly or indirectly exposed. For example, dangerous persons may be present due to a lack of organized child care, or to parental activities such as procuring substances. Furthermore, the level of known sexual abuse and risk would seem to indicate that it is much more prevalent than official reporting suggests. Research shows that when adolescents provide self-reports of type of maltreatment, their rates of reporting sexual abuse experiences suggest higher levels than the rates of CPS sexual abuse cases (Tanaka et al., 2011).

The demographics of the victims involved in substantiated cases of child maltreatment in the United States have remained relatively stable for several years (USDHHS, 2011b). According to CPS reports, youngest children are at the greatest risk of maltreatment: More than one-third (34%) of all substantiated cases of maltreatment involved children who were under the age of 4 years, and children less than 1 year of age had the highest rate of victimization (12.7%, a rate of 20.6 per 1,000 children of the same age). Among these official reports, the rate and percentage of victimization of child maltreatment appear to decrease with age (USDHHS, 2011b). A more in-depth assessment of the age characteristics in substantiated cases warrants further attention; this decrease may, for example, reflect fewer new case openings as children age toward the CPS mandate cutoff for their state (typically 16 years of age). Males and females appear to be equally affected by child maltreatment: Boys account for 48.5% of substantiated cases, and females for 51.2% (USDHHS, 2011b).

U.S. Community-Based Reporting

The NIS-4 (which looked at reference periods in 2005 and 2006) used data from cases that went unreported to CPS, that were reported and not investigated by CPS, and that were reported and investigated by CPS. It was discovered that CPS investigated the maltreatment of only 32% of children whom the NIS found met the standards for having endured harm from child abuse or neglect (Sedlak et al., 2010b). This provides a context for comparing substantiation rates and case characteristics released in the *Child Maltreatment* report (which includes only CPS-involved cases) with those in the NIS-4 (which includes additional cases). This comparison indicates that the majority of cases of maltreatment may not be CPS-involved.

Historically, child fatalities have usually generated CPS investigations; otherwise, the highest investigation rates (greater than 50%) occurred in cases of potential physical abuse and sexual abuse, while all other types of maltreatment were investigated at much lower frequencies. Although the overall percentage of investigations did not change substantially, the investigation rates in cases of potential sexual abuse, emotional abuse, and emotional neglect did increase by more than 10% in the 10 years since the NIS-3. With respect to sentinel reports of potential maltreatment, the highest rates of investigation occurred with those children recognized by police or at public housing agencies as being victims of maltreatment (53% and 68%, respectively). Meanwhile, the lowest rates of investigation occurred for children recognized at schools, day cares, or shelters (less than 20%).

Unfortunately, the NIS-4 methodology does not investigate the processes leading to the end result (i.e., a CPS investigation or not). Therefore, when a CPS investigation does not occur, it is impossible to distinguish between a sentinel who recognized maltreatment and did not report it and a report to CPS that, through screening processes, did not lead to an investigation (Sedlak et al., 2010b). However, the overall picture raises some concerns: If CPS agencies follow their current screening policies, then according to the CPS Screening Policies Study (included in the NIS-4), more than 80% of reported cases of maltreated children would receive investigation. If we assume that these policies are being followed, this may indicate that at least two-thirds of uninvestigated cases of child maltreatment are not being reported by mandated reporters (Sedlak et al., 2010b).

Another way to consider child maltreatment reports is in terms of the extent of actual or potential harm to the child. The NIS-4 estimated that 1,185,000 U.S. children experienced maltreatment that resulted in some degree of harm, ranging from a life-threatening condition or long-term impairment to an injury or impairment lasting at least 48 hours (e.g., bruises, emotional distress), during the 2005–2006 reference period. This reflects an incidence rate of 17.1 children per 1,000 children in the U.S. population nationwide. The majority of children were neglected (10.5 per 1,000), while cases of both abuse and neglect occurred at estimated rates of 0.9 per 1,000 children in the U.S population (Sedlak et al., 2010a). Females had an overall maltreatment rate of 8.5 per 1,000 girls in the U.S. population, which was approximately 1.3 times the rate of child abuse and

neglect experienced by male children. This difference was primarily due to their significantly higher risk of sexual abuse [3.0 per 1,000 girls compared to 0.6 per 1,000 boys] (Sedlak et al., 2010a).

According to data involving community professionals, children between birth and 2 years of age appeared to experience the lowest overall rates of maltreatment (8.5 per 1,000 children), as well as the lowest rates of physical abuse, emotional abuse, and neglect when each subtype was viewed independently (Sedlak et al., 2010a). Although physical abuse rates remained low relative to those for other age groups, physical abuse was the second most common type of maltreatment experienced by those under the age of 1 year, perhaps reflecting the unique vulnerability of infants to certain types of physical abuse such as shaken baby syndrome (USDHHS, 2011b). In opposition to the official reporting (CPS), these community-based reporting rates of the various subtypes of maltreatment all *increased with age*, reaching a peak overall rate of abuse and neglect for those ages 12–14 years (21.3 per 1,000 children) (Sedlak et al., 2010a). The lower rates among the youngest children in the NIS-4 should be interpreted with caution: They may reflect undercoverage in these age groups because younger children have far less contact with community professionals (i.e., the sentinels) (Sedlak et al., 2010b). Thus the NCANDS may be a more robust source for understanding maltreatment among younger victims, and the NIS may be best for understanding maltreatment for older victims, such as those ages 12 years and above.

The *Child Maltreatment 2010* (USDHHS, 2011b) report and the NIS-4 (Sedlak et al., 2010a) both illustrate the high prevalence of child maltreatment in the United States: It affects children at rates higher than 10 per 1,000 children in the general population. Both reports are in agreement that neglect is among the most common type of child maltreatment experienced in the United States. The *Child Maltreatment* report, which included CPS-involved cases only, captured a much higher rate of substantiated maltreatment among younger children than did the NIS-4, which included sentinel information in addition to CPS-involved cases. Moreover, rates of sexual abuse and physical abuse cases have declined steadily since 2002, although child neglect rates have remained similar (Jones, Finkelhor, & Halter, 2006). These changes may be related to an enhancement in public awareness and policy focus with regard to physical and sexual abuse, while neglect has not received the same attention (Finkelhor, 2008; Jones et al., 2006).

Correlates of U.S. Maltreatment

The NIS-4 also assessed distribution of abuse and neglect by family characteristics, including employment status, socioeconomic status (SES), and household composition. In all cases, children with employed parents had the lowest rate of maltreatment. Children with no parent in the labor force had overall maltreatment rates that were two to three times higher than those of children with at least one parent in the labor force (22.6 versus 7.7 per 1,000 children, respectively). Neglect, in particular, had a strong association with employment status: Children with unemployed parents had rates of neglect two to three times higher than those of children with employed parents (12.1 vs. 4.1 per 1,000 children, respectively).

Living in a low-SES household (defined as having a household income below $15,000 a year, parents' highest education level being less than high school, or having a household member participating in a poverty-related program) was associated with significantly higher rates of all types of child maltreatment (a rate of 55.1 per 1,000 children, compared with a rate of 9.5 per 1,000 children not in low-SES families) (Sedlak et al., 2010a). Children living in low-SES households were three times more likely to be abused and about seven times more likely to be neglected than those living in higher-SES households (Sedlak et al., 2010b). This is consistent with recent research demonstrating an association between increased hospital admissions related to physical abuse in children, and changes in mortgage and foreclosure rates between 2000 and 2009 (Wood et al., 2012). Several other risk factors for child maltreatment were evaluated in the *Child Maltreatment 2010* report (USDHHS, 2011b): Sixteen percent of victims were reported as having a disability, 3.9% of victims were reported as having behavior problems, and 5.2% of victims had another type of medical condition. These issues, though, may not be evident at the stage of investigation, and ongoing evaluation of mental health needs is required as children continue in the child welfare system beyond investigation.

Maltreatment Rates in Other Countries

Canadian rates, estimated from CPS data in the CIS, are in line with the American CPS-based data. In 2008, the investigation rate for potential child maltreatment was 39.16 investigations per 1,000 children in the population, and child abuse and neglect rates were estimated at 14.1 substantiated cases of maltreatment per 1,000

children in the general population—approximately half of which had no history of prior CPS investigations (Public Health Agency of Canada [PHAC], 2010).

Factors that may contribute to higher rates of substantiated cases of maltreatment in Canada include, first, a broader catchment mandate: The CIS and NCANDS both collect detailed information about included cases, but the decision as to whether or not a case meets CIS or NCANDS definitions of abuse is subjectively determined by the investigating workers; this may be reflected in the considerably higher rates of substantiation in the cases investigated in Canada. Second, Canada has a higher rate at which child exposure to adult intimate partner violence (IPV) is reported to child welfare as emotional maltreatment (34% of substantiated cases according to the most recent CIS; PHAC, 2010). Third, there are differences in Canadian and U.S. standards with respect to acceptability of the use of corporal punishment (Fallon et al., 2010). In 82% (11.60 per 1,000 children) of Canadian cases, the maltreatment was of a single type; the other 18% of substantiated cases involved multiple forms of maltreatment. The most common combinations were neglect and exposure to IPV; neglect and physical abuse; neglect and emotional maltreatment; and emotional maltreatment and exposure to IPV (PHAC, 2010).

Overall, child neglect in Canada is not as dominating a form of maltreatment as it is in the U.S. (4.81 per 1,000 children vs. 7.9–10.5 per 1,000 children, respectively); this finding may be related to Canadian universal health care and other forms of government assistance to low-income families (PHAC, 2010; Sedlak et al., 2010a; USDHHS, 2011b). Physical harm to the child victim was noted in 9% of substantiated cases of maltreatment in 2008, resulting in a rate of 1.17 cases per 1,000 children. In one-third of these cases with physical harm, harm was sufficiently severe that it required medical treatment (PHAC, 2010).

With regard to international prevalence rates of sexual abuse, approximately 20% of women and 5–10% of men report being sexually abused as children (Finkelhor, 2008; Pereda, Guilera, Forns, & Gómez-Benito, 2009; Stoltenborgh, van IJzendoorn, Euser, & Bakermans-Kranenburg, 2011). WHO roughly estimates that 150 million girls and 73 million boys under the age of 18 have experienced forced intercourse or other forms of sexual violence involving physical contact; most of the violence is inflicted by family members or other people either residing in or visiting the children's homes (WHO, 2006). Child prostitution and pornography constitute an especially pernicious form of abuse, and affect an estimated 1.8 million children annually worldwide (International Labour Organization [ILO], 2002). Child involvement in sexual exploitation is difficult to estimate accurately, but recent reports propose that, globally, 4.5 million people are victims of forced sexual exploitation; an estimated 21% of these are children under the age of 17 years, and 98% are females. Cross-border movement is strongly associated with sexual exploitation: 78% of all those involved in sexual exploitation are forced to leave their place of origin or residence (ILO, 2012).

Female genital mutilation/cutting (FGM/C) continues to exist in Yemen and several African countries, although its prevalence may be declining. Younger women are less likely to have undergone any form of FGM/C than older women, and fewer daughters have undergone it than have mothers. Nevertheless, UNICEF (2009) estimates that more than 70 million females ages 15–49 years have undergone FGM/C in 28 African countries, and that each of those countries has a national prevalence of FGM/C greater than 1%. Furthermore, FGM/C continues to be practiced (although to a much lesser degree) in other countries, including immigrant communities in Europe, North America, and Australia (UNICEF, 2009). In countries where prevalence continues to be high, the data indicate that opposition to the practice is increasing among women, but this opposition has not translated into behavioral changes (UNICEF, 2009).

Emotional maltreatment is a similarly global issue, with rates varying between countries. The World Studies of Abuse in the Family Environment (WorldSAFE) project (Sadowski, Hunter, Bangdiwala, & Munoz, 2004) discovered that 48% of parents in the Philippines reported having threatened their children with abandonment in the last 6 months; 24% of parents in the United States reported having cursed at their children in the last 6 months; and, in Egypt, more than 40% of parents reported that they having cursed and called their children names in the last 6 months. Exposure to IPV is considered by many to be another form of emotional maltreatment, as noted above. The first ever attempt to estimate the number of children exposed to violence in the home was conducted in 2006, using the limited data available from the UN Secretary-General's Study on Violence against Children. It was estimated that between 135 and 275 million children worldwide are exposed to violence in the home. In developed countries, it is estimated that 4.6–11.3 million children are exposed to domestic violence. Other regional estimates of the number of children exposed to IPV include

those for sub-Saharan Africa (34.9–38.2 million), Latin America and the Caribbean (11.3–25.5 million), southern Asia (40.7–88.0 million), eastern Asia (19.8–61.4 million), and western Asia (7.2–15.9 million) (UNICEF, 2006).

As a summary, Table 16.2 shows the overall incidence of all types of child maltreatment, based on comparable substantiated reports from the United States, Canada, Australia, and New Zealand. Australia's overall substantiation rate per year is lowest (6.5 per 1,000 children), followed by the U.S. (10.1), New Zealand (11.7), and Canada (14.1). Table 16.2 also breaks down the primary types of substantiated child maltreatment for these four countries, based on percentage of cases and rate per 1,000 children in the population (when available). Child neglect is the most common type of maltreatment in both the United States and Canada (7.9 and 4.81 per 1,000, respectively), whereas emotional abuse is more common in New Zealand (7.39 per 1,000) and Australia (no rate reported; 36% of all cases). Rates of physical abuse are comparable for these countries (ranging from 1.7 to 2.8), whereas rates of sexual abuse are higher in the United States and New Zealand (0.92 and 0.83, respectively) than in Canada (0.43). As we consider cross-country comparisons, it is evident that there is a primary issue for families in providing for their children (neglect), and that poverty, while it is not causal for maltreatment, is a frequently accompanying adverse condition. Emotional abuse, especially when exposure to IPV is included, is highly prevalent, and there is ongoing work in supporting women's vulnerabilities and investment in healthy relationships. Most certainly, sexual abuse is not detected sufficiently in CPS cases that come to attention for other forms of maltreatment, as CPS agencies do not thoroughly assess across types and (since disclosure is an ongoing process) do not repeatedly assess maltreatment history across childhood.

Based on trends across six developed countries, there is no consistent evidence for a decrease in any indicators of child maltreatment since record keeping began in the 1970s, with the possible exception of injuries to infants (Gilbert et al., 2012). These disappointing findings may be due to increased reporting, to ineffective prevention, or both, and draw attention to the need to expand and evaluate more child protection and prevention initiatives.

Rates of Harsh Physical Discipline

Harsh physical discipline has come under greater scrutiny because of its inherent connection to forms of maltreatment, particularly where a hard object is used and bruising is consequential. The WorldSAFE Project collected parents' self-reports of the disciplinary measures they used on their children in Egypt, rural India, and the Philippines. Between 21 and 31% of parents in these three countries reported hitting their child with an object, on an area other than the buttocks, in the previous 6 months. The same self-report measures revealed rates of 4% in the United States and Chile in this category. Furthermore, parents in Egypt and rural India reported slapping their children on the face and head as a frequent form of punishment (Hunter, Jain, Sadowski,

TABLE 16.2. Child Maltreatment Incidence Rates in Canada, the United States, Australia, and New Zealand

Incidence	Canada[a]		United States[b]		Australia[c]		New Zealand[c]	
	Percent of all cases	Rate per 1,000	Percent of all cases	Rate per 1,000	Percent of all cases	Rate per 1,000	Percent of all cases	Rate per 1,000
All maltreatment reports		14.1		10.1		6.5		11.7
Specific types								
Neglect	34	4.81	78.3	7.9	29	—	—	3.63
Physical abuse	20	2.86	17.6	1.76	22	—	—	2.05
Sexual abuse	3	0.43	9.2	0.92	13	—	—	0.83
Emotional abuse	9	1.23	8.1	0.81	36	—	—	7.39

[a]Data from *Canadian Incidence Study of Reported Child Abuse and Neglect* (Public Health Agency of Canada, 2010).

[b]Data from *Child Maltreatment 2010* (U.S. Department of Health and Human Services, 2011).

[c]Data from *World Perspectives on Child Abuse*, ninth edition (International Society for Prevention of Child Abuse and Neglect, 2010).

& Sanhueza, 2000; Straus, 1979, 1995; Straus, Hamby, Finkelhor, Moore, & Runyan, 1998). Similar parental and child self-reports from other countries confirm severe violence as a frequent form of physical punishment against children: 8% in Italy, 22.6% in China, and 51.3% in South Korea (Kim et al., 2000; Tang, 1998).

The UNICEF Multiple Indicator Cluster Survey Version 3 collected data from over 30 low- to middle-income countries on child discipline. Between 39 and 95% of children between the ages of 2 and 14 years were reported to have received violent discipline. These rates may not differ substantially from those found in high-income countries (Fluke, Casillas, Chen, Wulczyn, & Cappa, 2010). Not surprisingly, the belief of caregivers that a child needs physical punishment in order to be raised properly was identified as having the strongest association with the prevalence of violent discipline (Fluke et al., 2010).

Child Fatalities

Child fatalities, of course, represent the most severe form of maltreatment. The WHO (2010) estimates that there are 31,000 deaths attributed to homicide among children younger than 15 years of age every year. Using countries where data were available, the UN's World Report on Violence Against Children concluded that (1) those 15–17 years of age faced the highest risk of child homicide by any perpetrator; and (2) those under the age of 1 year held the second highest risk, usually at the hands of one or both parents, frequently the mother (UN Secretary-General's Study, 2006].

The U.S. national child maltreatment fatality rate has remained fairly stable over the years (USDHHS, 2011b). The NIS-4 estimated that approximately 2,400 children died as a result of maltreatment in 2005–2006, resulting in an incidence of maltreatment-related fatalities of 3.0 per 100,000 children in the U.S. child population (Sedlak et al., 2010a). The most recent reports, based on CPS data alone (NCANDS), have lower estimates of child fatalities from maltreatment: 2.07 deaths per 100,000 children in the general population, largely accounted for by children age 1 year or younger (47.7%) (USDHHS, 2011b). Of the children who died, many of them suffered neglect (68.1%), either exclusively or in combination with another form of maltreatment, or physical abuse (45.1%), also either exclusively or in combination.

True global and national numbers are likely to be much larger than all of the available estimates; many deaths are incorrectly attributed to other causes such as accidental falls, burns, and drowning. In low-income countries in particular, many births are not registered, and many deaths are not assigned a cause by a doctor (WHO, 2010).

COST OF CHILD MALTREATMENT

The many issues related to child maltreatment detection, prevention, and treatment services exact enormous costs from society. For example, legal, protective, and foster care services, mental and physical health services, and treatment and rehabilitation services are required on a regular, ongoing basis; additional costs are related to longer-term limitations in education and employment opportunities, family instability, and chronic addiction and mental health disorders. Maltreated children require immediate, high-cost health care services (e.g., emergency room treatment, specialists), as well as longer-term high usage of medical, psychological, and other services (Gelles & Perlman, 2012). For example, compared to the general population, CPS youth show greater special education class placement and longer time to complete schooling (Lang, Stein, Kennedy, & Foy, 2004). IPV shows substantial comorbidity with maltreatment, and it drove CPS cases in the Canadian province of Ontario up by over 300% when children in these families were considered in need of protection due to emotional abuse and risk for revictimization (Fallon et al., 2010). These figures persuasively argue for prevention as a fiscally (as well as socially) responsible approach.

DEVELOPMENTAL COURSE AND PSYCHOPATHOLOGY

Understanding the major consequences of child maltreatment requires consideration of the basic developmental processes that are typically impaired or delayed. Maltreatment requires a child to make social and emotional adjustments that may compromise development. For example, an offender's coercive strategies to ensure psychological control over a child (including fear-based tactics such as threatening harm to the child or others), as well as tactics aimed at destroying the child's sense of self (e.g., verbally denigrating the child), affect how the child learns to relate to others. As a result, maltreated children are more likely than other children to show an

absence of an organized attachment strategy (Baer & Martinez, 2006; Cyr, Euser, Bakermans-Kranenburg, & van IJzendoorn, 2010). This attachment context is important to understanding the impact of child abuse because the child's conceptualization of self and of others represents both a belief system and a relationship prototype (Waters, Posada, Crowell, & Lay, 1993).

Maltreatment challenges all domains of development, given the task of processing a highly affective aversive experience that may be ongoing. Common developmental issues emerge for traumatized children that are nonspecific to maltreatment type. These include social-cognitive adaptations (e.g., cognitive vigilance, dissociation, social-cognitive deficits) and socioemotional adaptations (conceptualization of the self, conceptualization of the other, affect regulation). Yet resilience and adaptation are noted among survivors, particularly in cases where resources in the environment can be marshaled to effect positive opportunities and social connections, and to maximize inner resources and self-righting tendencies (Afifi & MacMillan, 2011; Wekerle, Waechter & Chung, 2011).

Social-Cognitive Development

Social-cognitive development (i.e., a child's emerging view of the world and development of moral reasoning) is fostered by healthy parental guidance and control. It stands to reason that because abused children have been raised in an atmosphere of power assertion and external control, their level of moral reasoning would be significantly below that of their nonabused peers. Typically, abusive parents fail to invoke in their children concern for the welfare of others, especially in a manner that the children will internalize and imitate. The maltreated children must embark on creating some defensive structure, to protect themselves and to support their development.

Cognitive Vigilance

Hypervigilance includes not only a child's constant scanning of the environment, but also development of the ability to detect subtle variations in it to alert the child about possible abuse. Children can become adept at processing nonverbal communication, such that facial expressions, tones of voice, and body language cues signifying danger states (e.g., adult anger, sexual arousal, intoxication, or dissociation) seem to be automatically processed without much conscious awareness. Indeed, a maltreated child can learn to respond to danger signals because they have evoked a feeling of alarm, without being able to verbally label or identify such cues. In other words, it appears that the "feeling state" is most accessible to the child. However, once alarmed, the maltreated child must make quiet efforts at escape, avoiding visible displays of agitation and instead attempting to be inconspicuous—avoiding the perpetrator if possible, or placating or complying if necessary.

Some evidence supports maltreated children's sensitivity to a particular class of affective cues—unresolved anger. Hennessy, Rabideau, Cicchetti, and Cummings (1994) found that children with a history of maltreatment and exposure to domestic violence reported greater fear following videotaped presentations of interadult anger than did matched low-SES children who were exposed to domestic violence. However, this heightened emotional reaction occurred in the context of unresolved (but not resolved) anger, suggesting that maltreated children are particularly sensitive to cues of conflict termination. The placating behavior often observed in maltreated children may represent fear-based attempts to calm or soothe angry parents, so as to avoid becoming the recipient of parental aggression (Hennessy et al., 1994; Koss et al., 2013).

In a psychophysiological experiment, Pollak, Cicchetti, Klorman, and Brumaghim (1997) found that maltreated children evidenced different brain event-related potentials (ERPs), specifically P300, as compared to nonmaltreated controls when exposed to angry or happy visual depictions. Maltreated children had larger ERP amplitude in response to the angry than to the happy stimulus, consistent with a more efficient or preferential cognitive processing of such negative affect. Thus maltreated children appear to be primed for detecting negative affect, which can have a subsequent impact on their own adult parenting style and affect (El-Sheikh & Erath, 2011; Hildyard & Wolfe, 2007).

Dissociation

"Dissociation" denotes the situation of altering one's usual level of self-awareness, in an effort to escape an upsetting event or feeling (Trzepacz & Baker, 1993). It is a normal reaction to an emotionally overloaded situation, enacted in the service of self-preservation when neither resistance nor escape is possible (Herman, 1992). With dissociation, a child diverts attention away from the maltreatment (especially sexual or physical abuse), psychologically escaping from it. This process

can include actively pretending to be somewhere or someone else, experiencing amnesia, and having the ability to "cut off" pain perception from parts of the body. The cognitive outcome of dissociation is a fragmentation of abuse-related information in memory, such that informational details may be separated from each other and from affective and physiological responses. This fragmentation can translate into patchy and disorganized event recall, seemingly illogical associations, and seemingly extreme affective reactions, such as extreme rage in reaction to relatively minor interpersonal "offenses." The trauma may lead to the experience of intense emotion without clear memory of an event, accompanied in some instances by flat affect.

Although children often emit dissociative experiences (e.g., daydreaming, forgetfulness, attentional shifts), essential features of atypical dissociation include amnestic periods, trance-like states, and marked changes in behavior and functioning (e.g., abruptly disrupted play) (Putnam, 1993). Friedrich, Jaworski, Huxsahl, and Bengtson (1997) compared nonabused controls, nonabused psychiatric clients, clients with substantiated sexual abuse, and clients with suspected sexual abuse on self-reported dissociation symptoms. All three clinical groups scored significantly higher than normal controls, with no significant differences among clinical groups. In predicting dissociation symptoms, the duration and nature of the sexual abuse were significant contributors beyond age and gender. Young adolescents with a longer duration and greater severity of abuse were more likely to endorse dissociative symptomatology. Trickett and colleagues (2001) found that dissociation at initial assessment (referral within 6 months of disclosure) described youth who had experienced abuse by multiple perpetrators (nonbiological father figures or other relatives) that was probably accompanied by physical violence, in contrast to those who had experienced chronic incest by a single perpetrator with low physical violence (all sexual abuse involved genital contact). When data were collapsed across subgroups, sexually abused girls had greater dissociation in adolescence at the follow-up assessment 7 years later (Trickett et al., 2011).

Dissociation does not apply only to sexually abused children, however. Macfie, Cicchetti, and Toth (2001) examined dissociation among maltreated and nonmaltreated preschoolers, using a narrative story stem completion task. Developmentally, an integrated self would be evident in toddlerhood and the preschool period. Normative, nonmaltreating experiences facilitate this process to create a sense of self as separate but connected to others. In contrast, maltreatment experiences may promote the development of a dissociated self, with concomitant disruptions in the normal integration of memories, perceptions, and identity; this development supports denial, amnesia for the experiences, blurring of self and fantasy characters, and grandiose self-representations. Macfie and colleagues found that maltreated preschoolers did have higher dissociation scores than nonmaltreated controls. These differences described the sexually abused and physically abused groups, but were less striking for the neglected group. The nature of these differences indicated an increasing level of dissociation over the two time points (initial assessment and 1 year later). This finding does not indicate a "recovery" or greater subsequent coherence in the self, and raises the preschool period as a possible time of "sensitivity" for self-consolidation versus self-fragmentation.

Social-Cognitive Deficits

Social cognition is an important dimension of development to consider because it may mediate the link between maltreatment experiences and a child's subsequent social behavior. Domains of social cognition can include inferences about the thoughts, feelings, and intentions of others, as in person perception and causal attributions (Smetana & Kelly, 1989). For example, maltreated children have been found to have greater difficulties with affect recognition, leading to greater conflict with peers and more psychopathology (Kim & Cicchetti, 2010).

These difficulties may be a function of a lower mastery of verbal expressiveness about inner feelings. To illustrate, Cicchetti and Beeghly (1987) found that maltreated toddlers used fewer "internal state" words (e.g., talking about the feelings and emotions of self and other—"Ouch," "I be good," "You hurt my feelings") than their nonmaltreated counterparts in interactions with their mothers, and they spoke less often about their negative internal states. Furthermore, the maltreated children produced fewer utterances about negative affect and about physiological states (hunger, thirst). These researchers suggest that inhibition of emotional language may be adaptive in a maltreating environment because its expression may function as a parental trigger for maltreatment. That is, certain class-

es of children's affect (e.g., distress) may not be tolerated in maltreating families, and this may be reflected in maltreated children's inappropriate responses to other-distress (e.g., Main & George, 1985).

Alternatively, maltreating parents may be poor models for children in their decoding abilities, perhaps because they overlabel affect as negative. Cicchetti (1990) found similarities in the level of emotional language of maltreated and insecurely attached children, which again emphasizes the relational context as a main environment for teaching a child about emotional states, labeling of emotions, and affective perspective taking. Toddlers at greatest risk for delayed internal-state language were maltreated children with insecure attachments, as compared to maltreated toddlers with secure attachments and comparison toddlers with insecure attachments (Beeghly & Cicchetti, 1994). This finding suggests that maltreatment occurring within a generally problematic relational context is particularly toxic for young children's developing social-communicative abilities.

Thus cognitive development among maltreated children may be altered by their experiences to such an extent that various adaptational strategies, such as hypervigilance and dissociation, form to become a cognitive "style" that is highly responsive to signs of personal danger. Maltreated children, moreover, have difficulties verbally describing their experiences. Ipso facto, when the environment changes (as when a child starts school), such strategies are no longer adaptive, making cognitive flexibility more challenging.

Conceptions of the Self

Maltreated children appear to struggle with core deficits in the self—including poor self-integration, self-destructiveness, low self-esteem, low self-efficacy, self-blame, and negative affect toward the self, as seen in depression and suicidal ideation. Finkelhor and Browne (1988) identify the sense of "powerlessness" as being a salient component to the disruption of the self, as well as the process of "stigmatization," in which negative connotations about the maltreatment experience become incorporated into the child's self-image. In neglect, a child's personal power or self-efficacy is diminished by his or her low value and status as a recipient of inadequate care. In child physical or sexual abuse, power is usurped from the child as a function of the invasion to his or her physical space and subjugation. The child's self-efficacy may be further diminished when his or her attempts to avoid or end the abuse meet with no or limited success. Thus the emotional undercurrent to the self as a function of childhood maltreatment is one of disrespect, being valued only as an "object," and lack of self-determination.

Limited work has been directed to self-conceptualization, especially as it evolves over time and with new salient experiences (e.g., romantic relationship formation). Awareness of a negative or "bad" sense of self was inferred from findings in which maltreated toddlers responded to their mirror reflections with neutral or negative affect more often than controls did (Schneider-Rosen & Cicchetti, 1991). Furthermore, chronic negative self-esteem and a low sense of self-efficacy are reported clinically among sexual abuse survivors, although self-esteem is not a strong discriminator between samples of abused and nonabused adults (Kendall-Tackett, Williams, & Finkelhor, 1993). Studies in the 1980s addressing the issue of self found that young maltreated children inhibited negative affect (Cicchetti & Beeghly, 1987; Crittenden, 1988), with Crittenden (1988) noting that some maltreated children displayed false positive affect. Toth, Cicchetti, Macfie, and Emde (1997), using a narrative story stem task to elicit material considered to reflect internalizations of maltreating and other caregiving experiences, found that maltreated children expressed more negative maternal and self-representations than did nonmaltreated children in their completions of the stories. Physically abused children had higher levels of negative self-representations, and neglected children had lower levels of positive self-representation. Thus maltreated children are challenged to develop an integration of positive and negative aspects of the self and realistic self-appraisal (Cole & Putnam, 1992).

These issues may generalize to other domains. For instance, persistence in problem solving is less among maltreated children than among cognitively comparable controls (Egeland & Sroufe, 1981; Gaensbauer, 1982). Also, a child's achievement may be met with acceptance and positive regard from others outside the maltreating environment, but the child's ability to take credit for and appreciate these sentiments is limited by his or her sense of self as "bad." In extreme cases, these alternate views of the self form the core of alternate personalities and dissociative identity disorder.

Studies converge in identifying self-blame as an important construct for understanding symptomatology

in children. Self-blame may serve a preventative function; that is, a child may know "better" what to do next time or how to prevent further maltreatment (Janoff-Bulman, 1979). However, the literature on sexually abused children in particular suggests that greater self-blame is associated with greater psychological distress (Feiring, Taska, & Lewis, 1998; Wolfe, Sas, & Wekerle, 1994). In a CPS sample, most teens spontaneously attributed blame to the perpetrators (McGee, Wolfe, & Olson, 2001). However, when teens were probed about their possible role in the abuse, the physically/emotionally abused teens identified "misbehavior," and sexually abused teens identified their own failure to prevent the abuse. Physically/emotionally abused youth showed a relationship between abuse severity and self-blame. Self-blame cognitions decreased with increased abuse severity, and self-blame negative affect also increased with severity among females. Also, self-blame was inversely related to perpetrator blame. Across all forms of maltreatment, self-blaming affect added unique variance to the prediction of internalizing problem scores. For physical/emotional abuse and sexual abuse, self-blaming affect also predicted externalizing problems. These authors suggest that *feeling* one is to blame for maltreatment may be more salient than *thinking* one is to blame, in terms of adjustment (McGee et al., 2001). Shame and a self-blaming attributional style appear to mediate the relationship between number of abusive events and depressive symptoms, self-esteem, and eroticism among sexually abused children and adolescents (Feiring, Taska, & Lewis, 2002; Simon, Feiring, & McElroy, 2010).

The functional value of self-blame in a child's interpretation of physical or sexual abuse may be to absolve parents of blame and responsibility, thereby preserving the attachment relationship (Herman, 1992). Toward this end, the child may use other strategies in addition to self-blame, including minimalization, rationalization, suppression of thoughts, denial, and dissociative reactions. The meaning of the abuse may be changed from bad to "less bad," or even "good"—an interpretation that may be conveyed directly to the child by others in his or her environment (positive benefits or rewards, experience of pleasure, etc.). This process of adaptive misperception of adult behavior and self-blame is not unique to abused children, however. It also differentiates preschool children who are anxiously attached from those who are securely attached to their caregivers, and such reactions are considered to be a strategy that serves attachment (Waters et al., 1993).

Conceptions of Others

Sexual abuse involving fathers and stepfathers is experienced as more traumatic than that involving nonrelative males. Finkelhor and Browne (1988) discussed this in terms of the betrayal dynamic of sexual abuse perpetrated by trusted persons, on whom the children were in some way dependent (see also Freyd's trauma betrayal theory, discussed subsequently). Betrayal involves the degree to which children feel their confidence was gained through manipulation and coercion, as well as the position of trust or authority held by the perpetrators. Since it is understood that caregivers take care of their children, any type of maltreatment may be experienced as a betrayal (including child abuse by persons involved with community institutions and organizations; Wolfe, Jaffe, Jetté, & Poisson, 2003). As a consequence, a child's interpersonal needs may be compromised by intense and contradictory feelings of need for closeness and the fear of it (Dodge, Pettit, & Bates, 1994).

Using a storytelling/completion task, Waldinger, Toth, and Gerber (2001) found that neglected preschoolers represented others as hurt, sad, and anxious more often than did physically abused, sexually abused, or nonabused controls. Abused/neglected children, as compared to controls, represented the self as angry and opposing others more often. Thus, over the course of development, this process may translate into interpersonal wariness, idealization, and conflict; affectively labile interpersonal interactions; and indiscriminate interpersonal relationships.

The disruption in relatedness caused by child maltreatment can also lead to general interpersonal patterns of withdrawal/isolation and anxious clinging. For example, physically abused and neglected children showed a high degree of proximity seeking to mothers, teachers, and peers, suggesting their anxiety about closeness to others (Lynch & Cicchetti, 1991). In addition, maltreated children show a high preponderance of insecure attachment to their caregivers—particularly the disorganized/disoriented type—as compared to nonmaltreated children. Without consistent stimulation, comfort, and routine to aid in the formation of secure attachment, maltreated infants and toddlers have considerable difficulty establishing a reciprocal, consistent pattern of interaction with their caregivers. Instead, they show an insecure pattern described as "disorganized" attachment, characterized by a mixture of approach and avoidance, helplessness, apprehension,

and a general disorientation (Barnett, Ganiban, & Cicchetti, 1999; Cyr et al., 2010). The lack of a secure, consistent basis for relationships places maltreated children at greater risk of falling behind in their cognitive and social development, and can result in problems regulating their emotions and behavior with others. Emotions serve as important internal monitoring and guidance systems, designed to appraise events as beneficial or dangerous, and provide motivation for action.

Another disruption in relatedness is heightened conflict. For example, although children exposed to domestic violence did not differ from children not thus exposed in the number of friends they claimed or their frequency of peer contact, they reported feeling lonelier and having more conflict with a close friend (McCloskey & Stuewig, 2001). The mothers of these children also reported their children to have more problems with friends than mothers from nonviolent families reported about their children. Likely contributors to such peer conflict are problems with aggression, as would be expected, given social learning influences and learned relational schemas (El-Sheikh & Erath, 2011).

Finally, maltreated children are at greater risk for peer rejection. A prospective, longitudinal design of three cohorts of public school children distinguished those who were identified as maltreated children in a statewide central registry of substantiated cases from a matched comparison group (Bolger & Patterson, 2001). Maltreated children were predominantly neglected (75%) and physically/emotionally abused (64%), with neglect only and overlapping neglect/abuse the most common patterns, and most maltreated children received one substantiated report. Based on annual sociometric testing, chronically maltreated children (5 years or more of maltreatment) experienced peer rejection more often on a single assessment occasion, as well as consistently across childhood to early adolescence.

The longer maltreatment continued, the more likely a child was to be rejected repeatedly by peers over time. For example, 73% of the control children, 64% of the children maltreated up to 5 years, and 50% of the children maltreated for 5 years or more were classified as never being rejected by peers. Importantly, the relationship between maltreatment and peer rejection was accounted for in part by aggressive behavior for both boys and girls, whereas social withdrawal did not account for this relationship. These researchers concluded that chronicity rather than type of maltreatment best predicted aggression and rejection by peers. Chronic maltreatment by caregivers emerged as a significant predictor of both high levels of aggression and repeated peer rejection across the school years. One suggested mechanism for the maltreatment–aggression–peer rejection pathway is a coercive pattern of parent–child interactions; that is, the propensity to employ a coercive, aggressive interactional style with peers has probably been "trained up" in the family of origin (Snyder, Schrepferman, Bullard, McEachern, & Patterson, 2012).

Socioemotional Development and Emotion Regulation

Parent–child attachment and the home climate play a critical role in emotion regulation, another early developmental milestone. "Emotion regulation" refers to the ability to modulate or control the intensity and expression of feelings and impulses, especially intense ones, in an adaptive manner (Kim & Cicchetti, 2010). A child's self-regulation of affect involves the ability to modulate, modify, redirect, and otherwise control emotions (especially intense ones) in a way that facilitates adaptive functioning (Cicchetti, Ganiban, & Barnett, 1990). Two categories of emotion regulation problems are (1) modulation difficulties (i.e., inability to alter emotion intensity with self-soothing strategies, etc.) and (2) experiential avoidance (i.e., inability to accept or tolerate affect, and hence efforts to avoid, control, or suppress the experiencing of emotion; Cicchetti, Ackerman, & Izard, 1995). For maltreated children, affective issues seem in particular to involve difficulties with modulation, resulting in experiencing affective extremes, and the more fundamental difficulty of lack of awareness of body states or physiological responses (Herman, 1992).

Difficulties in modulating emotions can be expressed as depressive reactions, as well as intense angry outbursts. Accordingly, as maltreated children grow older and face new situations involving peers and other adults, poor emotional regulation becomes more and more problematic, resulting in unusual and self-harmful behavior. Over time, this inability to regulate emotions is associated with internalizing disorders, such as depression and fearfulness, as well as externalizing disorders, such as hostility, aggression, and various forms of acting out (Brensilver, Negriff, Mennen, & Trickett, 2011; Teisl & Cicchetti, 2008).

Considering depressive symptomatology and the timing of maltreatment, any maltreatment during ado-

lescence, as compared to childhood-only maltreatment, increased the risk for depressive symptoms in adolescence (Thornberry, Ireland, & Smith, 2001). Maltreatment experiences during either period were related to risk for internalizing disorder. Maltreated children, as compared to sociodemographically matched control children, were also more likely to show clinical-level internalizing behavior problems (e.g., elevated self-reports of depression or teacher-rated internalizing problems; Cicchetti & Rogosch, 2001). Furthermore, cortisol dysregulation was found in these internalizing maltreated children, in that higher cortisol levels were noted in the morning, in the afternoon, and on daily average. The typical cortisol pattern is that the highest level is evident at the time of awakening, with a decline to low levels by sleep onset. Because cortisol levels would be elevated in response to acute trauma, internalizing maltreated children's patterns would suggest chronic hyperactivity of the limbic–hypothalamic–pituitary–adrenocortical (LHPA) axis,[1] which may indicate the presence of brain impairment (e.g., neuronal damage, neuronal loss in the hippocampus, retarded myelination, atypical synaptic pruning; Cicchetti & Rogosch, 2012). De Bellis and colleagues (1999) found that maltreated prepubertal children with PTSD and comorbid depressive disorder evidenced dysregulation of the LHPA axis. These findings suggest cortisol dysregulation and an association with poorer socioemotional functioning (Carpenter, Shattuck, Tyrka, Geracioti, & Price, 2011).

Difficulties with affect regulation may lead to maladaptive and self-destructive behavior in an attempt to manage the painful affect or avoid it. For example, child self-injurious behavior may be a pathological form of self-soothing, replacing intolerable psychological pain with physical pain (Herman, 1992). A compulsion to self-mutilate is preceded by a strong dissociative state, tends to develop before puberty, and is often a source of shame and is practiced in secret. Other maladaptive attempts at negative affect regulation among survivors include purging and vomiting; compulsive sexual behavior; compulsive risk taking or exposure to danger; and alcohol and drug use (Beitchman, Zucker, Hood, daCosta, & Akman, 1991; Lanier, Jonson-Reid, Stahlschmidt, Drake, & Constantino, 2010). The functional value of such maladaptive behavior may include positively reinforcing a negative self-construct, escaping from emotional numbing, and self-medicating aversive affective states by decreasing negative and increasing positive affect (Stewart & Israeli, 2002). Substance misuse may also bolster self-esteem, increase a sense of peer affiliation, and reduce feelings of isolation.

Neurobiological Development

The effects of childhood maltreatment on cognitive development are believed to occur by two distinct mechanisms that disrupt the brain's development. The first is through direct injury to the brain, as occurs in physical abuse causing injury to the head, or neglect resulting in malnutrition. The second mechanism is mediated through stress pathways, as seen in all forms of abuse including emotional and sexual abuse, which have also been associated with impaired cognitive functioning.

The brain undergoes its most rapid growth and organization early in development, especially from birth to 2 years of age. The changes that occur during this sensitive period of rapid growth may become permanent and thus influence further development. In the case of childhood maltreatment, this means that maltreatment exposure early in life could influence further development even when that adversity is no longer present (McCrory, De Brito, & Viding, 2010). Thus it is possible that early childhood stress may have enduring effects on cognitive function and development. Studies with maltreated children and adults with a history of childhood abuse show long-term alterations in the LHPA axis and norepinephrine systems, which have a pronounced effect on one's responsiveness to stress (McCrory et al., 2010). Brain areas implicated in the stress response that can lead to long-term mental health problems include the hippocampus (involved in learning and memory), the prefrontal cortex, and the amygdala (Cicchetti, Rogosch, Howe, & Toth, 2010; Nunes, Watanabe, Morimoto, Moriya, & Reiche, 2010; Roth & Sweatt, 2011).

Neuroscientists have connected the behavioral signs of poor emotion regulation among maltreated children to alterations in the developing brain, resulting in abnormalities in their ability to manage stress (Danese et al., 2011). Gunnar and Quevedo (2007) define "stress" as the phenomenon that occurs when an individual's well-being is challenged to an extent that exceeds his or her ability to cope. Whereas acute stress is adaptive and increases survival, chronic stress can be detrimental to brain development. Children who are chronically maltreated tend to experience this chronic stress and demonstrate abnormal stress hormone production, resulting in high levels of circulating catecholamines and cortisol (Carpenter et al., 2011; De Bellis et al., 1999).

Chronically elevated cortisol levels are associated with poorer performance on many neuropsychological tasks, including IQ measures (Starkman, Giordani, Schork, & Schteingart, 2001).

Chronic exposure to stress hormones at any age affects the brain structures involved in cognition (Lupien, McEwen, Gunnar, & Heim, 2009). The specific consequences of this phenomenon depend on the time and duration of exposure, and may also depend on the interaction between genes and an exposure to previous environmental adversity.

An acute stress response activates the LHPA axis, which causes cortisol and catecholamines to be released by the adrenal glands. These stress hormones have potentially long-lasting effects on brain functioning (Lupien et al., 2009). Elevated levels of stress hormones can act on structures in the brain such as the hippocampus and the amygdala to disrupt learning and memory, and can lead to adverse brain development through accelerated neuronal loss, myelination delays, inhibition of neurogenesis, and decreased brain growth factors (McCrory et al., 2010; Smith, Makino, Kvetnansky, & Post, 1995). It is thought that each brain region has its own sensitive period, or window of vulnerability, during which that region's development may be altered by elevated levels of stress hormones (Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001). Chronic abuse is more likely to occur during sensitive periods, and these sensitive periods are likely to occur early in life (Pechtel & Pizzagalli, 2011). Complex cognitive functions associated with regions of the brain with longer periods of development are especially vulnerable to the negative impact of early life stress. Thus it would appear that stressful childhood life experiences can influence brain development and lead to both anatomical and functional brain changes. Late childhood and adolescence are considered to be critical periods for the brain's prefrontal cortical development. These regions are responsible for the maturation of executive functioning, including attention and cognitive flexibility, and are among the last areas of the brain to develop (Anderson et al., 2001). Therefore, because executive skills develop later in life, difficulties in executive functioning would not become apparent until children became a little older.

Nearly two-thirds of children who were physically abused and sustained nonaccidental head injuries have been found to have speech and language difficulties, which are usually associated with other neurological abnormalities (Barlow, Thompson, Johnson, & Minns, 2004; Stipanicic, Nolin, Fortin, & Gobeil, 2008). Many of these children have varying combinations of cognitive, motor, language, and behavioral issues (Barlow et al., 2004). These children are reported to have poor concentration and a decreased attention span, resulting in worsening school performance (Barlow et al., 2005). Neuropsychological testing often reveals significant intellectual impairment after traumatic brain injury (Ewing-Cobbs et al., 1998; Prasad et al., 2005). Children who suffer from traumatic brain injuries on average have lower IQs and greater deficits in executive functioning than their noninjured peers (Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005; Stipanicic et al., 2008).

Children from birth to 6 years of age are more vulnerable than older children to adverse outcomes following traumatic brain injury (Babikian & Asarnow, 2009). Infants, in particular, are more likely to develop severe and widespread brain injuries. Their open fontanels cannot help absorb the impact; they are unable to support their disproportionately large heads; and their rapidly developing brains are more vulnerable to injury (Hahn et al., 1988). Infants less than 1 year of age are at greatest risk for the poorest outcomes following traumatic brain injury, as they are more likely to suffer diffuse injuries (Anderson et al., 2009).

In one study, children who sustained brain injuries in infancy or preschool were more likely to demonstrate problems with global cognitive processing, including verbal and performance skills, and their recovery took longer on average than children who obtained brain injuries later in life. They also demonstrated greater reading difficulties than physically abused children who had already learned to read at the time of their traumatic brain injury (Barnes, Dennis, & Wilkinson, 1999). This increased susceptibility toward adverse outcomes before 6 years of age is likely due to the rapid brain development occurring during this relatively early stage of life. Children who acquire brain injuries early in development are less likely to acquire new age-appropriate skills. Thus they tend to have poorer outcomes than children who sustain brain injuries later in life, in whom fundamental cognitive skills have already developed. These children also notably fail to catch up to their peers in terms of intellectual development (Keenan & Runyan, 2001).

Children who were school-age at the time of their head injuries had IQ scores that improved over time. Their verbal skills also seemed to improve, although verbal deficits became apparent in settings where these

children were put in performance situations (van Heugten et al., 2006), and their speed of cognitive processing was often slower (Bawden, Knights, & Winogron, 1985). School-age children who sustained severe brain injuries performed at an average level on academic testing, but many required additional help and remedial education (Ewing-Cobbs et al., 1998; Ewing-Cobbs, Barnes, & Fletcher, 2003).

Not surprisingly, severity of traumatic brain injury is a key predictor in identifying cognitive outcomes later in life (Barlow et al., 2005; Catroppa, Anderson, Ditchfield, & Coleman, 2008; Taylor et al., 2008). Children younger than 7 years of age who sustained traumatic brain injury tended to recover well if their injuries were less severe, and were often able to demonstrate average cognition, though they struggled with executive functioning after more severe injuries (Anderson et al., 2005; Nadebaum, Anderson, & Catroppa, 2007). In children ages 2–7 years at the time of injury, severe traumatic brain injury was more likely than milder injury to result in ongoing memory issues (Anderson, Catroppa, Rosenfeld, Haritou, & Morse, 2000). Thus two important predictors of cognitive outcomes in physically abused children are the age at which the brain injury occurs and the severity of the injury.

Learning and Language Problems

The current consensus in the literature is that childhood maltreatment is associated with cognitive deficits and difficulty with school adaptation and learning (Cicchetti & Valentino, 2006). Formerly, the cause of these cognitive differences between maltreated and nonmaltreated children was a source of debate, as child maltreatment is also associated with other factors related to delayed cognitive development; these include economic disadvantage, poor nutrition, parental psychopathology, poor parenting, poor stimulation by caregivers, family dysfunction, and low parental education attainment (Ayoub et al, 2006; Cicchetti & Lynch, 1993; Jaffee & Maikovich-Fong, 2011).

IQ and Academic Achievement

Academic performance and language development are delayed among physically abused children, who score significantly lower than nonabused peers on cognitive functioning and language skills measures (Mills et al., 2011). Among adolescents with a history of physical abuse, expressive and receptive language deficits have been noted (McFadyen & Kitson, 1996). In one study, they used significantly less self-related language, had impaired syntactic expression, and were more likely to engage in self-repetition compared to nonabused adolescents (Prasad et al., 2005). In research using event history analysis, an intensification of academic risk has been noted in adolescence (after age 14), when maltreated children are at increased risk for absenteeism and decline in grade point average (Leiter & Johnsen, 1997). Cognitive deficits may be due to the limited stimulation received in the home from parents who are overly concerned with a child's behavioral appearance and obedience—impairing the child's freedom to explore, attempt new challenges, learn cooperatively with others, and engage in a variety of cognitive and social stimuli.

Maltreated children tend to have impaired intellect, have worse academic performance (as demonstrated by at-risk test scores and failure of core subjects), be held back a grade, attend fewer than 80% of classes in one academic year, and need more attention and individualization of their education through additional services (De Bellis et al., 2009; Shonk & Cicchetti, 2001). One of the reasons maltreated children are more likely to have academic issues is that they may be less engaged academically than nonmaltreated comparison children (i.e., less self-initiated, less self-regulated, and less able to pay attention and complete schoolwork; Shonk & Cicchetti, 2001).

These effects of maltreatment on cognitive abilities are not transient. A longitudinal study on the effects of maltreatment in early life on cognitive functioning in later childhood followed a cohort from birth (Enlow, Egeland, Blood, Wright, & Wright, 2012). Maltreated children between birth and 5 years of age constituted the cohort, and their IQs were assessed at multiple points from birth to 8 years of age. Maltreatment was significantly associated with decreased scores in cognition at every point of measurement compared to controls. One poignant finding was that children exposed to trauma within the first 2 years of life scored 0.5 standard deviations lower on all cognitive assessments throughout the study. Thus children in this study exposed to trauma in the first 2 years of life experienced significant and long-lasting effects on cognitive functioning, persisting into later childhood. This same group was found to have cognitive scores an average of 7 points lower than those maltreated later in life, indicating the greater detrimental effects associated with abuse earlier in life.

Studies using IQ as a surrogate outcome for cognitive functioning have also found that maltreatment results in cumulative harm, which impairs a child's developmental trajectory.

Chronically maltreated children, defined as having been maltreated in multiple periods of development from infancy to early school age, had lower IQ scores than children abused in only one period of development, in a dose–response relationship (Jaffee & Maikovich-Fong, 2011).

Emotionally abused children demonstrate higher levels of impulsivity, which may adversely affect academic functioning (Fishbein et al., 2009). Children from homes with high levels of domestic violence (a surrogate of emotional maltreatment) had IQs an average of 8 points lower than those of children without this history. Studies have also shown that families with domestic violence had an elevated risk of child maltreatment. Koenen, Moffitt, Caspi, Taylor, and Purcell (2003) used a twin study to assess the effects of domestic violence on IQ. They found that domestic violence was associated with IQ suppression in a dose–response relationship, in both monozygotic (identical) and dizygotic (fraternal) twins. This demonstrates that domestic violence has an environmental effect on cognition in young children, independent of genetic predisposition. The negative effects of domestic violence persisted even after child maltreatment was controlled for as a potential confounding variable. Domestic violence may also have an impact on IQ, as IPV is threatening and extremely stressful for children (Grych & Fincham, 2001; Turner et al., 2012).

Findings from a longitudinal study of at-risk families, followed from infancy to late adolescence, are informative about long-term cognitive outcomes (Erickson & Egeland, 2002; Sroufe, Coffino, & Carlson, 2010). Overall, children who were physically neglected had high rates of school failure and dropout, and the emotionally neglected group had high rates of psychopathology (i.e., 90% received a psychiatric diagnosis, with 73% displaying comorbidities). Cognitive and academic deficits were found across development, from infancy (e.g., Egeland & Sroufe, 1981) and toddlerhood (e.g., Egeland, Sroufe, & Erickson, 1983; Strathearn, Gary, O'Callaghan, & Wood, 2001) through to school age (e.g., Erickson, Egeland, & Pianta, 1989) and adolescence (e.g., Egeland, 1997). Specifically, even when gender and welfare status were controlled for, maltreated children had lower IQs, scored significantly lower in reading and math achievement, received more suspensions, received more disciplinary referrals, and repeated a grade more often than matched control children did. Also, maltreated children in general and physically neglected children in particular showed lower academic initiative (e.g., ability to work independently, persistence, responsiveness to directions) than controls.

Rowe and Eckenrode (1999) found a pattern of academic difficulties across the years in a sample of maltreated children, the majority of whom were neglected. Compared to nonmaltreated children, these children were at greater risk for repeating kindergarten and first grade, which is consistent with lower school readiness. From second through sixth grade, maltreated and nonmaltreated children were similar in terms of first-time grade failure. Residential mobility mediated the relationship between reported child maltreatment and academic performance (Eckenrode, Rowe, Laird, & Brathwaite, 1995): Maltreating families averaged twice as many moves during the children's school-age years.

Studies with matched controls indicate the presence of maltreatment-related cognitive deficits in the areas of delayed language, cognitive development, low IQ, and poor school performance (e.g., Perez & Widom, 1994; Shonk & Cicchetti, 2001; Veltman & Browne, 2001; Widom, 1998). In a study of 6-year-old children in low-income families who were recruited from inner-city pediatric clinics, a history of both FTT and maltreatment was related to greater impairment in school performance and cognitive functioning than among children with neither of these experiences (Kerr et al., 2000). Neglected children were found to have impaired cognitive development by age 5, averaging almost an entire standard deviation below a comparison nonmaltreated control group (Dubowitz, Papas, Black, & Starr, 2002). In a prospective study of extremely low-birthweight infants, Strathearn and colleagues (2001) found that infants with substantiated neglect showed a significantly progressive decline in their cognitive function over time (at 1, 2, 3, and 4 years), and had significantly smaller head circumference at 2 and 4 years (but not at birth), as compared to the control group. These authors found that disability (defined as cerebral palsy, blindness, or deafness) was not associated with a higher rate of CPS referral. Although Sullivan and Knutson (2000) did find that disability status was related to maltreatment, rates for children with physical disability status were lower than for children with cognitive-based or behavioral disabilities.

Executive Functioning

Executive functions consist of those mental abilities underlying goal-directed actions, and are as diverse as directing attention, self-restraint, planning/problem solving, working memory, and self-monitoring. These functions allow individuals to adapt to novel or diverse environmental contexts (DePrince, Weinzierl, & Combs, 2009). However, executive functioning is often deficient following exposure to early life stress, as experienced by maltreated children (Bos, Fox, Zeanah, & Nelson, 2009; Colvert et al., 2008; Pollak et al., 2010). For instance, Mezzacappa, Kindlon, and Earls (2001) compared adolescent boys with substantiated histories of abuse to boys without this history. They discovered that children who had been abused showed decreased rates of improvement with age in their ability to avoid behavior associated with negative consequences. This demonstrates decreased self-regulation in the maltreated population.

Nolin and Ethier (2007) looked at the effects of physical abuse and neglect, combined and in isolation, on executive functioning. They found that children who were subjected to both neglect and physical abuse tended to have poorer cognitive functioning than individuals who were exposed to either form of maltreatment alone. They had decreased auditory attention and responsiveness, and more difficulty with problem solving, abstraction, and planning. This study thus suggests a cumulative impact on cognitive function when a child experiences multiple forms of abuse.

Exposure to familial trauma was associated with poorer executive functioning on measures such as working memory, self-inhibition, attention, and processing speed. A relationship between IQ and executive functioning was also found, suggesting that executive functioning difficulties may be one way in which abused children are at risk for academic, peer, and behavioral issues compared to their nonabused peers (DePrince et al., 2009). These deficits in functioning persist into adulthood in terms of greater deficits in visual memory, executive functioning, and emotional processing (Gould et al., 2012).

Language

Language deficits are significantly more common in severely neglected children than in children who experience other forms of maltreatment (Culp et al., 1991; Gowan, 1993). These language delays include significant delays in receptive and expressive language, difficulties with articulation, and less syntactically complex language than expected for age. Sylvestre and Merette (2010) found that 35.3% of the neglected children in their cross-sectional study demonstrated a language delay. This result is probably attributable to the fact that neglected children have decreased parental support and more strained parent–child interactions than children who experience other forms of maltreatment, such as physical abuse. Severe neglect begins to affect language development as early as 9 months of age, during the prelinguistic stage.

Deviant development at this early stage can lead to significant negative outcomes in terms of language development, as demonstrated by the increasing prevalence of language delay with age (Adamson, 1996). Approximately 50% of neglected children found to have a language delay before age 3 will be diagnosed with persistent language issues by age 4 or 5 (Law, Garrett, & Nye, 2003). Children who had language delays in kindergarten were at greater risk of developing reading disabilities in grades 2 and 4 (Catts, Fey, Tomblin, & Zhang, 2002). These children are also less interested in play and socialization, more serious, more withdrawn, and more depressed, and thus prone to psychological and social problems from an early age (Hammond, Nebel-Gould, & Brooks, 1989; Irwin, Carter, & Briggs-Gowan, 2002). Children with language delays tend to score lower on reasoning and arithmetic measures as well, demonstrating that language is associated with weakness across multiple scholastic domains (Bates, Tomasello, & Slobin, 2005; Manor, Shalev, Joseph, & Gross-Tsur, 2001).

Eigsti and Cicchetti (2004) observed and compared the interactions between two groups of mothers and their preschool-age children; one group contained children with a history of maltreatment, and the other group had no such history. All abused children had their first maltreatment experience before the age of 2, so the authors were able to assess long-lasting effects of maltreatment on language delay. Mothers of maltreated children were less talkative with their children, regardless of baseline verbal ability. Maltreated children showed a 3-month delayed in their syntactic language production, which continued until 5 years of age. They produced less complex language and had decreased knowledge of vocabulary compared to their age-matched peers. Toddlers 31 months of age were assessed in a similar study during a free-play session with

their mothers. The maltreated children in the study used fewer words per utterance, had delays in expressive vocabulary, and used fewer self-descriptive words, reflecting possible deficits in the development of emotional or self-concepts (Beeghly & Cicchetti, 1994; Coster, Gersten, Beeghly, & Cicchetti, 1989).

Childhood sexual abuse also affects language acquisition and subsequent educational attainment. Sexually abused females in one study acquired receptive language at a significantly slower pace throughout their development, and these differences were pronounced as early as midadolescence (Noll et al., 2010). These girls also achieved a lower maximum proficiency overall, relative to nonabused peers. In addition, sexually abused children were more likely to have a greater diversity of deficits in executive functioning, including areas of spatial working memory in adulthood (Gould et al., 2012).

Emotional and Behavioral Problems

Children with histories of physical abuse or neglect stand out in school as having the most severe and wide-ranging emotional and behavioral problems. They are described by teachers as lacking maturity and academic readiness. These descriptions indicate problems completing schoolwork, lack of initiative, overreliance on teachers for help, and behavior that is both aggressive toward and withdrawn from their peers (Egeland, Yates, Appleyard, & van Dulmen, 2002). They perform worse than other children on standardized tests of reading, language, and math (Mills et al., 2011). Child-welfare-involved youth with mild to moderate intellectual disability are an invisible subpopulation within CPS, with research pointing to higher psychological distress levels than their average-IQ counterparts (Weiss, Waechter, & Wekerle, 2011). In a population-based study of adolescents (grades 7–12), any CPS involvement was linked with greater psychological distress, number of visits to professionals for mental health issues, and likelihood to be prescribed medication for depression/anxiety, as compared to their non-CPS-involved counterparts (Hamilton, Paglia-Boak, Wekerle, Danielson, & Mann, 2011). There is evidence, though, that young children are underserved, with an overall mental health service rate of 33% among youth investigated for child maltreatment in a U.S. national cohort study (Horwitz et al., 2012). This pattern of poor adjustment often persists over time, contributing to higher rates of physical and mental health problems in later adolescence and adulthood (Clark, Thatcher, & Martin, 2010; Trickett et al., 2011).

More work has gone into examining the connection between maltreatment and schizophrenia or psychosis. The disentanglement is challenging, given the comorbid conditions of marijuana use, PTSD, and severe personality dysfunction. However, across different study types, there appears to be an elevated risk of psychosis, with an estimated attributable population risk of 33% to childhood adversity (primarily maltreatment types) (Varese et al., 2012).

Aggression and Hostility

The most notable behavioral signs associated with physical abuse are heightened aggression and hostility toward others (especially authority figures), and angry outbursts, sometimes to minor provocation (for reviews, see Kolko, 2002). Physically abused teens had higher rates of conduct disorder and oppositional defiant disorder (ODD) than nonabused youth recruited from a social services department (64% of youth with physical abuse histories also had exposure to domestic violence; Pelcovitz, Kaplan, DeRosa, Mandel, & Salzinger, 2000). Physical abuse during the preschool period, especially when it overlaps with emotional maltreatment, predicts externalizing behavior problems (Manly, Kim, Rogosch, & Cicchetti, 2001). Physically abused children are more disliked and less popular than their nonabused peers (Salzinger, Feldman, Hammer, & Rosario, 1993). This relationship is mediated by the children's aggressive versus prosocial behavior toward others (Salzinger, Feldman, Ng-Mak, Mojica, & Stockhammer, 2001). With close friends, maltreated children exhibit less intimacy, more conflict, and more negative affect than their nonabused counterparts (Parker & Herrera, 1996). These peer difficulties remain even when poverty and negative life events are taken into account (Okun, Parker, & Levendosky, 1994).

In addition, physically abused children may form a hostile attributional bias toward peers (i.e., they automatically presume that a peer means harm), which facilitates an aggressive response. For example, Brown and Kolko (1999) found that self-oriented attributions (e.g., self-blame) were associated with internalizing symptoms, and that other-oriented attributions (e.g., seeing the world as dangerous) tended to be linked to externalizing symptoms. The relationship between

physical abuse and aggression may be mediated by impairments in acquired social knowledge, where learning is hampered by the abusive context, especially in social problem-solving skills (Rogosch, Cicchetti, & Aber, 1995).

Children do find naturally what behavior works in their home environments. Another behavioral pattern among younger physically abused children has been labeled "compulsive compliance," which may be related to a child's level of interpersonal sensitivity and sensitivity to performance demands (Crittenden & DiLalla, 1988). This term refers to a child's ready and quick compliance to significant adults, which occurs in the context of the child's general state of vigilance or watchfulness for adult cues. A child's compulsively compliant behavior may be accompanied by masked facial expressions (e.g., false positive affect, suppressed fear or anger), ambiguous affect, nonverbal–verbal incongruence, and rote verbal responses. Such behavior seems to emerge in pace with the child's abstraction abilities, at about 12 months of age, concurring with the child's ability to form a stable mental representation of the caregiver. It has been suggested that abused infants learn to inhibit behavior that has been associated with maternal anger (e.g., requests for attention, protests against intrusions), and that in toddlerhood, such children may actively behave in a manner designed to please their mothers. This early pattern may lead to inflexible strategies of behavior, with the consequence of reduced reciprocity in interactions (Crittenden, 1992; see also Crittenden & Claussen, 2002). In this regard, it may be noted that childhood maltreatment history has been linked with relationship violence in youth (Flett, Druckman, Hewitt & Wekerle, 2012; Flett, Goldstein, Hewitt, & Wekerle, 2012; Flett & Hewitt, 2002; for a special issue, see Flett & Hewitt, 2012).

The general nature of maltreated children's peer relationships can be organized into two prominent themes (Cicchetti & Lynch, 1995). First, maltreated children, particularly physically abused children and those who witness violence between parents, are more physically and verbally aggressive toward their peers. They are more likely to respond with anger and aggression equally to friendly overtures from peers and to signs of distress in other children (Shields & Cicchetti, 1998; Teisl & Cicchetti, 2008). As a result, they are less popular and have atypical social networks marked by aggression and negative attention seeking. Given their propensity to mistakenly attribute hostile intent to others and their lack of empathy and social skill, it is not surprising that abused and neglected children are rejected by their peers (Anthonysamy & Zimmer-Gembeck, 2007; Kim & Cicchetti, 2010).

The second theme is that maltreated children, especially neglected children, withdraw from and avoid peer interactions. Neglected preschool and school-age children tend to remain isolated and passive during opportunities for free play with other children, and seldom display overtures of affection or initiate play with their mothers or peers (Hildyard & Wolfe, 2002; McSherry, 2007).

Longitudinal studies of girls who were sexually abused in childhood or early adolescence reveal deleterious effects across a host of biopsychosocial domains (the impact on boys has not been well established to date). The most illustrative of these studies followed a sample of sexually abused girls for 23 years, documenting problems and concerns at home, school, and with peers. The pattern and extent of harm to these girls was substantial: Compared to a nonabused comparison group of girls, those with histories of sexual abuse had significant neurodevelopmental differences in their responses to stress; earlier onsets of puberty; greater cognitive deficits; more mental health problems (especially depression and PTSD); higher rates of obesity; and more major illnesses and health care utilization. They also had higher rates of dropping out of high school; self-mutilation; physical and sexual revictimization; teen motherhood; drug and alcohol abuse; and domestic violence in adulthood (Trickett et al., 2011). These findings, along with those pertaining to physical abuse and neglect, speak strongly to the need for greater prevention and early intervention, as we discuss at the end of this chapter.

Substance Abuse

Teens with histories of maltreatment have a much greater risk of substance misuse (Kilpatrick et al., 2000). CPS-involved youth are at increased risk for cigarette smoking (Goldstein, Faulkner, & Wekerle, 2013), alcohol problems (Goldstein, Vilhena-Churchill, Stewart, & Wekerle, 2012), and illicit drug use (chiefly marijuana; Goldstein et al., 2011). Consistently, the link between child maltreatment and youth substance use is reported in large surveys (Bensley, Spieker, Van Eenwyk, & Schoder, 1999; Chandy, Blum, & Resnick, 1996b). In a study comparing sexually abused males to females, males reported greater substance use before and dur-

ing school, greater weekly alcohol and marijuana use, and more binge-drinking episodes (five or more drinks per occasion) than females (Chandy, Blum, & Resnick, 1996a). Furthermore, being physically abused, in addition to experiencing sexual abuse, increased the likelihood of binge drinking (Luster & Small, 1997) and the use of multiple substances (Harrison, Fulkerson, & Beebe, 1997). Finally, substantiated early abuse or neglect (before age 12) was related to subsequent arrest for an alcohol or drug violation as an adult, but not as a juvenile (Ireland & Widom, 1994).

A newer direction is to consider personality vulnerability as a driver of substance abuse and, potentially, other health risk behaviors. Work to date indicates that CPS-involved youth with hopelessness, sensation seeking, and impulsive orientations are more likely to report earlier age of onset of drinking and alcohol-use-related problems, whereas anxiety-sensitive youth (fear of experiencing anxiety symptoms) are less likely to use alcohol (Stewart, McGonnell, Wekerle, & Adlaf, 2011). Brief, personality-targeted cognitive-behavioral interventions have shown promising results, delivered in school settings (e.g., Conrod et al., 2013).

Impairments in Relational Development

The above-described behavioral symptoms of aggression and excessive compliance can be understood in terms of the nature of the caregiver–child interaction, which provides a basis for the child's formation of an interpersonal style (Sroufe & Fleeson, 1986). The primary attachment relationship has been theoretically linked to the intergenerational transmission of abuse (e.g., Kaufman & Zigler, 1989), the failure of maltreated children to form harmonious relationships with others (Erickson, Sroufe, & Egeland, 1985), and their vulnerability to additional developmental failures that rely to some extent on early attachment success (Aber & Allen, 1987). Attachment research shows that the vast majority of maltreated infants form insecure attachments with their caregivers (70–100% across studies; Cicchetti, Toth, & Bush, 1988). This suggests that such a child lacks confidence in the mother as an available and responsive provider, and that the mother has difficulty in providing sensitive, nurturant, and responsive care. Of note is a greater likelihood of a disorganized/disoriented attachment, where no clear attachment strategy is utilized; rather, a mixture of approach, avoidance, and atypical (e.g., freezing) behavioral responses is deployed by the child (Barnett et al., 1999; Cyr et al., 2010). Although these reactions may be adaptive in the short term, it is suggested that such nonoptimal attachment may be most significant in terms of influencing a child's relationship formation with peers, future partners, and future offspring (Cicchetti, Toth, & Maughan, 2000).

As abused children enter school, their development of relationships with both peers and adults is challenged. At this time, their manifestations of sensitivity to others' emotions and problems in their early prosocial behavior development become paramount. Because a positive bond or relationship between parent and child is an important learning context, abused children would be expected to show problems in the affective domain. Physically abused children have a higher incidence of depressive symptoms and diagnoses than either nonabused controls or neglected children do (Kolko, 2002). For example, Toth, Manly, and Cicchetti (1992) compared physically abused, neglected, and nonmaltreated children, using several measures of depression and social adjustment. After the researchers controlled for age and cognitive functioning, the physically abused group differed significantly from both the neglected and nonmaltreated samples, which did not differ from each other.

Abused children do tend to isolate themselves, to respond aggressively under a range of circumstances, and to respond with anger and aversion to the distress of others (Main & George, 1985). Adolescents who were physically abused and witnessed domestic violence were at greater risk for major depression, separation anxiety disorder, and PTSD than were their nonabused counterparts (Pelcovitz et al., 2000). Physically abused children had difficulties recognizing emotions such as sadness and disgust, although their accuracy in recognizing anger did not differ from that of controls (Pollak, Cicchetti, Hornung, & Reed, 2000). These authors conclude that physically abusive environments appear to compromise the ability to recognize and differentiate some emotions, while concurrently heightening the awareness of others (e.g., anger), perhaps due to an overabundance of hostile emotional cues and a familial context of limited affective range.

Like physically abused children, most neglected children form insecure attachments with their caregivers (Stronach et al., 2011). Consequently, some neglected children never learn strategies for engaging adults and for independently exploring their environments, tending to be passive interactants with peers and adults alike (Crittenden & Ainsworth, 1989). Neglected chil-

dren, however, have been rated by teachers and parents as having more internalizing behavior (withdrawal, sadness) than comparison children (Manly et al., 2001). The extent to which such withdrawal from relationships indicates differences in psychological difficulties (e.g., depression, anxiety, repressed anger), acquired social skills (e.g., social reciprocity), motivation, or cognitive–affective abilities remains to be fully understood. In regard to the last-mentioned point, Pollak and colleagues (2000) demonstrated that physically neglected children accurately recognized emotions less frequently than did nonmaltreated or physically abused children, even after receptive language abilities were controlled for. Neglected children displayed deficits in discriminating among emotions (e.g., neglected children saw greater similarity between happy and sad expressions than did the other groups) that were not attributable to problems at the visual-perceptual level, but rather at the level of understanding particular emotion displays. Neglected children, then, would seem to be exposed to fewer emotional learning opportunities and greater restriction of parental affect (Hildyard & Wolfe, 2002).

In observed interactions, neglected toddlers showed little persistence and enthusiasm, much negative affect and noncompliance, and little positive affect, yet were found to be highly reliant on their mothers. As preschoolers, these neglected children showed poor impulse control, which is associated with later behavioral issues, and were found to be highly dependent on teachers for support and nurturance (Erickson et al., 1989). Neglected children were more likely than child victims of other forms of abuse to suffer from impairments in emotional processing and inhibition in adulthood (Gould et al., 2012). Koenig, Cicchetti, and Rogosch (2000) found that neglected children displayed more negative affect during an observed cleanup session that followed a free-play period (physically abused children were not significantly different from controls). One interpretation of interactional differences may be that neglected children are in a stronger position than physically abused children to express negative affect directly in interactions with their caregivers. Similar interactional themes are found in observational studies of children with FTT and their families (Benoit, 2000). These mothers show fewer positive behavior, less affect, more negative perceptions of their infants, and more adult insecure attachment patterns; have experienced more maltreatment themselves in childhood (physical and sexual abuse, neglect) and adulthood; and have more mental illness (e.g., anxiety, depression).

Symptoms Specific to Child Sexual Abuse

Reviews of the child sexual abuse literature converge in identifying a range of common symptoms and adjustment problems (Maniglio, 2009, 2010; Paras et al., 2009). Sexual abuse is often related to specific symptoms of sexualized behavior, as well as to clinical indications of aggression, depression, withdrawal, and anxiety. The range of symptoms can be meaningfully described in reference to (1) acute symptoms, representing a primary stress response to the abuse trauma; and (2) secondary symptoms, representing an accommodation and adaptation to the abuse experience.

"Sleeper" effects of maltreatment have been suggested as those that emerge subsequently when developmental maturity for their expression has been reached, as in the case of sexual dysfunction (e.g., Beitchman et al., 1992). The domain of risky sexual behavior includes early entry into sexual activity, lack of protection during sex, a high number of sexual partners, and early pregnancy and prostitution. Childhood maltreatment has been found to be a risk factor for subsequent engagement in prostitution (Maniglio, 2009) and teen pregnancy (e.g., Gershenson et al., 1989), as well as teenage parental status in both males and females (e.g., Herrenkohl, Herrenkohl, Egolf, & Russo, 1998). Other studies, though, have found that maltreatment is not a necessary and sufficient antecedent for teen promiscuity, pregnancy (e.g., Widom & Kuhns, 1996), or prostitution (e.g., Nadon, Koverola, & Schludermann, 1998). In a retrospective cohort study of boyhood exposure to maltreatment and risk of impregnating a teenage girl (N = 4,127 men), Anda and colleagues (2001) reported that 32% endorsed physical abuse, 15% endorsed sexual abuse, and 11% had witnessed domestic violence. Compared to no maltreatment, each of these maltreatment types significantly increased the risk of impregnation, by 70–140%. Although the mechanisms are yet unclear, such risk behavior may reflect a means of regulating affect (induction of positive affect, distraction from negative affect).

For many maltreated youth, risky sexual practices overlap with other risky behaviors considered to assist with affect regulation (Stewart & Israeli, 2002), notably heavy substance use. In studies of collegiate females, experiencing date rape is associated with a history of childhood sexual abuse, a greater number of sexual partners, and heavier alcohol consumption (Abbey, 2000). It has been suggested that one long-term implication of early maltreatment is the increased likelihood

of "drifting" into higher-risk situations and engaging in a greater array of risky behavior (Wekerle & Wolfe, 1998). In a study of pregnant or parenting adolescent females, age at first pregnancy was predicted by family risk factors (drinking problem, physical abuse) and individual risk factors (early age of intoxication, early age of first wanted sexual experience). Furthermore, younger age at first unwanted sexual experience predicted earlier entry into wanted sexual experience (Kellogg, Hoffman, & Taylor, 1999).

As a useful summary of the information presented above, Table 16.3 shows the major dimensions of development that are affected by physical abuse, neglect, and sexual abuse.

DISORDERS IN ADULTHOOD

Although child maltreatment often poses major challenges to a child's cognitive, emotional, and behavioral coping strategies, many such children and adolescents still remain capable of becoming well-functioning adults (Afifi & MacMillan, 2011). However, evidence from community sample studies attests to the clinical reality that childhood maltreatment can result in significant negative sequelae that persist into adulthood (Hillberg, Hamilton-Giachritsis, & Dixon, 2011; Mersky & Topitzes, 2010). Thus, although many maltreatment survivors can function adequately in later life, the lives of others can be replete with serious psychological distress and disturbance.

Generally speaking, adolescents and adults with histories of physical abuse are at increased risk of developing interpersonal problems accompanied by aggression and violence (Malinosky-Rummell & Hansen, 1993). This relationship between being physically abused as a child and becoming abusive toward others as an adult supports the cycle-of-violence hypothesis, which infers that those subjected to violence become perpetrators of violence (Widom, 1989b). Those with histories of sexual abuse, in contrast, are more likely to develop chronic impairments in self-esteem, self-concept, and emotional and behavioral self-regulation, including severe outcomes such as PTSD, depression, and dissociative states (Hillberg et al., 2011).

As adulthood approaches, the developmental impairments stemming from child maltreatment can lead to more pervasive and chronic psychiatric disorders, including panic and other anxiety disorders, depression, eating disorders, sexual problems, substance use disorders, and personality disturbances (Bentley & Widom, 2009; Irish, Kobayashi, & Delahanty, 2010; Mersky & Topitzes, 2010). For instance, a prospective study of children with documented child abuse and neglect found that they had a fourfold increased risk for personality disorder, as compared to those without a maltreatment history. A wide range of personality

TABLE 16.3. Range of Child Characteristics Associated with Physical Abuse, Neglect, and Sexual Abuse

Dimension of Development	Physical abuse	Neglect	Sexual abuse
Physical	Minor: bruises, lacerations, abrasions; major: burns, brain damage, broken bones	Failure-to-thrive symptoms: slowed growth, immature physical development	Physical symptoms: headaches, stomachaches, appetite changes, vomiting; gynecological complaints
Cognitive	Mild delay in areas of cognitive and intellectual functioning; academic problems; difficulties in moral reasoning	Mild delay in areas of cognitive and intellectual functioning; academic problems; difficulties in moral reasoning	No evidence of cognitive impairment; self-blame; guilt
Behavioral	Aggression; peer problems; "compulsive compliance"	Passivity; "hyperactivity"	Fears, anxiety, PTSD-related symptoms; sleep problems
Socioemotional	Social incompetence; attributions of hostile intent; difficulties in social sensitivity	Social incompetence; withdrawal, dependence; difficulties in social sensitivity	Symptoms of depression and low self-esteem; "sexualized" behavior; behavior that accommodates to the abuse (e.g., passive compliance; no or delayed disclosure)

disorders was noted (i.e., antisocial, borderline, dependent, depressive, narcissistic, paranoid, and passive–aggressive), even when parental education and psychiatric disorders were controlled for (Johnson, Cohen, Brown, Smailes, & Bernstein, 1999; Johnson, Smailes, Cohen, Brown, & Bernstein, 2000). Particular associations include the link between officially reported physical abuse cases and a pattern of antisocial behavior in adolescence and adulthood (Cohen, Brown, & Smailes, 2001; Crooks, Scott, Wolfe, Chiodo, & Killip, 2007). Community surveys have highlighted the salient risk to mothers; childhood abuse is associated with more mood, anxiety, and substance use disorders in both single and married mothers, increasing the odds for psychopathology two- to threefold (Lipman, MacMillan, & Boyle, 2001).

We now examine six prominent adult outcomes of maltreatment—substance use disorders, mood and affect disturbances, posttraumatic-stress-related problems, sexual adjustment, criminal and antisocial behavior, and eating disorders—and note similarities and differences in these outcomes according to particular forms of maltreatment whenever appropriate.

Substance Use Disorders

Although a causal relationship has not been demonstrated, studies have consistently found that women who misuse alcohol and other drugs are likely to have a history of sexual and/or physical abuse and/or neglect as children; the literature for men remains equivocal (Lansford, Dodge, Pettit, & Bates, 2010; Wekerle & Wall, 2002c). About two out of three women entering substance abuse treatment have a maltreatment history (Dunn, Ryan, & Dunn, 1994; Resnick, Kilpatrick, Dansky, Sanders, & Best, 1993). In a study of substance-using women who were admitted to a community-based family service agency (N = 171, with most being single, low-income mothers), it was found that half had experienced sexual and/or physical abuse in childhood, with the majority (82%) abused by relatives. Maltreated women had higher drug use severity and psychological distress levels than control women (Kang, Magura, Laudet, & Whitney, 1999). In a similar study of teens and young adults presenting to an addiction treatment agency (N = 287), half of females reported a history of childhood sexual and/or physical abuse, with 64.7% using substances to cope with the maltreatment (Ballon, Coubasson, & Smith, 2001). For males, about a quarter reported a physical abuse history and about 10% reported being sexually abused, with 37.9% reporting using substances to cope with the maltreatment. Self-medication for maltreatment-related distress (e.g., Stewart & Israeli, 2002) would seem to characterize a substantial number of persons seeking treatment for substance addictions.

Longitudinal studies considering substance use problems and childhood maltreatment have yielded inconsistent results, in part due to varying methodology. Prospective research by Widom and colleagues (e.g., Widom, Ireland, & Glynn, 1995) found that neither sexual or physical abuse history increased the risk of alcohol problems, although having a parent with an alcohol/drug problem did. For females—after controls for parental alcohol/drug problems, child sexual and physical abuse, childhood poverty, race, and age—a history of childhood neglect predicted number of lifetime alcohol-related symptoms, but not lifetime diagnosis. Another longitudinal study, but with a community sample and self-reported maltreatment, found that 43.5% of the sexually abused females met diagnostic criteria for alcohol abuse or dependence in young adulthood, as compared to 7.9% of the nonabused females. Similar associations were not found for child physical abuse (Silverman, Reinherz, & Giaconia, 1996). Kendler and colleagues (2000) found a nearly threefold increase for alcohol and drug dependence among women who retrospectively reported childhood sexual abuse, as compared to those who did not. Using both official and self-reports of maltreatment, Cohen and colleagues (2001) found elevated substance misuse in young adulthood for officially reported child physical abuse and retrospectively reported sexual abuse cases, but not for officially identified neglect cases. Although maltreatment and substance use disorders overlap, greater prospective work needs to be completed in which both maltreatment and substance misuse are assessed comprehensively to capture acute and chronic forms; such work must also take into account the range of potential confounds (e.g., parental psychopathology beyond substance abuse; Lansford et al., 2010; Wekerle & Wall, 2002b).

Mood and Affect Disturbances

Emotional trauma resulting from the chronic rejection, loss of affection, betrayal, and feelings of helplessness that may accompany chronic maltreatment by trusted adults may be responsible for the emotional and behavioral disturbances shown among child, adolescent,

and adult survivors. If symptoms of depression and mood disturbance go unrecognized among those who were sexually or physically abused and/or neglected in childhood, they are likely to increase during late adolescence and adulthood (Brown, Cohen, Johnson, & Smailes, 1999; Mironova et al., 2011). In an important cotwin cohort study, a history of child sexual abuse increased the likelihood of a lifetime diagnosis of major depression, suicidal ideation, and past suicide attempt (as well as increasing the rates of conduct disorder, panic disorder, and alcoholism) for both genders (Dinwiddie et al., 2000). For women, the presence of childhood sexual abuse more than doubled the risk for major depression; for men, it nearly quadrupled the risk for depression. Concordance for childhood sexual abuse was not greater for identical than for fraternal twins, indicating that genetic effects did not play a significant role for either men or women. Rates of major depression and suicidal ideation (as well as conduct disorder) among adult survivors were higher when both cotwins were abused than if the study respondent alone reported childhood sexual abuse. This latter finding suggests that the link between child sexual abuse and adult depression is in part due to the influence of shared familial factors.

In another population-based twin study that controlled for parental psychopathology and family background factors, Kendler and colleagues (2000) found an approximately twofold increase in major depressive disorder (as well as generalized anxiety and panic disorders) among women who reported a childhood history of sexual abuse, compared to women who did not. In these cotwin studies, there were few significant findings among twin pairs who were discordant for sexual abuse history, raising the possibility that shared familial factors influenced the risk of psychopathology; however, sexual abuse was assessed in a limited fashion (e.g., retrospectively, in a single question) and did not consider other types of maltreatment experiences. Nonetheless, there is mounting evidence supporting a link between maltreatment and mood/affect disorders related to neuroendocrine and genetic factors. In particular, the concept of "limbic irritability" has been coined to account for symptoms of internalizing psychopathology following maltreatment, through its impact on the limbic system. Symptoms of limbic irritability include somatic, sensory, and behavioral phenomena believed to be due to increased excitatory neurotransmission following early childhood maltreatment (Dackis, Rogosch, Oshri, & Cicchetti, 2012).

Community surveys using retrospective recall have found an elevated lifetime risk for major depression in women, but not men, where there is a history of physical and/or sexual abuse; a trend for physically abused males has been found (MacMillan et al., 2001). MacMillan and colleagues (2001) note that females reporting physical abuse are more likely to have coexisting sexual abuse than males, raising the issue of whether females are exposed to more types of maltreatment. The sex difference in depressive symptoms has been advanced as a feature of greater child sexual abuse representation among women (Whiffen & Clark, 1997). However, those sexual abuse victims who perceive having an intimate relationship as being high in quality show fewer depressive symptoms, suggesting that positive relationships can be healing (Whiffen, Judd, & Aube, 1999).

Depressive symptoms are a serious concern, as they can lead to life-threatening suicide attempts and self-mutilation. Dinwiddie and colleagues (2000) found that a history of childhood sexual abuse increased the odds ratio for a serious suicide attempt greater than sevenfold for both genders. In a study of women presenting for nonemergency, routine gynecological medical care, prior suicide attempts were significantly higher in women who endorsed a childhood history of sexual abuse, physical abuse, emotional abuse, or witnessing domestic violence than they were in women who did not endorse any type of maltreatment (Wiederman, Sansone, & Sansone, 1998). In a study of college women measuring self-reported depression, suicide attempt, PTSD symptoms, and childhood maltreatment, women who witnessed domestic violence had significantly higher depression and trauma scores than did their counterparts who were not maltreated (Maker, Kemmelmeier, & Peterson, 1998). No significant differences were found for suicide attempts. Furthermore, it was noted that witnessing overlapped with physical abuse, sexual abuse, and paternal alcohol and other drug use. Thus it would seem that sexual and physical abuse, in particular, are related to suicide attempts.

Posttraumatic-Stress-Related Problems

A significant number of men and women who have been subjected to severe physical or sexual abuse during childhood suffer long-term stress-related disorders. About a third of the individuals who were sexually abused, physically abused, or neglected as children meet criteria for lifetime PTSD (Widom, 1999). PTSD-

related symptoms are also more likely in cases of abuse if the abuse was chronic and the perpetrator relied on some method of coercion or trickery to force compliance (Rodriguez, Vande Kemp, & Foy, 1998; Wolfe et al., 1994). In a study of college women, after controls for demographic variables (age, ethnicity, parental occupation, family mental health risks, presence of adult maltreatment), childhood abuse added 9% variance to the prediction of self-reported PTSD symptoms, and witnessing domestic violence added a further 2% of unique contribution (Feerick & Haugaard, 1999). Thus, although maltreatment in childhood is a distal variable, it remains a significant direct predictor of PTSD symptoms in adulthood, especially among women (Koenen & Widom, 2009).

Another consideration would be how PTSD interacts with other problems. For example, Brady, Killeen, Saladin, Dansky, and Becker (1994) compared women with PTSD and substance use disorders to those with only substance use disorders, and found that those in the combined-disorder group were more likely to have experienced childhood sexual and physical abuse and to have greater addiction severity. It has been suggested that substance misuse exacerbates PTSD symptomatology (e.g., Stewart & Israeli, 2002). PTSD may also include symptoms of dissociation—a form of psychological escape from stressful or traumatic events, leading to profound disruptions to self and memory. Over time, this fragmentation of experience and affect can progress into borderline personality disorder, dissociative identity disorder, or chronic pain (Briere, Hodges, & Godbout, 2010; Raphael & Widom, 2011; Widom, Czaja, & Paris, 2009).

Sexual Adjustment

A history of any type of maltreatment among males is a significant risk factor for inappropriate sexual behavior, alienation, and social incompetence in adolescence (Haviland, Sonne, & Woods, 1995; Wolfe, Scott, Wekerle, & Pittman, 2001). Women with childhood histories of sexual abuse, in contrast, are more likely to report difficulties in adulthood related to sexual adjustment—ranging from low sexual arousal to intrusive flashbacks, disturbing sensations, and feelings of guilt, anxiety, and low self-esteem concerning their sexuality (Meston & Heiman, 2000). In a survey study of undergraduates, frequency of childhood sexual abuse was related to a higher frequency of intercourse, a greater variety of sexual experiences, and greater frequency of masturbation, but lower subjective sexual drive (Meston, Heiman, & Trapnell, 1999). These findings are consistent with sexual traumatization's leading to a sexualization of relationships; that is, a sexually abused child may have been rewarded for sexual behavior, which may promote the use of sexual behavior as an interpersonal strategy in adulthood.

Because their normal development of self-awareness and self-protection was compromised, adult survivors of child sexual abuse may become less capable of identifying risky situations or persons, or knowing how to respond to unwanted sexual or physical attention. Consequently, they are more likely to be subjected to further violence in adulthood, such as rape or domestic violence (McIntyre & Widom, 2011; Widom, Czaja, & Dutton, 2008; Wolfe, Francis, & Straatman, 2006). Also, compromised self-protection ability may relate to the risk for unintended pregnancy. A community survey study found that the strongest association between childhood maltreatment and first unintended pregnancy was for psychological abuse, followed first by witnessing physical abuse of the mother, and then by physical abuse. Women who experienced four or more types of maltreatment were 1.5 times more likely to have an unintended first pregnancy during adulthood than control women, even after marital status and age at first pregnancy were controlled for (Dietz et al., 1999).

Criminal and Antisocial Behavior

Although many persons convicted of child abuse and other heinous crimes report significant histories of child abuse and neglect, most maltreated children do not go on to commit crimes. Even so, the risk for antisocial outcomes is higher than in typically developing children. As longitudinal studies demonstrate, there is a significant connection between early maltreatment (before age 12) and subsequent arrest as a juvenile or an adult (Widom, 1989a) or engaging in sexual and physical violence as a young adult, especially for males (Feldman, 1997). A history of maltreatment is associated with an earlier mean age at first offense; a higher frequency of offenses; a higher proportion of chronic offending (Widom, 1989b, 2000); and a greater frequency of self-reported violence and delinquency in adolescence and adulthood (Kelley, Thornberry, & Smith, 1997; Thornberry, Henry, Ireland, & Smith, 2010). Heck and Walsh (2000), in a study of European American males processed by Idaho juvenile probation authorities (N = 388), found that child maltreatment

history had a greater impact on violent delinquency (i.e., rape, assault) than did type of family structure, SES, verbal IQ, family size, or birth order. Maltreatment was also predictive of property crime (e.g., burglary, theft) and misbehavior (e.g., truancy, running away), and emerged as the most powerful predictor of overall delinquency. In a longitudinal, inner-city community study, maltreatment was related to property and violence offenses, and the risk of court contact was about double for maltreated individuals as compared to nonmaltreated controls (Stouthamer-Loeber, Loeber, Homish, & Wei, 2001). In this study, the maltreatment predominantly involved substantiated neglect, emotional maltreatment, or physical abuse, with most perpetrators family members. Given that antisocial and aggressive behavior precedes delinquency, Stouthamer-Loeber and colleagues (2001) examined the sequencing of officially detected maltreatment and delinquency, and found that CPS involvement tended to precede or co-occur with overt (e.g., physical fighting, rape) and covert (e.g., lying, property damage, theft) antisocial behavior problems. For instance, in the case of physical fighting, there was over a fourfold increase in likelihood when maltreatment was present than when it was not. Overall, these findings suggest a different process underlying the transition to delinquency for maltreated versus nonmaltreated children (Topitzes, Mersky, & Reynolds, 2012).

One consideration for a mediator of such delinquency outcomes (in addition to PTSD symptomatology noted earlier) may be relationship functioning—in particular, the success or failure of close romantic relationships during adolescence. Indeed, girls and boys who grew up in violent homes report more violence (especially verbal abuse and threats) toward their dating partners, as well as toward themselves (Wolfe, Wekerle, Reitzel-Jaffe, & Lefebvre, 1998; Wolfe et al., 2001). Dating violence during adolescence and a past history of family violence are strong prerelationship predictors of intimate violence in early adulthood and marriage (O'Leary, Malone, & Tyree, 1994). A history of childhood sexual or physical abuse is associated with more than 3.5 times greater risk of involvement in adult domestic violence (Coid et al., 2001). Thus adolescence may be an important time period for preventing a trajectory toward continued relationship violence, as it may represent the initiation period in the formation of a violent dynamic in intimate partnerships.

Growing up with power-based, authoritarian methods of child management—even if they do not result in physical injuries or identified maltreatment—can be toxic to relationship and social patterns. The amount of routine violence (frequently being hit with objects or physically punished) one experiences as a child is significantly associated with violent delinquent behavior later on (Straus & Donnelly, 1994). This connection is especially noteworthy, given the previous description of how routine violence toward children is commonplace throughout North America.

Eating Disorders

Early clinical suspicions that child sexual abuse could be an underlying cause of eating disorders among some individuals have been supported by ongoing investigations of this important issue. Conceptually, bingeing or purging (a symptom of an eating disorder) and self-mutilation (a feature of borderline personality disorder) have been considered to be maladaptive tension-reducing activities (Briere & Runtz, 1991), reflecting maladaptive self-conceptualizations. In a general population sample, women with bulimia nervosa were about three times more likely to have been sexually abused as children than were women without the disorder (35% and 12.5%, respectively; Garfinkel et al., 1995). Similar findings have been reported among population samples of school-age youth; that is, youth at risk for disordered eating report more negative perceptions of their families and parents, and more sexual or physical abuse experiences (Neumark-Sztainer, Story, Hannan, Beuhring, & Resnick, 2000). In addition, sexually abused children report many of the early risk signs of eating disorders, such as higher levels of weight dissatisfaction and of purging and dieting behavior (Wonderlich et al., 2000). In a study of college women, Tripp and Petrie (2001) found support for their conceptual model of sexual abuse and eating disorders. Sexual abuse predicted higher levels of bodily shame, which in turn predicted increases in body disparagement (low body satisfaction, greater body degradation and loathing), which were predictive of eating disorder symptoms.

Reviews on the link between childhood sexual abuse and disordered eating continue to suggest that it is one of many problem outcomes in the area of self-care. It is unclear how several issues may interrelate; for example, child sexual abuse more than doubles the odds of lifetime diagnoses of eating disorders, depression, anxiety disorders, and PTSD, but increases the likelihood of sleep disorders more than 16-fold (Chen et al.,

2010). The impairment of child sexual abuse may be that, either chronically or episodically, the victims are catapulted into experiences that fundamentally shake their sense of self-efficacy. The role of stigma and psychological isolation needs greater attention, given that about 95% of child sexual abuse survivors in one study never disclosed or had their assault histories detected by authorities (Martin & Silverstone, 2013).

The above-described connections between child maltreatment and mental disorders should be tempered by the awareness that maltreatment is a general risk factor for psychopathology, rather than a *specific* risk factor for eating disorders, antisocial behavior, or other disturbances. Such events are not uncommon in the background of individuals with eating disorders, as well as those with other psychiatric disorders. As well, maltreated individuals share in common a lack of perceived social support, most likely stemming from their early history of negative relationships, which accounts for a significant degree of variability in adult outcomes (Sperry & Widom, 2013). Childhood maltreatment is associated with many undesirable adolescent and adult outcomes, of which the six types of disorders we have described here are prominent.

THEORETICAL FRAMEWORKS LINKING CHILD PSYCHOPATHOLOGY AND MALTREATMENT

The impact of maltreatment on a child's development was first assumed to be invariably negative and disruptive, until researchers began to recognize that maltreatment does not affect each child in a predictable or consistent fashion. Diverse outcomes are especially understandable when positive mediators of adjustment (such as supportive relatives or a child's coping abilities) and moderators (such as the developmental timing of the maltreatment) are taken into consideration (Oshri, Rogosch, & Cicchetti, 2013). Systemic influences—including parental marital/couple violence, separation of family members, and an aversive "everyday" environment (e.g., impoverished parent–child interactions, high levels of household "traffic," multiple residential moves, low educational stimulation)—also vary in their consistency over time, and may synergistically and uniquely contribute to a maltreated child's maladaptation. Furthermore, the maltreatment and environmental problems are embedded in a relational context. The *unique* impact that maltreatment has on child development may be difficult to separate from other family and environmental forces (Wolfe, 1999). The following theories explaining the effects of maltreatment on children's development take into account developmental processes and how they might interact with maltreatment. Two major theoretical perspectives are presented: (1) the childhood trauma model, which focuses on learning theory; and (2) developmental psychopathology, which includes developmental traumatology.

Childhood Trauma Model

Theoretical concepts emerging from the study of the psychological processes underlying an individual's reaction to traumatic events provide further clarification of the nature of PTSD-related disorders or symptomatology. Horowitz (1986), Foa and colleagues (e.g., Foa & Kozak, 1986; Foa, Steketee, & Rothbaum, 1989), and Briere (e.g., 1992, 1996, 2002) have focused their theoretical work on conditioning principles and escape/avoidance mechanisms. The relational context as the prime learning environment is emphasized in betrayal trauma theory (Freyd, 1996). A central postulate of these models is the individual's efforts to integrate a traumatic event into an existing cognitive schema. During this process, PTSD symptoms arise; either intrusions (Horowitz, 1986) or phobic avoidance (Foa & Kozak, 1986) is viewed as a primary symptom. The functional value of such symptoms is to allow for slower assimilation of trauma information, given the overwhelming cognitive–affective nature of the trauma. These viewpoints have not gone without criticism, since differences in the features of the abuse, such as the presence of danger, violence, or coercion versus seduction, have not been adequately considered (Finkelhor, 1988).

Learning-based mechanisms may account for the manner in which a traumatic experience can result in an individual's long-term response that continues well beyond the original stressor (Baum, O'Keefe, & Davidson, 1990). The process of classical conditioning—that is, the manner by which traumatic episodes become associated with particular eliciting stimuli (e.g., odors, places, persons)—can lead to maladaptive or atypical reactions (e.g., flight-or-fight "overreactions"). Repetitive acute episodes occur on an irregular basis and, as such, are more resistant to extinction due to their unpredictability and intensity (Wolfe & Jaffe, 1991). In addition to conditioning, major and minor stressful

life events (referred to as "secondary stressors") often occur as a result of the original traumatic event. For example, disclosure of sexual abuse gives rise to both immediate events (e.g., change in living arrangements, arrest of the perpetrator) and long-term events (e.g., loss of contact with the perpetrator) that also play a role in reducing an individual's coping resources. According to Baum and colleagues (1990), "new" stressful events may be sparked by intrusive imagery of the original trauma. The individual's recollections of the trauma in dreams or thoughts serve to renew the potency of the original stimuli and create generalization to other, previously unrelated events (e.g., dating in adolescence). These secondary stressors may support a chronic, stress-filled lifestyle that makes habituation to the original stressor(s) more difficult.

Briere's self-trauma model (e.g., 1996, 2002) accords self-dysfunction and the increased potential for retraumatization key roles. Because maltreatment impairs capacities for healthy coping (problem-based, proactive), it leads to reliance on avoidance strategies, which in turn preclude the further development of self-capacities, such as self-regulation. This negative cycle is exacerbated by the self-healing need to process conditioned emotional responses via reexperiencing and reenactments. This process further overwhelms self-capacities and produces distress. At its core, maltreatment reduces the likelihood of encountering benign interactive experiences that would promote positive self-development. Instead, the maltreated child psychologically attenuates or avoids certain attachment interactions, developing broad negative self-perceptions. This impairs functioning in terms of negative preverbal assumptions and relational schemas; conditioned emotional responses to maltreatment-related stimuli; implicit/sensory memories of maltreatment (e.g., sensory reexperiencing); narrative or autobiographical memories of maltreatment; suppressed or "deep" cognitive structures involving maltreatment-related material; and inadequately developed affect regulation skills. For example, conditioned emotional responses may elicit "out-of-the-blue" negative affect, in which the specific trigger may remain unclear to the maltreated individual, given the nonverbal nature of the conditioning. It is also postulated that verbally mediated memory material may be most aversive, since it activates associated nonverbal feelings, implicit/sensory memories, and maltreatment-related schemas. Through processes such as distraction and dissociative compartmentalization, thought suppression regarding the maltreatment may be achieved. The low capacity to control and tolerate strong negative affect may contribute to the use of affect avoidance strategies, such as dissociation, substance misuse, or external tension-reducing behavior (e.g., inappropriate or excessive sexual activity, eating, aggression, self-injury). Support for this model has been reported in longitudinal and cross-sectional studies (Briere et al., 2010; Hodges et al., 2013).

Freyd's (1996) betrayal trauma theory bridges the trauma and cognitive science literatures in addressing the motivations for, and mechanisms resulting in, impairment in memory for the maltreatment. Freyd asserts that knowledge is multistranded, with different kinds of knowing that can occur simultaneously. She points out that pain is a motivator for behavior change, and that human beings have a system of natural analgesia. Dissociation during trauma and traumatic amnesia are considered psychological defenses against psychological pain. Behind the motivation to dampen felt pain is a goal more closely related to survival than to pain relief per se. A central factor is that the traumatization occurs while the child is in a situation of dependence. Because of the survival importance of attachment to caregivers, attachment goals are important for the developing child to maintain even when social betrayals are detected. Freyd (1997, p. 27) notes that "child abuse is especially likely to produce a social conflict or betrayal for the victim. If a child processes the betrayal in the normal way, he or she will be motivated to stop interacting with the betrayer. However, if the betrayer is a primary caregiver, it is essential that the child not stop inspiring attachment." The mediator in the maltreatment–dissociation link is the threat to the attachment system. Thus the knowledge gets isolated (memory repression, dissociation, unawareness), and the information gets blocked from ready retrieval (e.g., it may be partially blocked, as seen in blunted affective responses). This process leads to a disruption in awareness and autobiographical memory. This continued information blockage contributes to later interpersonal distrust and difficulties in accurately assessing aspects of interpersonal and intrapersonal reality.

There is preliminary support for the belief that the closeness of the child and perpetrator is related to the probability of some degree of amnesia for childhood sexual abuse, with amnesia rates for parental abuse higher than those for nonparental abuse (see Freyd, 1996). Freyd and DePrince (2001) summarize their laboratory studies using a Stroop color-naming paradigm with college students; they have found that "high

dissociators" (i.e., students with high levels of dissociation) have impaired attentional capacities in tasks of selective attention, but not divided attention. High dissociators also have impaired memory for affectively laden words (e.g., "incest"), but not neutral words, as compared to low dissociators (i.e., the time to name the color of the word is a function of the threat level of the word). High dissociators endorse three times as much trauma in their history as low dissociators do. These findings suggest that divided attention is a mechanism by which the flow of information is controlled.

The implication of betrayal theory is that there are two conceptually independent dimensions of trauma. The dimension of life threat may involve the symptoms of fear, anxiety, hyperarousal, and intrusive memories. The dimension of social betrayal may relate to the symptoms of dissociation, amnesia, numbing, and abusive relationships. Survivors of childhood maltreatment have learned to cope with an inescapable social conflict by being disconnected internally (Foynes, Freyd, & DePrince, 2009). Freyd and DePrince (2001) note that treatment goals for the social betrayal dimension include a focus on social relationships and related cognitive mechanisms promoting internal integration and more intimate external connections.

Developmental Psychopathology

General Description and Some Examples of Applications

Maltreatment as a special instance of major parent–child conflict was seldom studied until the field of developmental psychopathology turned its attention toward these phenomena (e.g., Aber & Cicchetti, 1984; Cicchetti, 1989; Cicchetti & Toth, 1995). Developmental psychopathology is an organizational framework for understanding that a child's poor resolution of one stage of development will lead to a greater *probability* of incompetence in subsequent tasks or milestones (Cicchetti & Rogosch, 1996). Therefore, to understand the effects of maltreatment on children's progressive vulnerability and nonoptimal development over time, it is necessary to place their experiences in a broader context that includes their perceptions of their families' emotional climate; their previous experiences with conflict and abuse; their interpretations of violence and maltreatment; their available coping abilities and resources to countermand stress and inadequate caregiving; and the stability of toxic or growth-supportive environmental factors (Cicchetti & Tucker, 1994; Crittenden & Claussen, 2002; Wolfe & Jaffe, 1991). Developmental psychopathology also considers transactions among the biological, cognitive, affective, representational, and interpersonal domains of the individual. It recognizes that biological processes influence psychological functioning, and that psychological experience influences biological structure and function. Developmental traumatology (discussed below) is an excellent exemplar of developmental psychopathology's moving in the direction of integrating neurobiological and psychosocial mechanisms.

Developmental psychopathology centers on the dynamic interplay of risk and protective factors in contributing to the organization of an individual and the formation of the individual's particular developmental trajectory. Rather than a single prototype, different pathways are likely to exist in cases where there is marked vulnerability to psychopathology. In other words, diverse outcomes are likely to emerge from child maltreatment. Thornberry and colleagues (2001, 2010) provide support for a developmental psychopathology approach. In their longitudinal study, these investigators were able to classify the period of maltreatment and compare these periods as they relate to diverse outcomes. Children who experienced early-only maltreatment (birth to age 5) appeared to be a fairly resilient group with regard to adolescent outcomes. In contrast, those experiencing chronic maltreatment and adolescent-only maltreatment evidenced the widest range of maladaptation in late adolescence, including increased general delinquency, drug use, internalizing problems, and teen pregnancy. These authors suggest that substantiated maltreatment ending in the preschool years may be responsive to intervention, and that if the negative effects of maltreatment are not reinforced, then its effects may dissipate. Empirical support is consistent with this notion. A follow-up study of families that received a home-visiting intervention found no relation between number of maltreatment reports and early-onset problem behavior (e.g., binge drinking, arrests, sexual intercourse, smoking marijuana) for maltreated youth receiving the intervention, whereas a significant relationship did exist in the no-intervention maltreated group (Eckenrode et al., 2001).

Cole and Putnam (1992) provide a specific example of the application of developmental psychopathology to the study of sexual abuse. They argue that incest has a unique negative impact on domains of the self and related social functioning; it is thus linked to adult dis-

orders that have intrapersonal dysfunction as core features (e.g., borderline personality disorder; dissociative identity disorder; and somatic symptom, eating, and substance use disorders). These researchers also consider the developmental stage at which abuse begins as influential in symptom structure. For example, school-age children may be particularly vulnerable to guilt and shame, given their increased introspective abilities. Thus the timing of the maltreatment within a child's developmental context is an important consideration (Cicchetti & Manly, 2001).

Developmental Traumatology

Recently, our knowledge of the biological bases underlying the impairment associated with child maltreatment has been expanding. In part, this reflects the accumulation of neurobiological studies showing that stress stimulates the formation of gene products, which then influence cellular processes responsible for gene expression, protein formation, and associated biological and behavioral change (for reviews, see McCrory & Viding, 2010; Roth & Sweatt, 2011). In addition, this research is being driven by studies demonstrating that early environmental events can lead to lasting effects on brain structure and function, and hence on biopsychosocial functioning throughout the lifespan (Fox, Levitt, & Nelson, 2010).

Developmental traumatology is the study of the interactions among the complex factors of genetic constitution, psychosocial environment, and critical periods of vulnerability and resiliency in individuals experiencing child maltreatment, with the aim of disentangling the effect of trauma on neurobiological development (De Bellis & Putnam, 1994). Stress, known to influence gene expression, is responsible for initiating a predictable physiological response. In contrast to an acute event, chronic stress linked with the threat of or actual revictimization, is thought to impair the functioning of the body's stress-responsive systems. These systems include the immune system, the neurotransmitter systems (e.g., noradrenergic, serotonergic, and dopaminergic systems), the LHPA axis, and the sympathetic nervous system (e.g., activation of the fight-or-flight response). Also involved are such brain structures as the hippocampus (e.g., learning, memory, capacity for neuronal regeneration), amygdala (e.g., responding to fear-inducing stimuli in times of acute threat), and prefrontal cortex (e.g., planning, execution, inhibition of responses, extinction of fear response) (De Bellis, Hooper, Woolley, & Shenk, 2010; Lanius et al., 2010).

Child maltreatment encompasses a stressful acute event, as well as exposure to other stressful ongoing life circumstances (often including socioeconomically substandard and dangerous living situations, domestic violence, and parental psychiatric problems). High-level and long-term stress is detrimental to the optimal functioning of the body's stress response system and threatens sustained system dysfunction. Child maltreatment, whether acute or chronic, may generate changes in neurobiological systems that can result in augmented responses to subsequently experienced stressors. This can place survivors in vulnerable positions for the resurgence of PTSD and related problems.

Developmental traumatology advances the view that stress-induced changes in neurobiology underlie the development of psychopathology in maltreated children, and that the negative psychobiological sequelae of maltreatment may be more properly regarded as "an environmentally induced complex developmental disorder" (De Bellis, 2001, p. 540). There is evidence for its course over the lifespan. In a path-analytic design, a history of child sexual abuse was shown to be directly related to subsequent maltreatment in adulthood, as well as contributing substantially to adult PTSD symptoms (Nishith, Mechanic, & Resnick, 2000). In a prospective study of substantiated maltreatment in childhood, the prevalence of PTSD in the maltreated group (37.5% sexually abused, 32.7% physically abused, 30.6% neglected) exceeded that of the nonmaltreated, matched comparison group (20.4%) (Widom, 1999). Thus the best predictor of future PTSD may be childhood maltreatment; that is, ongoing vulnerability to maltreatment-related cues may play a reciprocal role with PTSD symptom experience (De Bellis, 2012).

The extreme stress associated with maltreatment may cause changes in brain development and structure, which may explain some of the symptoms of psychological trauma (Glaser, 2000). Figure 16.1 depicts the developmental traumatology model (De Bellis, 2001) and the specific pathways hypothesized to be affected by experiencing traumatizing levels of child maltreatment. As can be seen from the model, maltreatment-related PTSD is hypothesized to lead to alterations of the catecholamines (norepinephrine, epinephrine, dopamine) and the LHPA axis. Much of the current research has focused on atypical cortisol levels in maltreated children, as compared to their nonmaltreated counterparts. As a result of hormones flooding the brain before and

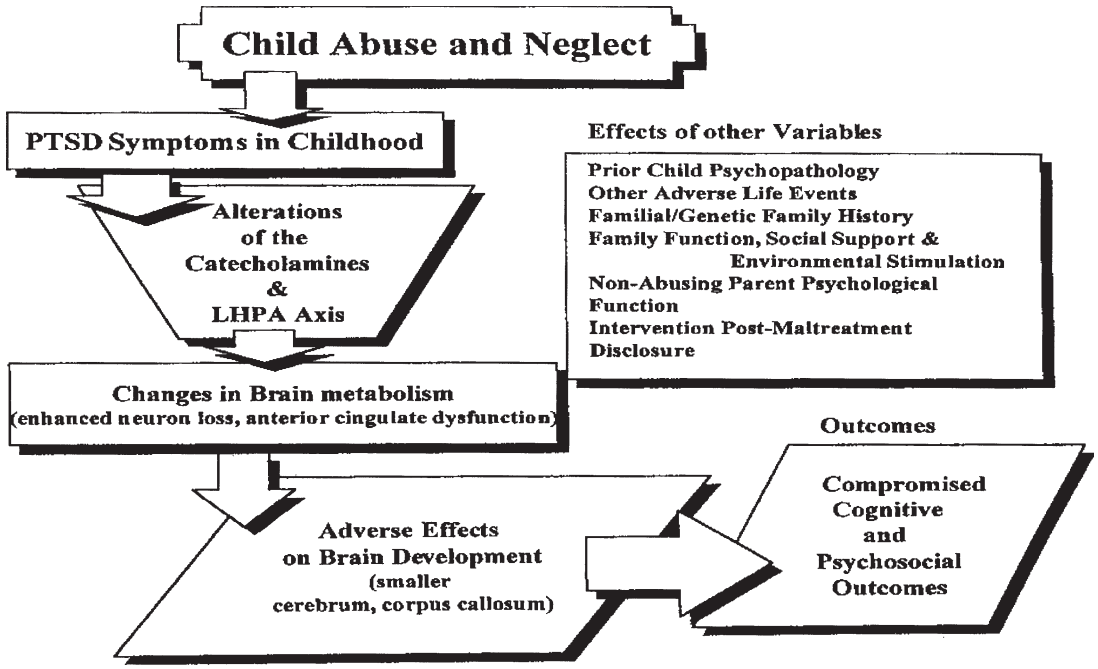

FIGURE 16.1. A developmental traumatology model of biological stress systems and brain maturation in maltreated children. In this model, compromised neurocognitive and psychosocial outcomes are understood as results of adverse brain development. From De Bellis (2001, p. 552). Copyright 2001 by Cambridge University Press. Reprinted by permission.

after a stressful period, the hippocampus—the part of the brain that deals with short-term memory, and possibly the coding and retrieval of long-term memory—may be functionally impaired. The hippocampus is particularly sensitive to high cortisol levels, which circulate for hours or days after stress. Low cortisol is linked with emotional numbing, and spasms of high cortisol coincide with disturbing memories (Heim et al., 2000). After prolonged stress, cortisol levels become depleted, and the feedback systems that control hormone levels in the brain may become dysfunctional. Stress floods the brain with cortisol; the brain in turn resets the threshold at which cortisol is produced, so that ultimately it circulates at a dramatically low level. The neuroendocrine system becomes highly sensitive to stress (De Bellis et al., 2010).

Developmental traumatology considers PTSD to be the key mediator linking childhood maltreatment and subsequent psychopathology in childhood, adolescence, and adulthood (see also Nader & Fletcher, Chapter 10, this volume). PTSD is regarded as a gateway illness and contributor to a wide range of problems of behavioral and affective dysregulation—often seen in other conditions, such as attention-deficit/hyperactivity disorder (ADHD), ODD, conduct disorder, depression, and substance use disorders (Mash & Wolfe, 2013). A study of consecutive admissions to a child psychiatry outpatient unit found that a history of physical or sexual abuse was related to ODD and ADHD. The group with combined ODD and ADHD (n = 40) had the highest prevalence rate of maltreatment: 73% were physically maltreated, and up to 31% were sexually maltreated. When symptoms that overlap among the disorders were taken into account, ODD (but not ADHD) continued to be related to PTSD (Ford et al., 2000). These authors advance the idea that maltreatment and subsequent PTSD may exacerbate ODD. More work is needed to assess whether PTSD is indeed a mediating or moderating factor in the link between child maltreatment and diagnosed psychiatric disorders.

De Bellis (2001) outlines seven postulations that underlie a developmental traumatology approach and that guide research in this area:

1. There are limited ways in which the brain and biological stress systems can respond to overwhelming stressors.
2. In maltreatment, the nature of the stressor is a dysfunctional and traumatized interpersonal relationship. As such, subtle interpersonal cues (e.g., indices of interpersonal trust) may trigger the trauma response.
3. Maltreatment in childhood may be more detrimental than adulthood trauma, given its potential to compromise development across multiple systems (e.g., behavioral, cognitive, emotional).
4. The biological stress system response will be based on individual differences (e.g., genetics); on the parameters of the stressor (e.g., severity, frequency); and on whether the system can maintain homeostasis in the context of severe and/or chronic stress, or whether it permanently changes in response to the stressor.
5. PTSD symptoms are normative responses to severe stressors.
6. Changes in biological stress systems cause psychiatric symptoms, particularly symptoms of PTSD. Lack of PTSD symptoms after experiencing a severe stressor will be associated with little psychopathology.
7. When trauma occurs during development, chronic PTSD symptoms represent a trajectory to more severe comorbidity and impaired cognitive and psychosocial functioning. The PTSD-mediated pathway underlies the intergenerational transmission of maltreatment via the presence of adverse brain development, consequent parental mental illness, and adverse parenting processes.

Thus the chronic mobilization of the stress response in maltreating environments is considered a key cause of persistent negative neurological effects. Maltreated children who do not develop psychopathology following trauma exposure may not have undergone such neurobiological changes. This may be consequent to an array of factors, including positive and "corrective" environmental experiences (such as attachment security or the child's perception and derived meaning of the maltreatment) that mitigate the stress response (e.g., by lowering the reactivity of the LHPA axis to stress) (Bremner & Vermetten, 2001). For example, a study of maltreated youth in the community and in the child welfare system found that teens who failed to endorse their maltreatment experiences as "abuse" obtained lower levels of self-reported trauma symptoms than did those who classified themselves as having been "abused" (Wekerle et al., 2001).

Whereas lower rates of PTSD are observed in children who experience single and/or noninterpersonal traumatic events, high rates of symptomatology are associated with chronic and/ or severe maltreatment (Pratchett & Yehuda, 2011). Retrospective and prospective research finds increased rates of PTSD symptoms in those with a history of childhood maltreatment (Boney-McCoy & Finkelhor, 1996; Widom, 1999), including physical abuse (Silverman et al., 1996; Widom, 1999), sexual abuse (Widom, 1999; Wolfe et al., 1994), and neglect (Widom, 1999). PTSD incidence rates in nonclinical samples as assessed within 2 months following disclosure have been 36% among sexually abused (McLeer, Deblinger, Atkins, Foa, & Ralphe, 1998) and 39% among physically abused (Famularo, Fenton, & Kinscherff, 1994), with a third of those positive for PTSD continuing to meet criteria at a 2-year follow-up (Famularo, Fenton, Augustyn, & Zuckerman, 1996). In general, estimates suggest that between 25 and 50% of children and adolescents with histories of maltreatment involving sexual abuse or combined sexual and physical abuse meet criteria for PTSD (McCloskey & Walker, 2000; Wolfe et al., 1994). At the 20-year mark in a prospective longitudinal study, maltreatment experiences continued to predict lifetime PTSD even after controls for family, individual child, and lifestyle confounds, with sexual abuse remaining highly significant (Koenen & Widom, 2009).

Although the diagnosis of PTSD appears to apply to a substantial minority of maltreated children, further research is needed to assess the ways in which maltreatment affects neurobiological development differently than other forms of trauma (Mehta et al., 2013). A dimensional study of PTSD may suggest contributory roles for individual clusters of symptoms (reexperiencing/intrusion, avoidance, and hyperarousal) in multisystem developmental delays or deficits (De Bellis, 2001). To emphasize, although the existing research has focused on PTSD, the proposed keystone mediator consists of PTSD *symptoms* in childhood, rather than a diagnosis of PTSD per se.

Future work needs to consider the mediational role of trauma symptoms in the prediction of subsequent outcomes. One study (Wekerle et al., 2001) found that the relationship between childhood maltreatment on the one hand, and violence both by and toward a dating partner on the other, was mediated by self-reported trauma symptoms in two samples of adolescent females: youth from a community sample, and youth on active CPS caseloads. For adolescent males, trauma symptoms added unique variance but did not achieve mediator status. These results support the value of considering PTSD symptoms as potential targets for reassessment when there is a history of child maltreatment, in an effort to reduce and prevent negative sequelae.

Understanding the psychobiology of maltreatment, in addition to the brain circuits and neuroendocrine systems that play a role in consequent psychopathology, remains a research priority for determining targets for treatment and early intervention. Brain maturation proceeds in an expectable sequential fashion. When expected experiences are absent (as in neglect), or when unexpected experiences occur (as in abuse), maturation may proceed in atypical ways that may result in compromised functioning. There remains a need to decipher developmentally sensitive periods as they pertain to age of onset of maltreatment, as well as differences between acute and chronic maltreatment. From a clinical perspective, chronic (multiple-event) and acute (single-event) maltreatment would seem to result in two distinct PTSD patterns, with greater memory for details and less denial, numbing, and dissociation when an acute traumatic event is experienced. Additional studies on the relationship between PTSD (as well as other psychiatric disorders) and child maltreatment are presented in the following sections.

ETIOLOGY

The consensus is that child maltreatment does not result from any single risk factor or etiological process that provides a necessary or sufficient basis for such behavior (National Research Council, 1993). Until recently, most models seeking to explain physical abuse and neglect, in particular, have focused their attention predominantly on the nature of the parent–child relationship and the factors that influence the normal formation of a healthy, child-focused relationship. Models of child sexual abuse, in contrast, have looked for evidence of deviant sexual histories of the adult offenders, as well as environmental and cultural risk factors that play a role in promoting the exploitation of children. Below are some of the major etiological factors that have been identified as part of this complex process.

Information-processing models have been applied to parenting, in recognition of the cognitive demands placed on the individual parent. These models focus on the internal processes in the parent, where child behavior *A* leads to parental behavior *B*. Typically, sequential stages of information processing are suggested, proceeding from parental attention to and perception of child behavior to the selection and implementation of a parental response. Four models focus on different abuse phenomena, with Crittenden's (1993) model centering on neglectful families, and Bugental's (1993), Milner's (e.g., 1993, 1998, 2000), and Dodge and colleagues' models emphasizing physically abusive families (e.g., Berlin, Appleyard, & Dodge, 2011; Dodge, Lochman, Laird, Zelli, & Conduct Problems Prevention Research Group, 2002).

Crittenden (1993) argues that neglectful parenting can occur as a function of a range of information-processing deficits: "Neglect occurs when there is a pattern in which mental processing is aborted before appropriate and necessary parental behavior is undertaken" (p. 32). Specifically, this pattern of deficits can include perceptual and interpretive "misses," in which a parent either does not perceive that a child is in need or, having accurately perceived a need, makes an inaccurate interpretation. This pattern can also include situations where a child's distress is misinterpreted (e,g., as seeking attention) or is unrealistically interpreted (e.g., in cases of overestimating the child's ability to care for him- or herself). Further deficits can occur at the response stage, where the neglectful parent "knows" a response is required but cannot develop a response strategy, or selects a response but fails to implement it. Thus the neglectful parent is considered to have a systematic bias toward not perceiving, not accurately interpreting, and/or not appropriately and effectively responding to the child's direct signals of need, as well as to contextual signals (e.g., time since last meal, mealtime).

Crittenden (1993) suggests a variety of parental factors that make these information-processing deficits more likely, such as parental depression, narcissism, intellectual disability, a low sense of self-efficacy, and inappropriate belief systems (e.g., a belief in early child independence). For example, a depressed neglectful parent may have a perceptual bias for automatically processing negative affective information that is linked

to depressive withdrawal and avoidance behavior. The depression will make more effortful cognitive processes, such as reflecting on the range of possible causes for child misbehavior (e.g., physical illness, lack of attention or understanding, need for assistance), less likely. This perceptual deficit is further linked to "higher-order" cognitive variables, such as a parent's internal models of relationships, developed from his or her own experiences of being parented. Thus a neglectful parent who has learned as a child that he or she is powerless in eliciting loving and caring responses from adults may come to detach from distress signals in his or her own child, in an effort to avoid being overwhelmed by distress yet maintain physical proximity.

Like Crittenden, Bugental and colleagues (e.g., Bugental, 1993; Bugental, Blue, & Lewis, 1990; Bugental & Goodnow, 1998; Bugental, Lewis, Lin, Lyon, & Kopeikin, 1999; Bugental, Lyon, Krantz, & Cortez, 1997; Bugental, Lyon, Lin, McGrath, & Bimbela, 1999) link information-processing deficits (in particular, a negative interpretive bias of personal powerlessness) to "higher-order" cognitive variables, such as stable, cognitive constructions about relationships. Physically abusive parents are proposed to interact with a "threat-oriented" relationship prototype, such that they are sensitive to and expect possible challenges to their authority. Given their own low perceived power, they are hypervigilant for dominance challenges. As a consequence, there is an elevated risk for invoking aversive response strategies to defuse the perceived or feared power of others. Given the enduring and well-practiced (overlearned) nature of these schematic guides, aversive response strategies are rapidly and automatically accessed. Bugental focuses on the power dynamics in abusive families, where parents attribute high levels of power to children, and children are placed in a reversed, parenting role. This role reversal leaves the children vulnerable to parental efforts to assume "counterpower" and make preemptive aggressive attacks, to counter perceived oncoming child hostile behavior. Women with low levels of perceived power attribute intentionality more often to ambiguous child behavior than to clearly responsive or unresponsive child behavior (Bugental, Lewis, et al., 1999). Thus abusive parents may see themselves as "victims" of aversive child behavior, which is perceived by the parents to be intentional and controllable by the children; therefore, they may minimize the severity of their actions as abusive. Parental aversiveness and abuse are seen as deriving from the parents' having a threat-oriented schema of interpersonal relationships, which may have originated from the parents' own early relationship experiences.

Several empirical studies support aspects of Bugental's proposed model. Compared to controls, abusive mothers were found to display higher levels of negative affect with their children, even during neutral or positive interactions (Bugental et al., 1990); moreover, the children of abusive parents showed speech patterns indicative of escalating levels of stress during interactions with their parents (Bugental & Lin, 1991, cited in Bugental, 1993). In an effort to control the stimulus of the child, Bugental and associates have observed adults "interacting" with a computer-simulated child on a computer-based teaching task. Women who were categorized as low in perceived control exhibited greater physiological arousal (heart rate, electrodermal activity) and negative affect to computer-simulated "unresponsive" child behavior, and minimal levels of arousal and negative affect to "responsive" child behavior, as compared to controls (Bugental, 1993). Thus women who perceive their power as low are more autonomically reactive to potential challenges to their authority.

Bugental, Lewis, and colleagues (1999) have clarified the importance of ambiguous control. Women with low perceived power, when placed in a situation of ambiguous (as compared to high or low) control, used higher levels of punitive force. This relationship was partially mediated by the elevated levels of autonomic arousal. The punitive response may temporarily reduce the perceived power threat. Children respond to low-power women with greater attentional disengagement, which is mediated by the ambiguous communication style of low-power women (Bugental, Lyon, et al., 1999). Experimentally induced adult ambiguity (in face and voice) was related to low levels of child attentional engagement, which may represent a means for children to regulate their distress. However, the reduced attention may impair the response formulation process. Furthermore, with experimentally manipulated stress (e.g., making judgments during engagement in a concurrent task), low-power women rated their children as in a position of greater power. This association did not hold in a non-stress-related context. These findings have been further supported by interventions to reduce a parental defensive interactional style that lacks clarity in intent and purpose—that is, to modify how the adult views interactions with his or her child as a "contest" to be won, and to help the adult learn more appropriate ways to cope with stress and ambiguous cues (Bugental et al., 2010).

In Dodge and colleagues' social information-processing model (e.g., Dodge, 1980; Dodge et al., 2002; Zelli & Dodge, 1999), emphasis is placed on patterns of encoding (e.g., hypervigilance to self-threats, deficits in attention to relevant cues) that take on features of an acquired personality characteristic—stable over time, with high internal consistency. Patterns link processing with affective and behavioral responses, such that rapid encoding of threat cues may lead to activation of attributions of hostile intent (e.g., the assumption that the child is misbehaving "on purpose"), angry reactions, instrumental goal setting (e.g., revenge or "win" goals), ready accessing of aggressive responses, and selecting and enacting an aggressive response (e.g., hitting the child). As applied to a parent, this would reflect knowledge garnered from his or her history of interaction with the child, as well as personal knowledge from his or her own historical interactions (e.g., a childhood history of being harshly parented). Compared to typical parents, abusive parents are expected to utilize "databases" or latent knowledge structures stored in memory that contain more negative knowledge about the child—negative, aggression-prone perceptual, interpretive, and response biases—possibly within a context of poor understanding of emotions (Dodge et al., 2002).

Milner (e.g., 1993, 1998, 2000) describes a social information-processing model of physically abusive parenting in which parental cognition and motivation are given central roles. Abusive parents are thought to be less attentive to child behavior in general. As such, they are considered to be "faulty discriminators." For example, the finding that abusive mothers are equally highly reactive to a crying and a smiling infant has been interpreted as suggesting that the abusive parent perceives *the child* as an aversive stimulus, failing to perceive accurately the distinct features of child behavior (Crouch, Skowronski, Milner, & Harris, 2008). Furthermore, Milner postulates that the personal "distress" of abusive mothers (resulting from both child-related and non-child-related events) decreases their perceptual abilities, such that greater inaccuracy in child-related perceptions results. In this model also, maternal depression in abusive mothers is cited as an important factor in accounting for a negative bias in abuse-relevant cognitive activities. For example, a lower threshold for perceived child misbehavior is suggested to be a function of depressive symptomatology.

The importance of parental perception of child behavior is indicated by Milner's proposing a direct path from perception to abusive parenting, via automatic processing. Automatic processing reflects rapid cognitive processing that is believed to occur outside of conscious awareness and to involve low demands on attention; because it is difficult to modify or suppress (especially under stress or threat), such processing generally proceeds to completion. Hence automatic processing is likely to be invoked under the low-attention condition presumed to be present in abusive parents. Milner notes that such rapid processing may account for the nature of abusive behavior: immediate, rapid, and explosive parental reactions, and a lack of consideration of mitigating details about the child. In accounting for abusive rather than aversive parental behavior, Milner places emphasis on the parent's estimation of "wrongness." That is, an abusive parent not only may perceive child problem behavior and attribute responsibility and negative intent to the child, but also may evaluate the behavior as "very wrong" and thus as deserving severe parental disciplinary actions.

Maltreating mothers in one study did report higher levels of perceiving child behavior as negative; they also inferred greater child responsibility, reported more anger and stress, and endorsed more punitive punishments. In regression analyses, the strongest proximal predictor of endorsed punishment was how angry a mother felt toward a misbehaving child. Support has thus been found for the pathway in which perceived negativity of child behavior predicts inferences of child responsibility, inferred child responsibility influences maternal anger, and maternal anger predicts maternal punishment (Graham, Weiner, Cobb, & Henderson, 2001). In considering parents scoring as having high potential for committing child abuse, Nayak and Milner (1998) found that, after controlling for IQ, such mothers showed neurocognitive deficits in the areas of conceptual ability, cognitive flexibility, and problem-solving skill. These differences dissipated when depression and anxiety were also controlled for, suggesting that physically abusive behavior is not directly related to parental cognitive functioning. Indeed, Caselles and Milner (2000) found that such high-risk mothers perceived children's conventional and personal transgressions as more wrong, expected less compliance from their own children, and appraised their disciplinary responses as less appropriate. Also, when presented with a noncompliant child, high-risk mothers rated the child's behavior as more stressful (Dopke & Milner, 2000). This theoretical model, though, remains to be tested among samples of substantiated maltreating parents.

OVERVIEW OF ADULT AND CHILD CHARACTERISTICS

Child Risk Characteristics

Although studies have sought to distinguish any characteristics a child might display that would place the child "at risk" of being the victim of neglect or physical or sexual abuse, the consensus is that certain child factors may increase the potential for maltreatment only in the presence of other important causal factors. Both longitudinal and comparative studies have failed to discern any child characteristics—such as age or gender, temperament, low birth weight, hyperactivity, or conduct problems—that clearly increase the risk of maltreatment, once environmental and adult factors are controlled for (National Research Council, 1993). Unintentionally, however, the child may still play a role in the continuation or escalation of abusive or neglectful relationships. For example, children with disabilities such as intellectual disability or physical impairments are more likely to be abused than are their nondisabled peers (Hershkowitz & Lamb, 2007; Sullivan & Knutson, 2000). Similarly, neglected children's early feeding problems or irritability may place an increased strain on the parents' limited child care abilities, again setting in motion an escalation in the children's dependency needs and demands, accompanied by further parental withdrawal (Drotar, 1999).

Factors that make it more difficult for a child to rebuff sexual abuse attempts in particular include an emotionally vulnerable child (e.g., an emotionally and/or physically deprived, compliant, or quiet child), the use of coercion and/or seduction by the perpetrator, the child's having witnessed parental conflict, the child's lack of education about sexual abuse, and the general social powerlessness of children. If subtler coercion methods (e.g., purchasing candy) are not successful, violence may be used. This can also be deceptive to a child, as in the offender's framing abuse as "discipline." Often the actual sexual behavior takes place only after a period of "grooming" or gradual indoctrination into sexual activity (Conte, 1992), suggesting that many sexually abusive adults are "sophisticated, calculating, and patient" (Singer, Hussey, & Strom, 1992, p. 884). In the case of neglect, a child's early feeding problems or irritability may place an increased strain on the parent's limited child care ability, which sets in motion a pattern of caregiver withdrawal from the child and a concomitant escalation in the child's dependency needs and demandingness (Drotar, 1992). Similarly, a physically abused child may learn from an early age how to elicit attention from his or her parent through aversive means (crying, hitting, clinging, etc.), which escalates in intensity due to the parent's further decline in appropriate child management and stimulation (for a review, see Wolfe, 1999).

Adult Characteristics

Abuse and Neglect in General

Studies of abusive parents have supported the development of the cognitive-behavioral models presented above. In a review of studies comparing abusive and nonabusive parents on psychological variables, Wolfe (1999) concluded that although abusive parents may not manifest any distinguishable personality or psychiatric disorders, they do exhibit behavioral differences and lifestyle patterns indicative of incompetence in the role of childrearing (see also Black, Heyman, & Smith Slep, 2001, and Milner, 1998, for reviews on physical abuse perpetration; see Flett & Hewitt, 2002, for a novel review on personality theory and empirical evidence). Abusive parents are not as effective or successful as nonabusive parents in the parenting role, in terms of either teaching their children new behavior or controlling child problem behavior. Abusive parents are less flexible in their choices of disciplinary techniques, and often fail to match their choice of discipline to a child's misdeed and the situation. Their overreliance on physical punishment as a control strategy, in combination with limited child management skills, is intensified by their failure to develop social supports to alleviate stress and to assist in family problem solving.

Empirical findings also suggest that both overcontrolled (e.g., obsessive) and undercontrolled (e.g., aggressive) parental responses may be present along with, or precipitants of, child- and family-mediated stress. Individual adult characteristics—such as low tolerance for stress, inappropriate or inadequate models or learning opportunities, and a poor repertoire of life skills—may be important psychological processes that are involved in determining the expression of these stressful life events. Furthermore, it is highly probable that abusive parents' perceptions of adverse family and environmental conditions are exacerbated by their failure to use social supports and to develop social networks.

In a 17-year longitudinal study of 644 families, Brown, Cohen, Johnson, and Salzinger (1998) reported

that three factors uniquely predicted physical abuse: low maternal involvement in childrearing, early separation of the child from the mother, and perinatal problems. Similarly, Bishop and Leadbeater (1999) found maternal depression, quality of social support from friends (low number of friends, contact with friends, and quality of friendship), and quality of current relationships (i.e., more negative) to be unique predictors of maltreatment status. These authors note that few maltreating mothers listed professionals as part of their formal social support system, despite higher-frequency and more varied service use. What remains unclear is how service use intersected with depression and relationship problems. It does, however, highlight the need to advocate for psychopharmacological and psychotherapeutic means of addressing maternal depression.

Neglectful parents have received far less attention than physically and sexually abusive ones, perhaps because omissions of proper caregiving behavior are more difficult to describe and detect (Dubowitz & Bennett, 2007). Hillson and Kuiper (1994), in their description of a stress-and-coping model of physical abuse and neglect, convincingly argued that neglectful caregivers engage in varying degress of behavioral disengagement (i.e., reducing their efforts to remove, avoid, or cope with a stressor). Neglectful parents may also engage in activities aimed at distracting themselves from the current stressor, in an effort to cope with the stress of childrearing and related family matters through escape and avoidance (Hildyard & Wolfe, 2007). These depictions of neglectful parenting, framed within a stress-and-coping model, are generally consistent with the existing empirical evidence. Schumacher, Smith Slep, and Heyman (2001) reviewed literature on the risk factors for neglect. Factors with moderate to strong effect sizes included fertility (e.g., more births, more unplanned conceptions), maternal self-esteem, impulsivity, lack of social support, daily stress, substance use disorder diagnosis, and poverty status.

In many other ways, however, the parental characteristics and lifestyle choices overlap (e.g., depression, substance abuse; Brent & Silverstein, 2013; Herrenkohl, Hong, Klika, Herrenkohl, & Russo, 2013). For instance, a positive association between substance abuse (past or current) and scores on a child abuse potential inventory for both mothers and fathers have been noted (Ammerman, Kolko, Kirisci, Blackson, & Dawes, 1999). In a prospective study, Chaffin, Kelleher, and Hollenberg (1996) found that parental substance abuse predicted parents' self-report of child physical abuse and neglect, even after controls for several confounds (including antisocial personality). Depression was a risk factor for physical abuse but not neglect, once confounds such as substance use disorder diagnoses were controlled for. These authors conclude that there is a direct effect for substance misuse, and also that substance misuse may be a mediator of the depression–neglect connection.

From this overview, we can highlight three key elements that stand out as common etiological features concerning the parent's role in child abuse or neglect: (1) the manner in which the parent interacts with the child on an everyday basis; (2) the frustration–aggression relationship that is learned by the parent in relation to childrearing, which accounts for the rapid and often uncontrollable escalation from annoyance to rage; and (3) the cognitive, social-informational processes that explain the distorted beliefs and attributions underlying a parent's actions (Wolfe, 1999). Social-interactional, social information-processing, and arousal–aggression processes are useful in explaining the constant changes in the behavior of family members in response to events within or outside of the family unit. Child maltreatment can best be explained as the result of an interaction between the parent and child within a system that seldom provides alternative solutions (e.g., through exposure to appropriate parental models, education, and supports) or clear-cut restraints (e.g., maltreatment laws, sanctions, and consequences). Importantly, a focus on the more distal events that may shape the childrearing environment (e.g., poverty, stress, etc.) and integration with neurobiological findings (discussed earlier) have not been accomplished to date.

Sexual Abuse

Research has shown pedophilic adults in general and incest offenders in particular to be heterogeneous groups, with an undercurrent being the association of violence and aggression with sexual abuse (Hartman & Burgess, 1989). Perpetrators of child sexual assaults are overwhelmingly male; data suggest that the majority of female offenders are usually in coercive relationships with male offenders (Friedrich, 1990). As a group, male offenders are more likely to have significant social and relationship deficits, including social isolation, difficulty forming emotionally close, trusting relationships, and low self-esteem (Marshall, Marshall, Serran, & O'Brien, 2009).

There is some evidence that sexual abuse victims are at increased risk of repeating such patterns in adult-

hood, although this is far from inevitable. The rate of self-reported history of sexual abuse among offenders is between 20 and 30%, with lower rates emerging when polygraph verification is used (Chaffin, Letourneau, & Silovsky, 2002). In a recent meta-analysis of 17 studies involving sexual offenders and nonoffenders, a higher prevalence of sexual abuse history was found among the child sexual offenders (over three times greater); no significant difference was found in physical abuse histories among these groups (Jespersen, Lalumière, & Seto, 2009). Although various mechanisms have been advanced (e.g., identification with the abuser, dissociative states, trauma reenactments), it would seem that a salient characteristic for offenders with a history of sexual abuse may be increased levels of deviant sexual arousal. A maltreatment history may portend an earlier onset of offending and selection of younger children, and diverse pathways can exist—for example, embedded in a broad range of social rule violations, low social competency, opportunity taking, or experimentation (for a review, see Chaffin et al., 2002). In a meta-analysis of 59 studies involving juvenile sexual offenders and nonsexual offenders, the largest group difference (based on effect sizes) was obtained for atypical sexual interests, followed by sexual abuse history, criminal history, antisocial associations, and substance abuse (Seto & Lalumière, 2010).

Critical features in classifying perpetrators identified from the literature include offense factors (such as degree of violence used, emphasis on coercion vs. seduction, relationship to the child, and age of the child), as well as offender factors (such as level of education, preoffense social and occupational adjustment, criminal history, personality traits, and substance misuse) (Hartman & Burgess, 1989). Personality features, on the other hand, are quite heterogeneous and overlap with neurocognitive impairments (Kruger & Schiffer, 2011). As well, there is emerging evidence of deficiencies in cerebral white matter in cortical regions of the brain that respond to sexual cues, suggesting that pedophilia may result from early neurodevelopmental problems that cause a partial disconnection within that network (Cantor et al., 2008; Cantor & Blanchard, 2012).

Finkelhor (1984) has identified the principal individual and situational conditions that foster child sexual abuse. Four offender preconditions are proposed as necessary before a sexual assault on a child can occur: (1) the motivation for sexual abuse (e.g., sexual arousal to children); (2) overcoming internal inhibitors (e.g., use of alcohol/drugs, impulsivity); (3) overcoming external inhibitors (e.g., lack of parental supervison of the child, opportunities to be alone with the child); and (4) overcoming the child's resistance (e.g., coercion through gifts, taking advantage of the child's curiosity). Finkelhor (1986) proposes that the first two conditions are necessary for abuse to occur; that is, the perpetrator must be inclined to abuse and uninhibited about it. This is consistent with the notion that the offender bears responsibility for the abuse. These perpetrator characteristics are considered to be fostered by societal practices, such as the erotic portrayal of children in mainstream advertising and in pornography, and the tolerance of male domination (Friedrich, 1990).

CURRENT ISSUES AND FUTURE DIRECTIONS

The developmental implications for children who have been abused or neglected have been emphasized throughout this chapter, in an effort to establish the significance and interconnectedness of these events vis-à-vis developmental psychopathology and the perpetuation of violence. These different forms of violence and maltreatment, although multiply determined, share common causes and outcomes; most importantly, the formation of healthy relationships is significantly impaired. This relational theme has emerged throughout the review and discussion of physical abuse, neglect, and sexual abuse, and one of the prominent issues in the field is establishing adequate services and supports for families and children that may serve to strengthen parent–child relationships and protect children from exploitation and harm. In closing, we discuss some ideas pertaining to this current direction of early identification and prevention.

How Can We Improve Our Definitions and Understanding of Different Forms of Maltreatment?

Defining child maltreatment in a manner that encompasses all of the social, methodological, and practical concerns poses a major challenge to research in this area. Typically, researchers have somewhat arbitrarily defined their groups of interest in a dichotomous manner, based on the most salient presenting characteristics of each child or family (e.g., evidence of physical abuse). However, this practice disguises other experiences these children may have had, resulting in a nonspecific categorization of maltreating families. More-

over, this common strategy treats each different type of maltreatment as a singular independent variable, when in reality such events often co-occur and are highly related. The categorical approach, therefore, fails to identify other relevant factors (such as other forms of maltreatment or family experiences) that can have a synergistic or unique impact on a child's development.

Researchers have also expressed dissatisfaction with current methodology in defining child maltreatment (Snarr, Heyman, Slep, & Malik, 2011). On the one hand, a categorization approach to defining forms of maltreatment can obscure differences in the severity of the different forms, and ignore the frequent co-occurrence of several forms in the lives of children (McGee & Wolfe, 1991). On the other hand, considerable light has been shed on the benefits and utility of applying a categorical, empirically validated approach to child maltreatment (Heyman & Smith Slep, 2009). Based on empirically derived definitions and criteria, the approach developed by Heyman and Smith Slep (2009) has shown strong reliability and validity in the field, and is often perceived as more "fair" and objective from a child welfare perspective in which parental rights are at stake. Because child welfare must have clear guidelines and definitions, a categorical approach based on scientific evidence remains highly supported in the field.

How Are We Currently Responding to Child Maltreatment?

The reduction or elimination of child maltreatment and related forms of family violence may be more readily achieved through a wide range of family support, education, and health promotion efforts (MacMillan et al., 2009; Wekerle & Wolfe, 1993). In contrast to the view that offenders can be identified and controlled, an inclusionary public health perspective strives to raise the level of understanding and skill among the broadest section of the population. Building healthy relationships is the central theme associated with violence prevention and enhanced family functioning. However, treatment needs will never be entirely supplanted by prevention, and continued investigation into efficacious treatment of maltreating parents will remain important.

Recently, our understanding of the causes and the developmental course of violence against women and children has grown significantly, allowing prevention efforts to be generated from a reasonable knowledge base. The developmental traumatology approach would argue for a national policy for general mental health screening (not just screening for PTSD) for all parents and children involved in CPS or law enforcement agencies, in cases where the perpetrator is not in a caregiving role (De Bellis, 2001). Given the cognitive and learning developmental risks to maltreated children, a developmental screening tool for children would be important to include. Medical examination and diagnoses need to be routine expectations for any child clinical presentation. This may be especially true for cases emerging in educational settings; for instance, school nurse examination should be available when abuse or neglect is suspected.

There is strong consensus that, in addition to detection and intervention, considerable benefit to children and families emerges from a public health model that aims at reducing the overall incidence of parenting disorders and emotional maltreatment (Eckenrode et al., 2010; MacMillan et al., 2009; Slep & Heyman, 2008). Such a strategy requires fewer resources per child and is typically more effective than those relying on detection and protection alone. A public health emphasis involves increasing protective factors, such as parental awareness of childrearing options, improved childrearing skills, community-based support during early years of parenting, school involvement, and many others (Wolfe & McIsaac, 2011). A public health model emphasizes healthy, positive parent–child relationships by informing the public what positive parenting involves and why healthy child development is important.

Few child-focused agencies, including protection agencies, routinely evaluate the history of maltreatment in adult caregivers, in addition to parental mental health. For example, children with a history of family disruption and violence have been shown to be at an elevated risk of either experiencing or perpetrating violence toward others, especially during middle to late adolescence and adulthood (Wolfe, Crooks, Chiodo, & Jaffe, 2009). Straus and Kantor (1994), using state records of offenses coupled with detailed histories of childrearing, contend that maltreatment experiences (including "milder" forms of corporal punishment) constitute the single most significant risk factor for subsequent relationship violence in adulthood. Thus it is believed that maltreatment experiences in one's family of origin create a vulnerability for further maltreatment by others (especially among young women), as well as a propensity to use power and control as a means of resolving conflict (especially among young men; Wolfe, Wekerle, Scott, Straatman, & Grasley, 2004). In more

severe cases of child maltreatment, children or youth can benefit from trauma-focused cognitive-behavioral therapy to reduce the impairments stemming from chronic fear and avoidance due to physical and psychological trauma (Cohen, Berliner, & Mannarino, 2010; Cohen, Mannarino, & Murray, 2011).

Whenever dating violence or IPV is a possibility or concern, maltreatment should be considered as well. For instance, whereas treatments for substance-abusing adults in couples consider partner violence, the adults' maltreatment histories and the presence of child maltreatment, either historically or currently, are not typically considered. In addition to prior maltreatment experiences, the risk of either experiencing or perpetrating violence increases as a result of negative influences from peers (i.e., condoning violence); the absence of compensatory factors (e.g., success at school, healthy relationships with siblings or friends); and the relative lack of alternative sources of information that serve to counteract existing biases, attitudes, and beliefs (Wolfe, Jaffe, & Crooks, 2006). Thus a thorough and comprehensive maltreatment evaluation is a necessity for all child and youth front-line health, education, mental health, justice, and CPS agencies.

Tertiary prevention or treatment studies to prevent recidivism with identified abusive parents have reported some degree of success at improving childrearing skills and knowledge of development, although limited follow-up data, evidence of recidivism, and high costs of delivery contribute to the inadequacy of this form of "prevention" (MacMillan et al., 2009). However, interventions with maltreating parents have not tended to operate within a multidisciplinary team perspective, and it may be prudent for CPS personnel to adopt a similar approach (e.g., ensuring psychiatric screening, including assessment of substance misuse and domestic violence, for all investigated parents). Selected or targeted prevention efforts, which range from interventions with high-risk to low-risk parents and expectant parents, favor assisting parents and children at an earlier point in time and have maintained gains over extensive follow-up periods. These wide-ranging strategies, and home-visiting approaches in particular, have demonstrated feasibility, cost-effectiveness, and effectiveness, and are beginning to be implemented at the statewide level (Appleyard, Berlin, Rosanbalm, & Dodge, 2011; Eckenrode et al., 2010; Kitzman et al., 2010; Moss et al., 2011; Prinz, Sanders, Shapiro, Whitaker, & Lutzker, 2009). With multiproblem families, home visiting provides direction to families in terms of service linkage, child physical health care and monitoring, enhanced parent–child interactions, and the prevention of physical abuse and neglect (Swenson, Schaeffer, Henggeler, Faldowski, & Mayhew, 2010; Thomas & Zimmer-Gembeck, 2011).

Universal prevention of child abuse has largely focused on educational strategies aimed at teaching school-age children and youth about safety issues (especially in relation to sexual abuse), or educating the public about norms, expectations, and laws related to childrearing. Evaluations of such programs are typically limited to demonstrations of knowledge gain, attitude change, behavioral intentions, and self-reported outcomes. However, behavioral gains supporting the preventative nature of such programs vis-à-vis childrearing ability have recently been reported in well-designed population-based studies (Prinz et al., 2009), showing promise for the wider-scale adoption of programs designed to assist families before maltreatment occurs. School-based sexual abuse prevention programs that focus on educating parents and children about personal safety have shown gains in children's awareness and abuse prevention skills, and have gained a major foothold in many jurisdictions in North America (Topping & Barron, 2009). The main concern for educational programs over the last two decades is that they place the weight of responsibility on the individual child to resist, deter, or avoid assault (Finkelhor, 2009). When the perpetrator of child sexual abuse is a determined adult, this is untenable as a dominant prevention strategy. If the child is not responsible for the abuse, the child should not be responsible for its prevention.

Child maltreatment prevention efforts have clearly advanced over the last decade, and have moved closer to the desired principle of building on individual, familial, and cultural strengths to reduce risk factors (rather than relying on detection and sanctioning), as well as promoting protective factors in an effort to deter maltreatment. This principle of risk reduction and strength promotion underscores the importance of the relational context to child maltreatment prevention. That is, learning to relate to others in a respectful, nonviolent manner is a crucial foundation for building a child maltreatment prevention strategy. Moreover, this principal can be applied at any point along the lifespan: pre- and postnatal parental assistance, parent–child treatment, youth dating violence prevention, adult supportive therapy, and many others opportunities for building healthy relationships (MacMillan et al., 2009). As we

have argued elsewhere (Wekerle & Wolfe, 1998), the most salient windows of opportunity for prevention and risk reduction may be adolescence and the formation of healthy intimacy and protection skills, and the first pregnancy in a young family. As society shifts toward a broader view of maltreatment beyond the individual parent or child, and as empirical evidence of risk and protective factors becomes established, we see the focus turning more toward reducing known risk factors for maltreatment (e.g., problems in child or adult emotion regulation, stress management, poor housing, harsh disciplinary techniques), through adoption of a family services and support orientation to address the needs of family members and enhance family dynamics. Efficient assessment, efficacious intervention, and effective prevention of child maltreatment are reasonable and achievable goals, and maltreating families and their children deserve nothing less.

NOTE

1. The LHPA axis is the pathway connecting the hypothalamus (a structure in the brain) to the adrenal and pituitary glands. The hypothalamus secretes corticotropin-releasing hormone (CRH), which then stimulates the pituitary gland to secrete adrenocorticotropic hormone (ACTH). ACTH is released into the blood, leading to the stimulation of the adrenal cortex to produce and release the steroid cortisol into the circulation. Specific brain centers receive cortisol and send messages via the LHPA axis to regulate the level of cortisol. Cortisol level is elevated in response to stress; cortisol actions include suppressing the immune response, increasing the level of circulating glucose, dampening fear responses to the stressor, and adversely affecting the hippocampus (Glaser, 2000).

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PART VII

EATING, PERSONALITY, AND HEALTH-RELATED DISORDERS

CHAPTER 17

Eating Disorders

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Eating disorders are severe disturbances in eating or eating-related behaviors that significantly diminish functioning or harm health. They typically begin in adolescence and disproportionately affect young females of European descent in Western countries—at least as eating disorders have been historically defined and studied. The specific types of eating disorders that are recognized have recently undergone expansion, and feeding disorders have been combined with eating disorders to form a single diagnostic category.

Symptoms of eating disorders, such as extreme food restriction and self-induced vomiting, have been described for centuries. However, only in recent decades have eating disorders seized the attention of clinicians, researchers, and the general public. Anorexia nervosa (AN) was first described by physicians in the 1870s, with other possible cases having been reported centuries earlier (e.g., Gull, 1874; Habermas, 1989; Lasègue, 1873). By contrast, the syndrome of bulimia nervosa (BN) is a more recent phenomenon. BN was not recognized until the 1930s (Habermas, 1989), but has become common in the decades since (Hudson, Hiripi, Pope, & Kessler, 2007). Beginning with the publication of the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) in 1980, the definition of eating disorders centered on AN and BN (American Psychiatric Association [APA], 1980, 1987, 1994, 2000) until the advent of DSM-5—when, as clinicians were faced with an excess of unspecified cases, new eating disorder diagnoses were added and existing diagnoses were revised substantially (APA, 2013a). Specifically, although diagnostic criteria for eating disorders had changed little between 1987 and 2013, in recent years evidence has accrued indicating that variations of eating disorder symptoms that were previously considered subthreshold, or that were often overlooked entirely, were actually more prevalent and problematic than initially realized (Fairburn & Bohn, 2005; Fairburn et al., 2007; Thomas, Vartanian, & Brownell, 2009). A critical problem was that when DSM-IV criteria were used, 40–60% of individuals seeking eating disorder treatment were receiving a residual diagnosis of eating disorder not otherwise specified (EDNOS) because they did not meet the specific criteria for AN or BN (Fairburn & Bohn, 2005; Fairburn et al., 2007; Ricca et al., 2001). The EDNOS category grouped together people with such a wide variety of eating disorder symptoms that it conveyed little information of predictive value about a patient, thus diminishing its clinical utility, as well as stifling research and treatment efforts (Fairburn & Cooper, 2011; Keel, Brown, Holland, & Bodell, 2012; Thomas, Vartanian, et al., 2009). One proposed solution was to create a single eating disorder diagnosis that emphasizes shared psy-

chopathology (Fairburn, Cooper, & Shafran, 2003). Other criticisms of DSM-IV eating disorder definitions were levied, such as that the criteria were excessively difficult to assess, did not adequately reflect symptoms of children and adolescents, and that certain criteria appeared to be unjustified (e.g., Birgegard, Norring, & Clinton, 2012).

Addressing many of these concerns and adopting a broader standard for defining an eating disorder, DSM-5 (APA, 2013a) includes the following eight categories of feeding and eating disorders:

AN
BN
Binge-eating disorder (BED)
Pica
Rumination disorder
Avoidant/restrictive food intake disorder (ARFID)
Other specified feeding or eating disorder (OSFED)
Unspecified feeding or eating disorder

We describe each of these disorders in detail below, as well as key terms. Note that these DSM-5 categories are largely consistent with those proposed for the forthcoming *International Classification of Diseases and Related Problems*, 11th revision (ICD-11), an update of the World Health Organization's classification system (Al-Adawi et al., 2013).

DEFINITIONAL AND DIAGNOSTIC ISSUES

Feeding Disorder versus Eating Disorder

The term "feeding disorder" applies to infants and small children who do not feed themselves, whereas "eating disorder" applies to those who feed themselves.

Binge Eating

A prominent symptom found in multiple eating disorders is binge eating. It is a hallmark symptom of BN and BED that can also occur in AN as well as OSFED. DSM-5's definition of binge eating for BN and BED involves two elements: (1) eating an unusually large amount of food in a limited period of time (i.e., within 2 hours); and (2) experiencing a subjective loss of control over eating (i.e., over what or how much food is eaten, or the perceived inability to stop eating). Determining whether the amount of food eaten is unusually large requires that one consider the context—that is, eating a "definitely" greater amount of food than most people would eat in a similar period of time under similar circumstances. For example, overeating at a holiday meal would not be considered to constitute a binge-eating episode. However, determining whether a given eating episode is "definitely" large necessarily involves subjectivity. No calorie requirement exists, but studies have indicated that average binge episodes for individuals with BN ranged in size from 1,100 to 4,500 calories, depending on the method of assessment (self-reported food diaries vs. laboratory studies; Wolfe, Baker, Smith, & Kelly-Weeder, 2009). Binge episodes among individuals with AN have received little systematic study (Wolfe et al., 2009), but are defined the same way as binge episodes found in other eating disorders.

Although evidence supports the validity of both the loss-of-control and 2-hour-duration attributes of a binge episode, the importance of size in defining a binge remains controversial (Wolfe et al., 2009). Factors other than the amount of food eaten appear to affect individuals' definitions of an eating episode as a binge, especially loss of control. An individual with an eating disorder, for example, might describe a binge episode as including a small amount of food (perhaps more than the person usually eats), or a larger quantity of food that has minimal calories (such as a head of lettuce), or as the size of a meal—all eaten while experiencing a loss of control. Whereas a binge episode involving an objectively large amount of food is termed an "objective binge episode," an eating episode that is identified as a binge due to the experience of loss of control, yet does not involve consumption of objectively large amounts of food, is termed a "subjective binge episode" (Fairburn, 2008). It has been observed that the size of binge episodes (i.e., the experience of objective vs. subjective binge episodes) did not distinguish treatment-seeking and community adults who otherwise met criteria for BN (Mond, Latner, Hay, Owen, & Rodgers, 2010; Watson, Fursland, Bulik, & Nathan, 2013). Evidence suggests that subjective binge episodes are linked to clinical impairment and eating disorder psychopathology (e.g., Fairburn et al., 2007; Latner, Hildebrandt, Rosewall, Chisholm, & Hayashi, 2007), thus casting into doubt the importance of size in defining a binge episode in adults. Similarly, loss of control over eating has been suggested to be more important in identifying children with eating disorder symptoms than the amount of food eaten (APA, 2013b;

Tanofsky-Kraff et al., 2007), in part because children and adolescents do not have the same control over their access to food as adults do (Hoste, Labuschagne, & Le Grange, 2012). Research criteria for loss-of-control eating in children have been developed (Tanofsky-Kraff, Marcus, Yanovski, & Yanovski, 2008). The provisional criteria specify that eating episodes must involve not only a sense of lack of control over eating, but food seeking in the absence of hunger or after satiation. To be perceived as a problem of clinical severity, the episodes must occur, on average, at least twice a month for 3 months, and must be associated with three or more of the following characteristics: eating in response to negative affect; secrecy regarding the episode; feelings of numbness (lack of awareness) while eating; eating more, or the perception of eating more, than others; and/or negative affect following eating.

Overvaluation of Weight and Shape

AN and BN share the core psychopathological feature of overvaluation of weight and shape. In other words, individuals with AN or BN judge themselves largely or entirely on the basis of their body shape and weight, rather than the gamut of other life domains that those without these disorders value, such as relationships, school, or work (Fairburn & Harrison, 2003). Overvaluation of weight and shape motivates the behaviors that characterize these disorders, and this shared psychopathology helps to explain the frequent diagnostic crossover that occurs among AN, BN, and their variants over time, particularly from restrictive symptoms to those involving binge eating (Eddy, Dorer, et al., 2008).

DMS-5 DIAGNOSES

Anorexia Nervosa

As defined in DSM-5 (APA, 2013a), AN is characterized by extreme food restriction, fear of gaining weight, and weight or body image disturbance (see Table 17.1). A number of changes have been made in the DSM-5 criteria for eating disorders, in large part to diminish the number of EDNOS cases (APA, 2013b). As a result, the definition of AN has been broadened substantively in four ways.

First, the wording of the criterion describing weight now focuses on behaviors, such as restricting calorie intake, that yield a "significantly low body weight." Previous wording of this criterion implied that those with AN were intentionally losing weight ("refusal to maintain body weight at or above a minimally normal weight for age and height")—an unnecessary assumption that was not necessarily true in every case (APA, 1994, p. 544).

Second, the criteria no longer reference a particular weight cutoff, although current severity descriptors specify particular body mass index ranges. In previous editions of the DSM, specific percentages (75–85%) of expected body weight were specified for operationalizing the low weight criterion, but evidence has not supported the validity of these cutoffs (Eddy, Doyle, Hoste, Herzog, & le Grange, 2008; Fairburn & Cooper, 2011). In addition, evidence suggests that weight cutoffs are somewhat arbitrary, in that they are calculated according to inconsistent standards, based on various life insurance company weight charts as well as body mass index (Thomas, Roberto, & Brownell, 2009). A diagnosis of AN demands a categorical decision about a variable (weight) that varies quantitatively, which is inherently challenging.

Third, the diagnostic criteria for AN no longer include amenorrhea, defined as the absence of three consecutive menstrual cycles. This criterion applied only to a subset of people—specifically, postmenarcheal and premenopausal women who were not taking hormones such as birth control pills. Although amenorrhea is an indicator of clinical severity in AN, its diagnostic utility has not been borne out in research. Studies generally have shown no consistent psychological or biological differences between AN patients with and without amenorrhea (Attia & Roberto, 2009; Fairburn & Cooper, 2011). Rather, most differences between patients with AN who do and do not have amenorrhea are attributable to nutritional status, as measured by current and lowest lifetime body mass index and exercise patterns. Exclusion of the amenorrhea criterion may facilitate the receipt of needed treatment by women who continue to have some menstrual activity, despite meeting the other criteria for AN (Attia & Roberto, 2009). A study comparing rates of AN diagnoses with DSM-IV versus DSM-5 criteria found that DSM-5 criteria captured a slightly greater percentage of eating disorder patients than did DSM-IV criteria (22% vs. 19% of eating disorder patients), with the AN diagnosis slightly more common among patients over age 14 when DSM-5 criteria were used (Birgegard et al., 2012). Thus this study demonstrated that the changes to DSM-5 criteria

TABLE 17.1. DSM-5 Diagnostic Criteria for Anorexia Nervosa

A. Restriction of energy intake relative to requirements, leading to a significantly low body weight in the context of age, sex, developmental trajectory, and physical health. *Significantly low weight* is defined as a weight that is less than minimally normal or, for children and adolescents, less than that minimally expected.

B. Intense fear of gaining weight or of becoming fat, or persistent behavior that interferes with weight gain, even though at a significantly low weight.

C. Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight.

Coding note: The ICD-9-CM code for anorexia nervosa is **307.1, which is assigned regardless of the subtype. The ICD-10-CM code depends on the subtype (see below).**

Specify whether:

(F50.01) Restricting type: During the last 3 months, the individual has not engaged in recurrent episodes of binge eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas). This subtype describes presentations in which weight loss is accomplished primarily through dieting, fasting, and/or excessive exercise.

(F50.02) Binge-eating/purging type: During the last 3 months, the individual has engaged in recurrent episodes of binge eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas).

Specify if:

In partial remission: After full criteria for anorexia nervosa were previously met, Criterion A (low body weight) has not been met for a sustained period, but either Criterion B (intense fear of gaining weight or becoming fat or behavior that interferes with weight gain) or Criterion C (disturbances in self-perception of weight and shape) is still met.

In full remission: After full criteria for anorexia nervosa were previously met, none of the criteria have been met for a sustained period of time.

Specify current severity:

The minimum level of severity is based, for adults, on current body mass index (BMI) (see below) or, for children and adolescents, on BMI percentile. The ranges below are derived from World Health Organization categories for thinness in adults; for children and adolescents, corresponding BMI percentiles should be used. The level of severity may be increased to reflect clinical symptoms, the degree of functional disability, and the need for supervision.

Mild: BMI ≥ 17 kg/m^2

Moderate: BMI 16–16.99 kg/m^2

Severe: BMI 15–15.99 kg/m^2

Extreme: BMI < 15 kg/m^2

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affected rates of AN among postmenarcheal women, but not youth under 14 years, who are less likely than adults to be eligible for the amenorrhea criterion.

Fourth, to be eligible for a diagnosis of AN, one need not state explicitly a fear of gaining weight or behaviors interfering with weight gain; rather, this fear can be inferred from other information, including behavior patterns or collateral reports. The symptoms of some individuals with extreme dietary restraint may fit an ARFID diagnosis better than AN if there is no evidence that their pattern of food restriction is motivated by fear of becoming fat or gaining weight (Bryant-Waugh, 2013). Cultural differences in the reasons given for food restriction in AN have been reported (e.g., Ngai, Lee, & Lee, 2000), including denial of a fear of gaining weight, which is termed "non-fat-phobic AN." A recent review concluded that non-fat-phobic AN occurs in both non-Western and Western cultures, and that although some evidence suggests those with non-fat-phobic AN report less psychopathology than those with AN (including fat phobia), thus far insufficient evidence exists to support the conclusion that non-fat-phobic AN is a distinct variant of AN (Becker, Thomas, & Pike, 2009). Interestingly, in ICD-11, to accommodate cultural variations in symptoms, fat phobia will *not* be required to be provided as the rationale for low weight status in AN (Al-Adawi et al., 2013). Denial of a fear of gaining weight is common among children, due to their lower level of cognitive maturation (Knoll, Bulik, & Hebebrand, 2011).

Consistent with DSM-IV, two subtypes of AN are defined in DSM-5, based on the presence or absence of recurrent binge-eating and/or purging behavior: restricting type and binge-eating/purging type. In the restricting type, weight loss occurs through some combination of dieting, fasting, and excessive exercise, but excludes those with recurrent binge eating or purging. In contrast, the binge-eating/purging type includes recurrent episodes of binge eating, purging, or both. Some individuals purge recurrently after eating small amounts of food. Purging (also called "purge behaviors") consists of self-induced vomiting or misuse of laxatives, diuretics, enemas, or other substances, with the aim of compensating for food eaten. Other, less common purging methods are use of thyroid hormone or, among those with Type I diabetes, reducing or omitting insulin doses to diminish the metabolism of foods eaten during a binge episode. AN subtypes can and do vary over time. Diagnostic crossover between AN subtypes and from AN to BN has been found to be common in treatment-seeking samples over 6–7 years' follow-up (Castellini et al., 2011; Eddy, Dorer, et al., 2008).

Bulimia Nervosa

BN has three essential features: recurrent binge eating, recurrent inappropriate compensatory behaviors, and overvaluation of body weight and shape (see Table 17.2; APA, 2013a). Compensatory behaviors, which typically follow binge-eating episodes, are intended to avoid weight gain. The minimum frequency of binge eating and compensatory behaviors has been reduced to once per week for 3 months in DSM-5, from twice a week in DSM-IV, as evidence suggests that those who meet the lower threshold have clinical characteristics and outcome similar to those of patients who meet the higher threshold (Wilson & Sysko, 2009). The most frequently used compensatory behavior in BN is self-induced vomiting; to a lesser degree, laxatives and diuretics are also misused (Mitchell, Hatsukami, Eckert, & Pyle, 1985). A distinction is made between purging and compensatory behaviors; that is, in addition to purging, the broader category of compensatory behaviors also includes fasting (e.g., for 24 hours or more) and excessive exercise that is associated with function-

TABLE 17.2. DSM-5 Diagnostic Criteria for Bulimia Nervosa

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:
   1. Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than what most individuals would eat in a similar period of time under similar circumstances.
   2. A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating).

B. Recurrent inappropriate compensatory behaviors in order to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, or other medications; fasting; or excessive exercise.

C. The binge eating and inappropriate compensatory behaviors both occur, on average, at least once a week for 3 months.

D. Self-evaluation is unduly influenced by body shape and weight.

E. The disturbance does not occur exclusively during episodes of anorexia nervosa.

Specify if:

In partial remission: After full criteria for bulimia nervosa were previously met, some, but not all, of the criteria have been met for a sustained period of time.

In full remission: After full criteria for bulimia nervosa were previously met, none of the criteria have been met for a sustained period of time.

Specify current severity:

The minimum level of severity is based on the frequency of inappropriate compensatory behaviors (see below). The level of severity may be increased to reflect other symptoms and the degree of functional disability.

Mild: An average of 1–3 episodes of inappropriate compensatory behaviors per week.

Moderate: An average of 4–7 episodes of inappropriate compensatory behaviors per week.

Severe: An average of 8–13 episodes of inappropriate compensatory behaviors per week.

Extreme: An average of 14 or more episodes of inappropriate compensatory behaviors per week.

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al impairment, such as exercising despite injury or illness, or that interferes with important activities (APA, 2013a). No subtypes of BN are specified in DSM-5, although previously BN had been divided into purging and nonpurging types. Severity of the current episode is measured according to the frequency of compensatory behaviors.

Binge-Eating Disorder

The essential feature of BED is recurrent binge eating at least once per week over 3 months, in the absence of regular compensatory behaviors (APA, 2013a; see Table 17.3). In addition, marked distress must accompany binge eating, and three of five features describing the binge episodes must be endorsed. Severity of BED is measured in terms of frequency of binge eating episodes per week.

After BED was introduced as a provisional diagnosis in DSM-IV, research on the topic flourished. In comprehensive reviews of research related to the validity of BED, experts concluded that BED is a clinically significant disorder associated with substantial impairment, and that it is distinct from other existing eating disorders (Striegel-Moore & Franko, 2008; Wonderlich, Gordon, Mitchell, Crosby, & Engel, 2009). In spite of concerns raised by a prominent critic that BED merely constituted "gluttony" (Frances, 2012, 2013), ultimately BED was included in DSM-5. It includes minor modifications paralleling those made in BN—namely, a reduction in frequency and duration of binge episodes from twice a week for 6 months to once a week for 3 months (APA, 2013a).

TABLE 17.3. DSM-5 Diagnostic Criteria for Binge-Eating Disorder

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:
   1. Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than what most people would eat in a similar period of time under similar circumstances.
   2. A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating).

B. The binge-eating episodes are associated with three (or more) of the following:
   1. Eating much more rapidly than normal.
   2. Eating until feeling uncomfortably full.
   3. Eating large amounts of food when not feeling physically hungry.
   4. Eating alone because of feeling embarrassed by how much one is eating.
   5. Feeling disgusted with oneself, depressed, or very guilty afterward.

C. Marked distress regarding binge eating is present.

D. The binge eating occurs, on average, at least once a week for 3 months.

E. The binge eating is not associated with the recurrent use of inappropriate compensatory behavior as in bulimia nervosa and does not occur exclusively during the course of bulimia nervosa or anorexia nervosa.

Specify if:

In partial remission: After full criteria for binge-eating disorder were previously met, binge eating occurs at an average frequency of less than one episode per week for a sustained period of time.

In full remission: After full criteria for binge-eating disorder were previously met, none of the criteria have been met for a sustained period of time.

Specify current severity:

The minimum level of severity is based on the frequency of episodes of binge eating (see below). The level of severity may be increased to reflect other symptoms and the degree of functional disability.

Mild: 1–3 binge-eating episodes per week.

Moderate: 4–7 binge-eating episodes per week.

Severe: 8–13 binge-eating episodes per week.

Extreme: 14 or more binge-eating episodes per week.

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Pica and Rumination Disorder

Pica involves the recurrent, developmentally inappropriate eating of non-nutritive, nonfood substances by individuals more than 2 years old. Rumination disorder is defined as the repeated regurgitation of recently ingested food, which may then be rechewed, reswallowed, or spat out. Rumination appears to be soothing or pleasurable (Nicholls & Bryant-Waugh, 2009). By definition, symptoms of both pica and rumination disorder must last at least 1 month. These disorders may vary in presentation, in part according to an individual's developmental level. Unlike AN and BN, pica and rumination disorder are not motivated by weight control or avoidance of weight gain. Pica and rumination disorder explicitly exclude cases in which symptoms can be attributed to another source, such as a medical disorder, or another psychiatric or eating disorder.

Avoidant/Restrictive Food Intake Disorder

Other feeding and eating disorders of infancy or young childhood have been subsumed into the diagnosis of ARFID in DSM-5 (APA, 2013a). The essential feature of ARFID is a persistent, clinically significant disturbance in eating, resulting in inadequate nutrition or energy consumption (see Lyons-Ruth, Zeanah, Benoit, Madigan, & Mills-Koonce, Chapter 15, Table 15.3, this volume). In other words, ARFID describes restrictive eating patterns that cause clinically significant impairment. ARFID differs from AN in that restrictive eating stems from sources other than weight concerns, shape concerns, or disturbance in the way one's body shape is experienced (Kreipe & Palomaki, 2012). Cultural practices or lack of access to food must not fully explain the restriction or avoidance of food intake seen in ARFID. Weight loss is not required for the diagnosis.

Three major subtypes of ARFID have been identified: (1) limited food intake associated with generalized emotional disturbance; (2) limited food intake associated with sensory sensitivities, including avoidance of food with certain textures, colors, tastes, smells, or temperatures; and (3) inadequate intake or phobic avoidance due to a specific, identifiable fear, such as fear of vomiting after an episode of choking on food (Bryant-Waugh, Markham, Kreipe, & Walsh, 2010; Kenney & Walsh, 2013). Notably, the diagnosis is not limited to these three types (Bryant-Waugh, 2013). Other previously described terms for syndromes that, when severe enough to cause problems, may fall under the ARFID umbrella include picky eating, selective eating, food neophobia, sensory sensitivity, sensory food aversions, infantile anorexia, feeding disorder associated with insults to the gastrointestinal tract, faddy eating, and perseverative feeding disorder (Lucarelli, Cimino, D'Olimpio, & Ammaniti, 2013; Nicholls & Bryant-Waugh, 2009; Wildes, Zucker, & Marcus, 2012).

It is worth noting that those guiding the development of DSM-5 explicitly worked toward ensuring that psychiatric diagnoses incorporated a lifespan perspective (Pine et al., 2011). Experts have encouraged the use of broader, more inclusive criteria to enable more developmentally sensitive diagnosis of eating disorders in children and adolescents, who may not present with, or comprehend, symptoms in the same way as adults do (Bravender et al., 2010; Workgroup for Classification of Eating Disorders in Children and Adolescents, 2007). For example, identifying eating disorder symptoms relatively early in the course of an eating disorder occurs more often in children and youth than in adults, which may mean that symptoms have not met a minimum duration (e.g., for BN or BED) or level of severity (e.g., for weight loss in AN). In addition, it may be developmentally inappropriate to require a child to verbalize fear of weight gain to be eligible for a diagnosis of AN. These arguments appear to have influenced DSM-5 criteria for eating disorders, in which numerous wording changes have been made from DSM-IV to broaden definitions and make them more suitable for children as well as adults, and to acknowledge that feeding and eating disorders can occur across the lifespan.

Other Specified Feeding or Eating Disorder

Another new diagnostic category in DSM-5 is OSFED, which comprises feeding or eating disorder symptoms that do not meet criteria for another feeding or eating disorder, accompanied by clinically significant distress or impairment in functioning (see Table 17.4). With OSFED, the clinician describes the specific reason that a person does not meet criteria for a specific feeding or eating disorder. Five types of OSFED are specified as examples, all of which are relatively common forms of the former EDNOS category; however, other presentations are possible as well. In addition to facilitating communication about details of an individual's symptoms for treatment purposes, the introduction of this category has the potential to facilitate systematic research into the validity of subtypes as potential eat-

TABLE 17.4. DSM-5 Diagnostic Criteria for Other Specified Feeding or Eating Disorder

This category applies to presentations in which symptoms characteristic of a feeding and eating disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not meet the full criteria for any of the disorders in the feeding and eating disorders diagnostic class. The other specified feeding or eating disorder category is used in situations in which the clinician chooses to communicate the specific reason that the presentation does not meet the criteria for any specific feeding and eating disorder. This is done by recording "other specified feeding or eating disorder" followed by the specific reason (e.g., "bulimia nervosa of low frequency").

Examples of presentations that can be specified using the "other specified" designation include the following:

1. **Atypical anorexia nervosa:** All of the criteria for anorexia nervosa are met, except that despite significant weight loss, the individual's weight is within or above the normal range.
2. **Bulimia nervosa (of low frequency and/or limited duration):** All of the criteria for bulimia nervosa are met, except that the binge eating and inappropriate compensatory behaviors occur, on average, less than once a week and/or for less than 3 months.
3. **Binge-eating disorder (of low frequency and/or limited duration):** All of the criteria for binge-eating disorder are met, except that the binge eating occurs, on average, less than once a week and/or for less than 3 months.
4. **Purging disorder:** Recurrent purging behavior to influence weight or shape (e.g., self-induced vomiting; misuse of laxatives, diuretics, or other medications) in the absence of binge eating.
5. **Night eating syndrome:** Recurrent episodes of night eating, as manifested by eating after awakening from sleep or by excessive food consumption after the evening meal. There is awareness and recall of the eating. The night eating is not better explained by external influences such as changes in the individual's sleep-wake cycle or by local social norms. The night eating causes significant distress and/or impairment in functioning. The disordered pattern of eating is not better explained by binge-eating disorder or another mental disorder, including substance use, and is not attributable to another medical disorder or to an effect of medication.

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ing disorder diagnoses, and the boundaries between syndromes. One example of an OSFED syndrome is purging disorder, an eating disorder variant that consists of a pattern of purging behaviors in the absence of objective binge eating. An alternate configuration of bulimic-variant symptoms is subjective binge eating with compensatory behaviors, which is more restrictive than purging disorder in requiring the presence of recurrent subjective binge episodes, but less restrictive in allowing compensatory behaviors such as excessive exercise or fasting in addition to purging (Watson et al., 2013).

Unspecified Feeding or Eating Concerns

The final DSM-5 feeding and eating disorders category is unspecified feeding or eating disorder. This diagnosis describes individuals with feeding or eating disorder symptoms that cause significant distress or impairment in functioning, but it does not require the diagnostician to specify details of why the individual does not meet criteria for a specific feeding or eating disorder. As noted in DSM-5, this category may be useful in situations in which little or incomplete information is available, such as emergency room settings.

CLINICAL CHARACTERISTICS

Anorexia Nervosa

The term "anorexia" (i.e., lack of appetite) is a misnomer, as those with AN usually do experience hunger (Lask & Frampton, 2009). Several characteristics of AN merit description. First, behavioral symptoms of food restriction (and compensatory behaviors, when present) in AN are fueled by individuals' intense concerns over weight and shape, sometimes described as fear of fatness or overvalued ideas about weight and shape. In severe cases, weight and shape concerns can become all-consuming, and one's life can narrow to eating disorder symptoms, including constant thoughts of weight, shape, and what one will and won't eat. These obsessional preoccupations only worsen with continued starvation and weight loss (Keys, Brozek, Henschel, Mickelsen, & Taylor, 1950). Second, body image disturbance in one with AN often involves the misperception that her or his body (or a part of it) is too big, despite being underweight. Alternatively, even if a person with AN recognizes that she or he is underweight, the person may persistently fail to recognize or may minimize the medical seriousness of the low

weight. Third, individuals with AN often view their low weight as a source of pride rather than a problem, which limits their willingness to change (Vitousek, Watson, & Wilson, 1998).

A classic study conducted in the 1940s, the Minnesota Semi-Starvation Experiment, has formed the basis of our understanding of psychological and behavioral symptoms associated with starvation (Keys et al., 1950). This study showed that many psychological symptoms commonly seen in AN actually result from starvation, buttressing the conclusion that many symptoms associated with AN resolve with refeeding to a higher weight. In this experiment, following a 3-month observation period, the calorie intake of 36 healthy young male volunteers was restricted for 6 months to approximately half of their previous intake. Participants lost approximately 25% of their body weight. The final 3 months of the study involved rehabilitation and gradual refeeding. During and after the starvation phase, participants became extremely preoccupied with food and hoarded both food-related and non-food-related items, and some began binge eating. They also experienced depression, anxiety, social withdrawal, impaired concentration, and lack of interest in sex. These symptoms tended to persist even during the refeeding phase of the experiment. Strikingly similar symptoms are observed in people with AN.

Medical complications of AN, which may arise from starvation as well as purging behaviors, are common and often serious (Mitchell & Crow, 2006). They involve every organ system, and include bradycardia (slowed heart rate), arrhythmias (irregular heartbeat), delayed gastric emptying, bone demineralization, lanugo (fine, dark hair on the back, abdomen, and forearms), gastric dilation, anemia, and severe electrolyte abnormalities. A recent meta-analysis concluded that AN has an annual mortality rate of 5 per 1,000 person-years, with 20% of deaths resulting from suicide (Arcelus, Mitchell, Wales, & Nielsen, 2011). This mortality rate is much higher than for other forms of psychopathology; for example, it is approximately double the mortality rate for schizophrenia.

Bulimia Nervosa

Individuals with BN tend to feel shame over their behaviors and keep them secret from others (Burney & Irwin, 2000). Many individuals with BN feel a sense of failure because they do not weigh as little as they want to.

Under previous diagnostic schemes, many adolescents seeking treatment for an eating disorder were diagnosed with subthreshold eating disorders (i.e., EDNOS) rather than AN or BN (Eddy, Doyle, et al., 2008). Experts have recommended the use of behavioral indicators in lieu of direct self-report—particularly for more complex cognitive features, such as the BN criterion requiring undue influence of body shape and weight on self-evaluation (Bravender et al., 2010)—because some children and adolescents may lack the complex abstract reasoning skills to rank and communicate internal experiences related to self-evaluation (Bravender et al., 2010). However, this criterion was not altered in DSM-5.

Medical complications of BN arise primarily from purging behaviors (Mitchell & Crow, 2006). Examples are Russell's sign (a scar or callus over the dorsal surface of the hand from repeatedly inducing vomiting), poorer outcomes among those with Type I diabetes, and many of the medical complications already mentioned that also affect those with AN (e.g., arrhythmias, electrolyte abnormalities, and gastric dilation). According to findings from a recent meta-analysis, BN has an annual weighted mortality rate of 1.7 per 1000 person-years, with a slightly higher rate (2.2) among female-only samples (Arcelus et al., 2011). This mortality rate meets or exceeds that of some other forms of psychopathology, such as unipolar and bipolar depression, highlighting the seriousness of this disorder.

Binge-Eating Disorder

Unlike a diagnosis of BN, a diagnosis of BED does not require the symptom of overconcern with shape and weight. Rates of both eating disorder psychopathology and comorbid psychopathology are high among individuals with BED (Spitzer et al., 1993; Wilfley, Wilson, & Agras, 2003). In contrast to individuals with BN, who tend to be normal-weight to overweight, individuals with BED are often overweight or obese, particularly in treatment-seeking samples (Carrard, der Linden, & Golay, 2012). The converse is not true, however: Most people with obesity do not binge-eat (Perez & Warren, 2012). The relationship of BED to obesity requires further investigation, particularly to examine the hypothesis that BED is simply a nonspecific marker for psychopathology among obese individuals (Wonderlich et al., 2009). Reported mortality rates have generally been low; unsurprisingly, the most elevated rates have been found among samples with longer-term follow-up

(Keel & Brown, 2010). As BED is associated with obesity, and obesity is associated with increased risk for premature death, it is possible that the mortality risk of individuals with BED increases over time.

Pica and Rumination Disorder

In contrast to AN, BN, and BED, little systematic research is available about pica, rumination disorder, and ARFID, which were previously included in a category that was eliminated from DSM-5: disorders usually first diagnosed in infancy, childhood, or adolescence. Feeding and eating disorders may affect a sizable number of infants and young children (e.g., Equit et al., 2013), including those with typical development, those with medical conditions, and those with developmental disabilities or disorders (Nicholls & Bryant-Waugh, 2009). Specifically, children at greater risk for feeding problems and/or disorders include children with developmental disabilities, chronic medical conditions, neurologic impairments, craniofacial anomalies, autism spectrum disorder, and certain genetic syndromes (Nicholls & Bryant-Waugh, 2009). Feeding and eating disorders of infancy and childhood are not well understood, due to lack of a common typology or suitable measurement tools (Nicholls & Bryant-Waugh, 2009). Progress has begun being made toward subtyping feeding disorders, however (Lucarelli et al., 2013).

Avoidant/Restrictive Food Intake Disorder

The creation of the ARFID diagnosis was intended to facilitate communication about, and future research into, these little-studied eating disturbances—which span DSM-IV feeding disorders of infancy or early childhood, as well as some cases that would have received a diagnosis of EDNOS according to DSM-IV (Kenney & Walsh, 2013). Like pica and rumination disorder, ARFID can occur across the lifespan (APA, 2013a; Bryant-Waugh, 2013; Bryant-Waugh et al., 2010; Wildes et al., 2012). However, symptoms of each of these eating disorders usually first appear in infancy or childhood (APA, 2013a).

In a study of the prevalence of eating problems in 1,090 young children averaging 5.8 years of age (SD = 0.5; range = 4–7), researchers found that many children avoided certain foods (53%), were unwilling to try new foods (26%), or ate only a narrow range of foods (23%), suggesting that picky eating is normative when unaccompanied by weight loss, behavioral or emotional problems (Equit et al., 2013). However, a minority of children experienced more concerning eating-related behaviors and attitudes: One-third exhibited more problematic selective and restrictive eating patterns, and 5% worried about their weight. Feeding problems among children are relatively common, and are particularly elevated in specific subgroups. A recent review indicates that 25–45% of normally developing children, and up to 80% of developmentally delayed children, experience some type of feeding problem (Bryant-Waugh et al., 2010). Many of these issues are transient, and will resolve without clinical intervention and without evolving into a feeding or eating disorder.

EPIDEMIOLOGY

Prevalence

Estimates of the prevalence of specific DSM-IV eating disorder diagnoses in the general population have ranged from less than 1% for AN to approximately 3% for BED, with estimates of the prevalence of BN falling in between. Under the DSM-IV diagnostic system, the most prevalent diagnosis was EDNOS, indicating that the majority of individuals with eating pathology of clinical severity did not meet criteria for a specific eating disorder diagnosis (Thomas, Vartanian, et al., 2009). However, the changes made in DSM-5 are likely to reduce the number of individuals whose eating pathology falls outside the specified eating disorder diagnoses, and thus to contribute to slight increases in the prevalence of AN, BN, and BED (Stice, Marti, & Rohde, 2013).

The National Comorbidity Survey Replication (NCS-R) is a recent, nationally representative survey of 9,282 U.S. English-speaking adults ages 18 years and older, wherein 2,980 participants were randomly assigned to have an assessment of eating disorders (Hudson et al., 2007; Hudson, Hiripi, Pope, & Kessler, 2012). According to the NCS-R, estimates of the lifetime prevalence of DSM-IV AN, BN, and BED were 0.5%, 1.0%, and 2.8%, respectively. The survey also provided lifetime prevalence estimates of subthreshold BED (1.2%) and any binge eating (4.2%). Twelve-month prevalence estimates were 0.0%, 0.3%, 1.2%, 0.6%, and 2.1%, for AN, BN, BED, subthreshold BED, and any binge eating, respectively. Similar prevalence rates were reported when BN and BED were surveyed in the World Mental Health Surveys (Kessler et al., 2013). The World Mental Health Surveys included 24,124 respondents ages 18 years and older in 14 mostly upper-middle and

high-income countries across four continents (North America, South America, Europe, and Australia). Lifetime and 12-month prevalence estimates were 1.0% and 0.4% for BN, respectively, and 1.9% and 0.8% for BED, respectively. In virtually all countries surveyed, both lifetime and 12-month prevalence rates were higher for BED than for BN. Prevalence of AN was not included in this report.

Recent estimates of lifetime and 12-month prevalence of eating disorders among adolescents were provided by the National Comorbidity Survey Replication—Adolescent Supplement (NCS-A), an interview-based survey of a nationally representative sample of 10,123 adolescents ages 13–18 years (Swanson, Crow, Le Grange, Swendsen, & Merikangas, 2011). Lifetime prevalence rates were 0.3%, 0.9%, 1.6%, 2.5%, and 0.8% for DSM-IV AN, BN, BED, subthreshold BED, and subthreshold AN, respectively. Twelve-month prevalence rates were 0.2%, 0.6%, 0.9%, and 1.1% for AN, BN, BED, and subthreshold BED, respectively (12-month prevalence of subthreshold AN was not assessed). Of adolescents with BN, 41.3% reported they had purged in their lifetime, whereas the remaining respondents reported nonpurging compensatory behaviors.

Despite the generally low prevalences of specific eating disorder diagnoses, eating pathology and specific disordered eating symptoms are highly prevalent, beginning at a young age. One-fifth of 5-year-old girls (Davison, Markey, & Birch, 2003), over one-third of 9-year-old girls (DeLeel, Hughes, Miller, Hipwell, & Theodore, 2009; Field et al., 1999), and approximately half of preadolescent girls (Rolland, Farnill, & Griffiths, 1997; Schur, Sanders, & Steiner, 2000) are concerned about their weight. By adolescence, not only is such concern prevalent, but increasing numbers of individuals are engaging in unhealthy weight loss behaviors in response to these concerns. A review of such pathology suggested that among adolescent girls in the United States, 46–80% reported dissatisfaction with their weight, 26–77% had dieted at some point, and 5–16% had engaged in purging behaviors (e.g., vomiting, laxatives, diuretics) (Chamay-Weber, Narring, & Michaud, 2005). Rates were similar in European countries. In regard to subthreshold eating disorders (defined in the review as inappropriate eating behavior that does not completely satisfy diagnostic criteria for a specific eating disorder), up to 14% of the general population may be affected. Such eating pathology, despite not reaching diagnostic thresholds, can be distressing and impairing (Chamay-Weber et al., 2005; Touchette et al., 2011); thus more clinical resources and research attention are needed for individuals suffering from such symptomatology.

Epidemiological data regarding the prevalence of eating disorders among children lag behind those available for adolescents and adults. A recent study involved surveillance for 14 months of new cases of early-onset (i.e., onset at age 13 years or younger) eating disorders among patients presenting to secondary care (Nicholls, Lynn, & Viner, 2011). Overall incidence was very low (i.e., 3.01 per 100,000), with the majority of identified cases among children demonstrating an AN-like illness. There was a clear association between incidence and increasing age, indicating that risk for an eating disorder increases as children get older and approach adolescence. Estimates of the incidence and prevalence of feeding disorders in children have been difficult to obtain with reliability, in part due to variability in definitions used. In regard to DSM-5 feeding disorders specifically, adequate epidemiological data for children are not yet available, but prevalence appears to be low (Bryant-Waugh et al., 2010; Hartmann, Becker, Hampton, & Bryant-Waugh, 2012).

Overall, epidemiological studies suggest some change in the incidence of eating disorders over the last century (Striegel-Moore & Bulik, 2007). For AN, incidence increased across the first two-thirds of the 20th century (Bulik et al., 2006; Hoek & van Hoeken, 2003), but over the past few decades it has remained fairly stable (Currin, Schmidt, Treasure, & Jick, 2005; Hoek & van Hoeken, 2003), although it has increased among 15- to 19-year-old girls (van Son, van Hoeken, Bartelds, van Furth, & Hoek, 2006). For BN, incidence increased during the latter half of the 20th century, with lifetime prevalence rates lower among age cohorts born before 1960 than among more recent age cohorts (Hudson et al., 2007; Kendler et al., 1991), but incidence levels were stable at the end of the 20th century (van Son et al., 2006). These changes roughly align with changes over time in the ideal female body size (i.e., increasing emphasis on the thin ideal), and may reflect the importance of gene–environment interactions (Striegel-Moore & Bulik, 2007)—specifically, genetic risk for eating pathology that is triggered within the context of increased societal pressure for a thin physique.

Gender

Research on eating disorders in males, which lags behind that of research on females, has begun to highlight both similarities and differences between females and

males. It has long been recognized that eating disorders are more prevalent among females, with approximately 10 women for every man affected (APA, 2000). However, this gender difference is more pronounced in AN and BN than in BED. For example, examination of gender differences in prevalence estimates provided by the NCS-R and the NCS-A indicated significant gender differences in lifetime rates of AN, BN, BED, and subthreshold BED among adults (Hudson et al., 2007), and BN, BED, and subthreshold AN among adolescents (Swanson et al., 2011). All significant differences for both adults and adolescents indicated increased prevalence among females, with one exception: Subthreshold BED was more common among adult males than adult females. These gender differences are less evident in younger adolescents and children, particularly those who are prepubertal.

Disordered eating attitudes and behaviors are also more prevalent among females than males, in both adult (Striegel-Moore et al., 2009) and adolescent (Croll, Neumark-Sztainer, Story, & Ireland, 2002) samples. Overall, gender differences in body image disturbance tend to emerge around ages 8–10 years, and gender differences in dieting and related behaviors appear to emerge around age 10 years (Ricciardelli & McCabe, 2001). The developmental trajectories and periods of greatest risk for the onset of disordered eating symptoms vary between females and males as well. For example, an 11-year prospective follow-up of 3,150 adolescents indicated that bulimic symptoms among females increased between ages 14 and 16 and then declined slowly thereafter, whereas bulimic symptoms among males decreased between ages 14 and 16 and subsequently increased in the early 20s (Abebe, Lien, & von Soest, 2012).

However, researchers have cautioned that these gender differences, although statistically significant, often represent small effect sizes, and thus may not reflect clinically meaningful disparities. Indeed, a substantial minority of males report clinically significant eating pathology, and are in need of increasing clinical resources and research attention (Striegel-Moore et al., 2009). For example, in a school-based survey of 81,247 students in grades 9 and 12, over half of female students and over one-quarter of male students self-reported engaging in at least one disordered eating behavior (Croll et al., 2002). The types of disordered eating symptoms reported often differ across sexes, however. In several studies, males were more likely to engage in excessive exercising and to report overeating, whereas females were more likely to engage in purging behaviors (e.g., self-induced vomiting), to report loss of control while eating, and to fast and/or skip meals (Croll et al., 2002; Striegel-Moore et al., 2009; Weltzin et al., 2005). In addition, males were more likely to desire a muscular physique, whereas females were more likely to desire a thin physique (Anderson & Bulik, 2004; McCreary & Sasse, 2000).

Beyond gender differences in the prevalence, development, and presentation of eating disorders and associated symptomatology, there are also gender differences in the outcome of eating disorders. For example, a retrospective cohort study of 1,015 patients with either AN, BN, or EDNOS consecutively admitted to a specialized eating disorder unit indicated that the median time from onset to remission of AN and EDNOS was longer for females than for males (Stoving, Andries, Brixen, Bilenberg, & Horder, 2011). Gender comparisons of time to remission for patients with BN were not possible in this study, as there were too few males with BN.

Ethnicity

There is a long-standing assumption that eating disorders are "culture-bound syndromes" that are rare among ethnic minority populations (Prince, 1985; Swartz, 1985). However, this assumption may have originated in part from observations made in clinical practice and treatment trials, in which few individuals from ethnic minorities have been represented (Striegel-Moore & Bulik, 2007). Recently, several studies have examined and compared eating pathology across diverse cultures. Although results have at times been discrepant, eating disorders have been documented across the globe (Kessler et al., 2013) and within diverse ethnic minority populations within the United States (Swanson et al., 2011) and Canada (Boisvert & Harrell, 2009). Overall, trends suggest that individuals in diverse cultures are susceptible to pathological eating behaviors and attitudes; however, some differences in the types of eating pathology and disorders most commonly suffered may exist across ethnic groups.

Conflicting reports have been provided regarding the prevalence of eating disorders across U.S. ethnic groups. However, the National Institute of Mental Health's Collaborative Psychiatric Epidemiological Studies (CPES) recently provided an authoritative examination of prevalence rates using pooled data from three samples, combined into a single nationally rep-

resentative sample of the U.S. population that included large sample sizes of Latino, Asian, African Americans, and non-Latino white Americans. The CPES indicated that the lifetime and 12-month prevalence rates for both AN and BED were similar across all four ethnic groups examined (Marques et al., 2011). In contrast, the CPES reported ethnic differences in the prevalence of BN. Specifically, significantly higher lifetime and 12-month prevalence of BN was observed among Latino and African Americans compared with non-Latino white Americans (Marques et al., 2011). Findings from the NCS-A largely corroborated these results among adolescents (Swanson et al., 2011). That is, differences in lifetime prevalence rates across ethnic groups did not reach significance for either AN or BED, whereas BN was more prevalent among Hispanic American adolescents than those of other ethnicities. More research is needed to better understand this group difference; however, the results could suggest a trend for elevated prevalence of BN that is developing over time among Hispanic and African Americans, or could suggest an earlier age of onset of BN among Hispanic and African Americans than among other ethnic groups.

Internationally, the World Mental Health Surveys indicated minimal variance in prevalence rates of BN across countries. Specifically, of the 14 countries surveyed, lifetime prevalence of BN was highest in Brazil (2.0%) and lowest in Romania (0.0%), with prevalence in the U.S. falling between these two extremes (1.0%; Kessler et al., 2013). Prevalence patterns reported for BED roughly aligned with that reported for BN, although a greater range in prevalence was noted: lifetime prevalence of BED was highest in Brazil (4.7%) and lowest in Romania (0.2%), with prevalence in the United States falling between these two extremes (2.6%; Kessler et al., 2013). AN was not included in this report.

When pathological eating attitudes and behaviors, rather than eating disorder diagnoses, are examined, some cross-cultural differences are noted. Research generally suggests that white females endorse greater body image disturbances than ethnic minority females, particularly in comparison to black females (Pike, Dohm, Striegel-Moore, Wilfley, & Fairburn, 2001; Striegel-Moore et al., 2000; White & Grilo, 2005), although the nature of these differences have shifted over time. A recent meta-analysis of black and white individuals indicated that, over time, between-group differences in body image disturbances have decreased on weight-focused measures and increased on measures that include items that do not pertain to weight or shape (Roberts, Cash, Feingold, & Johnson, 2006). In addition, the CPES indicated that lifetime prevalence of any binge eating was greater among Latino, Asian, and African Americans than among non-Latino white Americans (Marques et al., 2011).

Overall, research suggests that despite the existence of some cross-cultural differences, there are likely to be far more similarities than differences in eating pathology across ethnic groups, particularly in U.S. samples (Shaw, Ramirez, Trost, Randall, & Stice, 2004). Regardless of ethnicity, weight concerns and body dissatisfaction often develop at a very young age (Robinson, Chang, Haydel, & Killen, 2001), and for many individuals these concerns can evolve into a frank eating disorder by adolescence. Experts have emphasized that sociocultural pressures for thinness have become so widespread due to globalization that larger numbers of ethnic groups and peoples are increasingly at risk for the development of eating pathology (Shaw et al., 2004; Striegel-Moore & Bulik, 2007). For further consideration of ethnic and cross-cultural considerations regarding eating pathology, see "Sociocultural Influences" under "Etiology," below.

Sexual Orientation

Overall, research on the association between eating pathology and sexual orientation generally suggests that risk for eating disorders and associated symptomatology is higher among males who are homosexual or bisexual than among heterosexual males (Feldman & Meyer, 2007; Russell & Keel, 2002). A greater emphasis on thinness and appearance in gay male communities, and a tendency for homosexual and bisexual males to be more accepting than heterosexual males of gender noncomformist ideals, are hypothesized to contribute to such increased risk. In contrast, among females who are homosexual or bisexual versus heterosexual, risk for eating disorders and associated symptomatology is approximately equal (Beren, Hayden, Wilfley, & Grilo, 1996; Feldman & Meyer, 2007; Moore & Keel, 2003) or lower (Lakkis, Ricciardelli, & Williams, 1999; Share & Mintz, 2002). However, the majority of research has involved adult samples, with much less research available among youth.

The trend in research with adolescents generally mirrors that observed among adult samples, indicating that bisexual and homosexual adolescent males are at increased risk for disordered eating symptomatology

(Ackard, Fedio, Neumark-Sztainer, & Britt, 2008; Austin et al., 2009; Wichstrom, 2006). The trend is less clear among adolescent females, but generally suggests that bisexual and homosexual adolescent females are at equal (French, Story, Remafedi, Resnick, & Blum, 1996) or higher risk of disordered eating behaviors (Austin et al., 2009; Wichstrom, 2006), although their risk for body dissatisfaction is lower (Austin et al., 2004; French et al., 1996). More research is needed to clarify the nature of these associations among adolescent girls, and to discern mechanisms that may be influencing any associations.

Participation in Athletics

It has long been suggested that participation in sports increases risk for development of an eating disorder. Studies have reported widely varying prevalence of eating disorders among athletes, with prevalence of BN reportedly ranging up to 30% (Hildebrandt, 2005). However, more recent, methodologically rigorous research has questioned the nature and extent of such risk. A meta-analysis of 34 studies that explored associations between athletic participation and eating disorders concluded that athletes were at greater risk than nonathletes for disordered eating, but that the difference was small (Smolak, Murnen, & Ruble, 2000). Moreover, risk was largely associated with elite athletes, particularly those involved in sports that emphasized thinness, such as dancers. In contrast, nonelite athletes—particularly those in high school—were at reduced risk of disordered eating. Overall, it appears that the association between participation in athletics and eating pathology is probably small and largely specific to elite athletes involved in sports that emphasize thinness. Furthermore, some forms of athletic participation (particularly nonelite athletic participation during high school) may actually protect against disordered eating and should be encouraged.

COMMON COMORBIDITIES

Comorbid psychopathology is commonly observed among individuals with eating pathology (Swanson et al., 2011). Consistent with "Berkson's bias" (Berkson, 1946), whereby likelihood of seeking treatment increases with the number of problems an individual experiences, comorbid psychopathology is particularly prevalent among patient samples. For example, a study of 2,436 female inpatients admitted to a specialized eating disorder treatment facility in the United States, all of whom met diagnostic criteria for a primary diagnosis of AN, BN, or EDNOS, indicated that 97% of inpatients had one or more DSM-IV Axis I comorbid disorders (Blinder, Cumella, & Sanathara, 2006). Comorbid mood disorders were particularly prevalent: 94% of participants were diagnosed with a comorbid mood disorder (in almost all cases, a type of unipolar depression). Over half of the sample also evidenced an anxiety disorder, and over one-fifth endorsed a substance use disorder. The prevalence of either mood or anxiety disorders did not differ across eating disorder diagnosis, whereas the prevalence of substance use disorders was highest among inpatients with BN.

Overall, studies of treatment-seeking samples have consistently indicated that comorbid mood disorders are more common than comorbid anxiety disorders among patients with eating disorders (Fischer & le Grange, 2007; Grilo, White, & Masheb, 2009; Herzog, Nussbaum, & Marmor, 1996). However, studies of non-treatment-seeking samples have been less consistent, with some studies—including a national survey of a large, representative sample of U.S. adolescents (Swanson et al., 2011)—suggesting that comorbid anxiety disorders may be more prevalent than comorbid mood disorders. In addition, associations of eating pathology and eating disorders with substance use and misuse have been more modest in non-treatment-seeking samples than in treatment-seeking samples (von Ranson, Iacono, & McGue, 2002).

In general, prevalence and severity of comorbid psychopathology observed in studies of individuals with full-threshold eating disorders have been replicated in studies of individuals with subthreshold eating disorders (Ackard, Fulkerson, & Neumark-Sztainer, 2011; Touchette et al., 2011). Among those seeking treatment, individuals with subthreshold eating disorders may even demonstrate *higher* levels of comorbid psychopathology than those with full-threshold eating disorders, possibly because they may be less likely to seek treatment without comorbid psychopathology and associated distress. For example, a treatment trial for adolescents with either BN or specific variants of EDNOS, excluding BED, indicated more prevalent current depression, current obsessive–compulsive disorder (OCD), and childhood OCD among adolescents with EDNOS than among adolescents with BN (Schmidt et al., 2008).

Researchers have proposed that high rates of comorbidity among depression, anxiety, and eating pathology

suggest possible genetic associations among these disorders (Silberg & Bulik, 2005). Likewise, alternative classification schemes for psychopathology that rely on factor-analytically derived models indicate that these frequently comorbid disorders all belong to a common "internalizing factor" characterized by high negative affect (Forbush et al., 2010; Kotov et al., 2011). In addition, findings have indicated that mood and anxiety disorders often predate the onset of eating disorders (Brewerton et al., 1995; Kaye et al., 2004; Swinbourne & Touyz, 2007), suggesting that such early-onset psychopathology may predispose individuals to developing an eating disorder. For example, a retrospective comparison of the prevalence and age of onset of adult and childhood anxiety disorders and eating disorders indicated that an anxiety disorder predated the onset of an eating disorder in 90% of women with AN and 94% of women with BN (Bulik, Sullivan, Fear, & Joyce, 1997). The presence of certain anxiety disorders indicated risk for a specific eating disorder (e.g., OCD indicated specific risk for AN), whereas other anxiety disorders (e.g., social phobia) suggested nonspecific risk for various eating and affective pathology, including the development of AN, BN, or major depression.

However, comorbid psychopathology may also develop after the development of eating pathology, and/or may demonstrate reciprocal associations with eating pathology. A longitudinal study of 754 community girls assessed at ages 11, 14, and 17 years used cross-lagged path analyses to indicate that, overall, eating pathology predicted later depressive symptoms more strongly than depressive symptoms predicted later eating pathology (Marmorstein, von Ranson, Iacono, & Malone, 2008). Likewise, a school-based longitudinal study of 1,124 adolescent girls indicated that among initially nondepressed adolescents, initial body dissatisfaction, dietary restraint, and bulimic symptoms prospectively predicted the onset of depression over the 4-year study period (Stice, Hayward, Cameron, Killen, & Taylor, 2000). Notably, elevated body mass index—a ratio of weight to height—did not predict the onset of depression; this finding emphasizes the importance of cognitive aspects of body dissatisfaction, rather than objective physical body dimensions, in the association between eating pathology and depression. Given the previous finding that negative affectivity predicts subsequent onset of bulimic symptoms among adolescents (Stice, Killen, Hayward, & Taylor, 1998), the authors concluded that there are likely to be reciprocal relations between eating pathology and symptoms of depression and/or negative affectivity. Specifically, there may be a feedback loop wherein adolescents initially develop negative affect, which leads to binge eating and purging in an effort to regulate affect, which in turn contributes to even greater affective disturbances and depressive symptoms (Stice et al., 2000). Thus each disorder may serve to intensify and maintain the other disorder. Recognizing the significant contribution of eating disorders to functional impairment, particularly in social and family relationships (Swanson et al., 2011), it is not surprising that eating pathology can contribute to children's and adolescents' becoming vulnerable to emotional, interpersonal, and behavioral problems, including psychiatric comorbidity.

Anorexia Nervosa

According to the NCS-A, 55.2% of adolescents who met diagnostic criteria for AN and 79.8% of those who met subthreshold criteria for AN endorsed one or more lifetime comorbid DSM-IV psychiatric disorders (Swanson et al., 2011). Among those with AN, the most prevalent comorbidities were behavioral disorders (31.7%; predominantly oppositional defiant disorder [30.4%]), followed by anxiety disorders (23.9%; most commonly specific phobia [20.5%] and separation anxiety disorder [11.1%]), substance abuse or dependence (13.0%), and mood disorders (10.9%). The prevalence of comorbid OCD was not reported; however, previous research suggests that obsessive–compulsive symptoms and personality traits are common among individuals with AN, including children and adolescents. For example, among 97 individuals with AN in the Price Foundation Collaborative Genetics Study, 35% were diagnosed with lifetime comorbid OCD (Kaye et al., 2004). Assessment of 49 children and adolescents ages 11–18 years who met diagnostic criteria for AN or AN-like EDNOS at three specialist eating disorder clinics in the United Kingdom identified moderate to severe levels of obsessive–compulsive symptoms in approximately half of the sample (Serpell, Hirani, Willoughby, Neiderman, & Lask, 2006). In addition, approximately one-sixth of the sample demonstrated clinically significant obsessive–compulsive personality traits. Likewise, a meta-analysis of the prevalence of personality disorders in eating disorders indicated that Cluster C personality disorders—in particular, obsessive–compulsive personality disorder—are the most commonly diagnosed personality disorders among individuals with the restricting subtype of AN (Cassin & von Ranson, 2005).

Minimal research is available regarding personality disorders among individuals with the binge-eating/purging subtype of AN, but the few studies available have suggested elevated rates of both Cluster B and Cluster C personality disorders, similar to the personality disorders most commonly observed among individuals with BN or BED. Notably, the majority of individuals with AN with OCD or obsessive–compulsive personality disorder develop the disorder prior to developing AN, indicating that obsessive symptoms observed in individuals with AN are not simply effects of starvation (Thornton & Russell, 1997).

Bulimia Nervosa

Results from the NCS-A indicated that 88.0% of adolescents with BN endorsed one or more lifetime comorbid disorders, including 27.0% who endorsed three or more classes of comorbidities (Swanson et al., 2011). Sixty-six percent endorsed an anxiety disorder—most commonly specific phobia (36.7%), posttraumatic stress disorder (PTSD; 26.5%), separation anxiety disorder (26.5%), or social phobia (20.3%). Fifty-eight percent endorsed a behavioral disorder, 49.9% endorsed a mood disorder, and 20.1% endorsed substance abuse or dependence. Self-harming behaviors were also common; in particular, over one-third of adolescents with BN had attempted suicide. A treatment-seeking sample of 80 adolescents with BN demonstrated similarly high rates of past suicide attempts, as well as other high-risk behaviors (Fischer & le Grange, 2007). For example, almost one-third of the sample had used illegal drugs; over two-fifths of the sample had smoked cigarettes; and almost two-thirds of the sample had used alcohol. No control group was included, so it is unclear whether these findings were specific to this treatment-seeking sample. In regard to comorbid personality disorders, meta-analytic findings suggest that individuals with BN are most likely to endorse Cluster B and C personality disorders, including borderline, avoidant, and dependent personality disorders (Cassin & von Ranson, 2005).

High rates of substance abuse and dependence among individuals with BN have led to numerous hypotheses regarding a shared or causal etiology between the disorders (Wolfe & Maisto, 2000). A study of 490 female monozygotic twins, 354 female dizygotic twins, and 930 females from opposite-sex pairs examined whether there was a shared etiology between broadly defined BN and drug use disorders (Baker, Mazzeo, & Kendler, 2007). Data indicated that there was a large genetic contribution to the association between these disorders: Specifically, 83% of the correlation between BN and drug use disorders was due to genetic factors. A smaller contribution of nonshared environmental factors was also noted. In addition, the study considered shared correlates of the disorders, and indicated that neuroticism and major depression accounted for a small to medium proportion of the variance between the disorders. The authors interpreted the findings as suggesting that neurotic personality traits may predispose individuals to both disorders, while a history of major depression may encourage individuals to use substances to alleviate affect. In a subsequent study of 7,241 female twins, BN and alcohol use disorder were moderately correlated (Trace et al., 2013): The two disorders had a genetic correlation of 0.23 (95% confidence interval [CI] = 0.01–0.44), suggesting that liability to both disorders may be influenced by some of the same genetic factors.

Impulsivity has also been observed to contribute to the elevated prevalence of comorbid substance misuse in BN (Dawe & Loxton, 2004), as well as to the development of other comorbid disorders and risky behaviors. For example, a prospective examination of the development of bulimic symptoms among a child sample of girls with attention-deficit/hyperactivity disorder (ADHD) and a comparison control group indicated elevated bulimic symptomatology during adolescence among girls with ADHD, inattentive type in comparison to the control group, and even further elevated symptomatology among girls with ADHD, combined type (Mikami, Hinshaw, Patterson, & Lee, 2008). Moreover, baseline levels of impulsivity better predicted the development of bulimic symptoms than baseline levels of hyperactivity and inattention. Impulsivity has also partially accounted for associations between BN and increased sexual activity (Culbert & Klump, 2005). The role of impulsivity in the development of comorbid disorders is discussed further in "Personality" under "Etiology," below.

Binge-Eating Disorder

As in AN and BN, comorbidity is common in BED. Eighty-four percent of adolescents with BED and 70.1% of adolescents with subthreshold BED endorsed one or more comorbid disorders in the NCS-A (Swanson et al., 2011). This included 37.0% of adolescents with BED who endorsed three or more classes of comorbid dis-

orders. The most prevalent comorbid diagnoses among those with BED were anxiety disorders (65.2%)—in particular, specific phobia (32.1%) and social phobia (26.3%)—followed by mood disorders (45.3%), behavioral disorders (42.6%), and substance abuse or dependence (26.8%).

Psychiatric comorbidity often signals greater psychopathology, impairment, and distress. Among treatment-seeking individuals with BED, the presence of current psychiatric comorbidity corresponded with greater eating disorder psychopathology and negative affect, as well as lower self-esteem (Grilo et al., 2009). Current psychiatric comorbidity has also been associated with higher "lifetime-high" body mass index and earlier onset of dieting behaviors (Grilo et al., 2009). Among non-treatment-seeking individuals with BED, comorbid psychopathology and associated distress appear to be similar to that suffered by treatment-seeking individuals with BED, with one exception: anxiety. Specifically, a comparison of 37 treatment-seeking women and 108 non-treatment-seeking women with BED indicated that non-treatment-seeking women were at least nine times more likely to endorse a current anxiety disorder (Wilfley, Pike, Dohm, Striegel-Moore, & Fairburn, 2001). No other significant group differences in prevalence of comorbidities were observed. More research that extends these analyses to child and adolescent samples is needed.

Obesity is important to consider in examining psychiatric comorbidity among children and adolescents with BED, as it can have implications for additional psychiatric comorbidity and distress. Childhood obesity—a common correlate of loss-of-control eating among children, including episodes characteristic of BED—is associated with significant psychiatric comorbidity, including particularly high rates of major depression and ADHD (Kalarchian & Marcus, 2012). Researchers have recently questioned whether psychiatric comorbidity among children is a cause or consequence of obesity, or whether common factors trigger both psychiatric comorbidity and obesity in at-risk children (Kalarchian & Marcus, 2012). However, although obesity may contribute to the psychiatric comorbidity observed in BED, it cannot account for it entirely. Research with adults has indicated greater psychiatric comorbidity among obese individuals with versus without BED (Bulik, Sullivan, & Kendler, 2002; Grucza, Przybeck, & Cloninger, 2007), highlighting a specific association with BED. However, more research is needed with child and adolescent populations.

DEVELOPMENTAL COURSE AND PROGNOSIS

Anorexia Nervosa

The period of greatest vulnerability for the onset of AN is adolescence (Striegel-Moore & Bulik, 2007), and is shorter than the period of risk for any other eating disorder (Hudson et al., 2007). Age of onset is often reported to be bimodal, with peaks around the ages of 14.5 and 18 years (Halmi, Casper, Eckert, Goldberg, & Davis, 1979). Recently, the NCS-R (Hudson et al., 2007) indicated that the median age of onset for AN was 18.0 years. In that study, no cases of AN were reported to have onset after the mid-20s (Hudson et al., 2007). Notably, age of onset of AN may be decreasing in younger generations (Favaro, Caregaro, Tenconi, Bosello, & Santonastaso, 2009). In particular, incidence of AN among 10- to 14-year-old females has increased over each decade since the 1950s, whereas incidence of AN for men and women older than 25 years has remained relatively low and stable (Hoek & van Hoeken, 2003).

In the NCS-R, the average duration of DSM-IV AN was 20 months (Hudson et al., 2007). A review of recent studies describing eating disorder course and outcome indicated variable remission rates for AN (Keel & Brown, 2010). Within treatment-seeking populations, most AN patients ascertained through outpatient settings have demonstrated remission by 5-year follow-up (Keel & Brown, 2010). However, lower remission rates have been observed in studies of patients in inpatient settings, with only a minority of inpatients achieving remission, regardless of length of follow-up (Keel & Brown, 2010). Overall, patients with AN who receive treatment have generally demonstrated modest benefits, with younger patients being more responsive to treatment, and patients with more established, chronic cases of AN being more resistant to treatment (Wilson, Grilo, & Vitousek, 2007). Overvaluation of weight/shape and self-oriented perfectionism have been shown to maintain anorexic symptomatology (Lampard, Tasca, Balfour, & Bissada, 2013), by facilitating a dysfunctional system for evaluating self-worth and a relentless striving for personally demanding standards (such as a very thin physique) despite adverse consequences. Various biological and physiological processes that result from starvation and malnutrition additionally maintain anorexic symptomatology (Treasure, Cardi, & Kan, 2012), in part through contributing to alterations in mental state such as dysphoric mood and preoccupation with food and food-related behaviors.

Among patients with AN who do not achieve remission over treatment follow-up periods, many cross over to other eating disorder diagnoses, including BN and subthreshold variants of eating pathology (Keel & Brown, 2010). Some of these diagnoses may reflect AN in partial remission. A 7-year prospective study of 216 treatment-seeking women with AN or BN indicated that the majority of women with AN experienced diagnostic crossover, with half crossing between DSM-IV subtypes of restricting AN and binge-eating/purging AN, and one-third crossing over to BN (Eddy, Dorer, et al., 2008). Those who crossed over to BN were likely to relapse back to AN. Diagnostic crossover has been observed in non-treatment-seeking samples as well (Tozzi et al., 2005). Finally, a large proportion of patients with AN suffer from psychiatric comorbidity at follow-up (Steinhausen, 2002).

Bulimia Nervosa

Like AN, BN typically begins during adolescence (Keski-Rahkonen et al., 2009; Striegel-Moore & Bulik, 2007). However, the period of risk for BN is longer than for AN, and some cases of BN have been reported to begin later in middle adulthood (Hudson et al., 2007). The NCS-R indicated that the median age of onset for BN was 18.0 years.

A community-based study that followed 102 women with BN ages 16–35 over 5 years indicated a general trend for BN symptomatology to demonstrate marked initial improvement, followed by gradual improvement (Fairburn, Cooper, Doll, Norman, & O'Connor, 2000). In general, approximately one-third of the women achieved remission and approximately one-third relapsed during each year of the study. At each 15-month assessment point, between half and two-thirds of the women met DSM-IV criteria for some form of eating disorder, although only a minority continued to meet diagnostic criteria for DSM-IV BN. Reported frequency of diagnostic crossover from BN to AN is inconsistent across studies (Keel & Brown, 2010; Tozzi et al., 2005) but generally appears to be low. A recent 8-year prospective study of DSM-5 eating disorders in adolescents suggested that diagnostic crossover is greatest between threshold and subthreshold variants of BN and BED (Stice et al., 2013).

Among treatment-seeking individuals, remission rates generally increase as duration of follow-up increases, and most individuals with BN achieve remission over time. However, a review of recent studies describing the course and outcome in eating disorders indicated that individuals who have not achieved remission by 5 years following baseline assessments are likely to continue demonstrating a chronic course (Keel & Brown, 2010). Recent reports of the average duration of BN episodes have ranged from 6.5 years (Kessler et al., 2013) to 8.3 years (Hudson et al., 2007).

Overall, level of psychiatric symptom severity and burden, as well as extent of psychiatric comorbidity, have been associated with poorer prognosis in BN. In the aforementioned longitudinal study of the natural course of BN among community women (Fairburn et al., 2000), duration of disturbed eating, degree of overvaluation of shape and weight, level of social maladjustment, history of childhood obesity, and persistence of compensatory behavior all predicted persistence of binge eating (Fairburn, Stice, et al., 2003). Persistence of binge eating was the only predictor of the persistence of compensatory behavior.

Binge-Eating Disorder

Whereas AN and BN typically have their onset during adolescence, the onset of BED has been observed to occur at a later age and has a substantially longer period of onset risk. According to the NCS-R (Hudson et al., 2007), median age of onset of BED was 21.0 years, with some cases having onset after age 60 years. However, binge eating and/or loss-of-control eating behavior that does not reach diagnostic thresholds may begin at a much earlier age, including during childhood. Such behavior appears relatively common among children and adolescents, with reported prevalence estimates ranging from approximately 2 to 40% (Glasofer et al., 2007; Greenfeld, Quinlan, Harding, Glass, & Bliss, 1987; Lamerz et al., 2005; Tanofsky-Kraff et al., 2004, 2007; Walsh, 2013).

Recent large-scale surveys have indicated that the average episode duration for BED reported by community adults ranges from 4.3 years (Kessler et al., 2013) to 8.1 years (Hudson et al., 2007). Another study reported that on average, symptoms of BED endure for over 14 years, which is longer than AN and BN tend to last (Pope et al., 2006). Although one community-based study of 48 women ages 16–35 years with BED found that only 18% had any form of clinical eating disorder by 5-year follow-up (Fairburn et al., 2000), a study of community-based adolescents indicated that approximately one-third of girls with BED relapsed over an 8-year interval (Stice et al., 2013). Of the 15 girls with BED, the major-

ity demonstrated remission within 1 year, and the average episode duration was only 3.3 months.

Overall, rates of remission appear to be higher for BED than for AN and BN, and individuals with BED may be less likely than individuals with AN and BN to cross over to another eating disorder diagnosis (Keel & Brown, 2010). Evidence suggests that BED is associated with a poor health prognosis, including medical complications that develop independently of the effects of comorbid obesity (Bulik & Reichborn-Kjennerud, 2003; Bulik et al., 2002). However, more long-term data regarding BED outcome are needed. Few prognostic factors for BED have been explored and identified. Evidence suggests that factors such as greater interpersonal problems (Hilbert et al., 2007), increased impulsivity, and psychiatric comorbidity (Fichter, Quadflieg, & Hedlund, 2008) may be associated with poorer outcome.

ETIOLOGY

Eating disorders are clear examples of multiply determined problems that involve interacting sociocultural, psychological, and biological variables (Jacobi, Hayward, de Zwaan, Kraemer, & Agras, 2004; Polivy & Herman, 2002; Striegel-Moore & Bulik, 2007). As Striegel-Moore and Bulik noted, "The single best predictor of an eating disorder is being female" (2007, p. 182). Not all women develop eating disorders, of course, and indeed some men are affected, especially with BED. To increase our understanding of why only some people develop eating pathology, much research has focused on specific factors that place individuals at heightened risk.

Sociocultural Influences

Contemporary Western culture places high value on the "thin ideal"—that is, socially defined ideals of attractiveness that emphasize a thin physique. Awareness of the thin ideal is widespread, particularly among females; many children become aware of this sociocultural preference by the first grade, or around age 6 (Murnen, Smolak, Mills, & Good, 2003). Once individuals have become aware of the thin ideal, this ideal can subsequently become internalized. That is, individuals "cognitively '[buy] into' socially defined ideals of attractiveness and [engage] in behaviors designed to produce an approximation of these ideals" (Thompson & Stice, 2001, p. 181). Pursuit of the thin ideal can involve unhealthy eating and weight control behaviors, and, at severe levels, can lead to the development of an eating disorder. Empirical findings suggest that internalization of the thin ideal is a causal risk factor for body dissatisfaction and disordered eating (Thompson & Stice, 2001), and that internalization of the thin ideal accounts for significant variance in body dissatisfaction and disordered eating, even beyond that accounted for by awareness of the thin ideal (Heinberg, Thompson, & Stormer, 1995).

Sociocultural pressures to be thin are particularly important in the initiation of disordered eating symptoms, rather than the maintenance and/or cessation of such symptoms (Stice & Agras, 1998). As pathology progresses, the role of sociocultural influences may become less prominent than other powerful maintenance mechanisms that serve to perpetuate the disorder, such as clinical perfectionism, low self-esteem, poor social adjustment, mood intolerance, and impulsiveness, among others (Fairburn, Cooper, et al., 2003; Fairburn, Stice, et al., 2003; Schnitzler, von Ranson, & Wallace, 2012).

Recognition of the significance of thin ideal internalization, as well as other sociocultural influences, in the development of disordered eating has contributed to the development and promulgation of the "dual-pathway model" of eating disorders (Stice, 2001). Some researchers also refer to this model as the "sociocultural model," although they may only test a portion of it in a given study. The dual-pathway model is one of the most widely examined and supported models of disordered eating, including within child (Evans, Tovée, Boothroyd, & Drewett, 2013) and adolescent (Stice, 2001) populations. Originally designed to describe the development of bulimic symptoms specifically, it has since been applied to a range of pathological eating and weight control behaviors (e.g., Goodwin, Haycraft, & Meyer, 2011), including both nonclinical and clinical issues. The dual-pathway model hypothesizes that pressure to be thin and internalization of the thin ideal lead to body dissatisfaction, and subsequently increase risk for disordered eating via two pathways: dietary restraint and depression. Some, but not all, studies additionally suggest a direct pathway between thin-ideal internalization and disordered eating attitudes, even when associations with mediating variables of dietary restraint and depression are statistically controlled for (Field et al., 2001; Stice, Presnell, & Spangler, 2002; Vander Wal, Gibbons, & Grazioso, 2008).

Internalization and pursuit of the thin ideal is often socially reinforced, such as by comments or actions by family and peers that support the ideal, and messages that suggest widespread benefits of thinness (Thompson & Stice, 2001). The mass media in particular have been suggested to spread and encourage ideas about the thin ideal, and thus ultimately to contribute to body dissatisfaction and disordered eating. A recent review of research pertaining to the mass media as a causal risk factor for body dissatisfaction and disordered eating in females concluded that the content, use, and experience of media are possible causal risk factors for eating pathology, although further research is needed to determine whether media exposure precedes and predicts such outcomes (Levine & Murnen, 2009). Mass media messages can be communicated directly or indirectly, such as through synergistic messages from parents and peers. The relative contribution of various sources of mass media to eating pathology may vary across childhood and adolescence. In particular, fashion and glamor magazines have been reported to have greater influence than television on thin-ideal internalization among adolescent girls, whereas television has a greater influence than magazines among children (López-Guimerà, Levine, Sánchez-Carracedo, & Fauquet, 2010).

Sociocultural influences are generally considered to have a greater impact on the development of disordered eating among females than males, which has been suggested to contribute in part to the significant sex differences in the prevalence and associated characteristics of eating disorders (see "Gender" under "Epidemiology," above). For example, an examination of sociocultural influences and eating pathology among 1,266 female and male adolescents in grades 7–10 reported that girls, in comparison to boys, perceived greater pressure from the media to alter their weight (McCabe & Ricciardelli, 2001). Girls likewise reported receiving more feedback about body change from mothers, fathers, and both male and female peers. However, boys remain susceptible to sociocultural influences, particularly to pressure about increasing lean body mass and muscle tone (McCabe & Ricciardelli, 2001; Ricciardelli & McCabe, 2004). Indeed, media has increasingly presented boys with pressure to attain an ideal body that is characterized by a muscular physique, which has contributed to greater body dissatisfaction among boys in recent years (Arbour & Martin Ginis, 2006). Multiple studies have provided empirical support for sociocultural influences and parts of the dual-pathway model among boys in late childhood and adolescence (e.g., Goodwin et al., 2011; Halliwell & Harvey, 2006). Sex differences also exist in the pattern of associations between sociocultural influences and eating pathology, with boys being particularly susceptible to a moderating influence of depression (Rodgers, Paxton, & Chabrol, 2010).

Increasingly, researchers have engaged in cross-cultural research that has considered whether sociocultural influences involved in the dual-pathway model, originally developed among Western societies, are applicable in non-Western societies. Although epidemiological data has indicated a greater prevalence of eating disorders in industrialized societies than in developing societies, the dual-pathway model has generally held up well across several studies of culturally and industrially diverse samples (e.g., Austin & Smith, 2008; Rodgers, Ganchou, Franko, & Chabrol, 2012; Vander Wal et al., 2008). Some of the most important cross-cultural research pertaining to sociocultural influences and the development of eating pathology has emerged from a multiwave cross-sectional study that examined samples of Fijian schoolgirls before and after prolonged regional television exposure (Becker, Burwell, Herzog, Hamburg, & Gilman, 2002). This sample represented a relatively media-naive population that was undergoing significant social and economic change, including the introduction of television and other mass media influences. Thus the context facilitated a naturalistic examination of the impact of television and other mass media exposure on eating pathology. Prior to this period of change, disordered eating was considered to be rare in Fiji. Instead, traditional aesthetic ideals prevailed, wherein robust body types were preferred. Results indicated a significant increase in the prevalence of disordered eating attitudes and self-induced vomiting to lose weight—two key indicators of eating pathology—following introduction to television and other mass media. Disordered eating attitudes were particularly elevated among respondents who lived in a household with a television; however, social network media exposure was also associated with eating pathology, independent of any direct media exposure and other cultural exposures (Becker et al., 2011). Analysis of narrative interviews with Fijian schoolgirls suggested that increased eating pathology primarily reflected a means of reshaping one's body and identity, so as to model oneself after television characters and ultimately enhance one's social and economic positioning and opportunities (Becker, 2004; Becker et al., 2002). In sum, although cross-sectional, these data are compelling because the study examined eating attitudes and

behavior before and after the introduction of television into a relatively media-naive society with low a priori rates of eating disorders.

Dieting

Dieting (i.e., restriction of overall caloric intake and/or avoidance of specific foods in order to influence body shape and weight) is a key feature of most forms of disordered eating, including AN and BN. However, elevated dietary restraint has also emerged as a strong predictor of the later development of an eating disorder, including in child and adolescent populations; this finding highlights that dieting not only is part of the symptomatology of eating disorders, but also plays an important role in the development of such psychopathology. Emphasizing the potency of the effect of dieting on eating pathology, a large-scale, population-based study of 14- to 15-year-olds in Australia observed that dieting was the strongest predictor of the onset of new eating disorder cases 3 years later (Patton, Selzer, Coffey, Carlin, & Wolfe, 1999). Female adolescents who dieted at a "severe" level were 18 times more likely to develop an eating disorder than female adolescents who did not diet, and female adolescents who dieted at a "moderate" level were 5 times more likely to develop an eating disorder than those who did not diet. In addition, not only the behavior of dieting, but endorsement of expectancies for life improvement from thinness and restricting food intake, has been associated with increased risk for the development of an eating disorder (Combs, Pearson, & Smith, 2011).

However, dieting is extremely prevalent in the general population, with some indications that dieting is now a normative behavior, including among preadolescents and adolescents. For example, approximately one-third of females ages 9–14 years reported dieting in the past year in large samples from the United States (Field et al., 2003) and Canada (McVey, Tweed, & Blackmore, 2004). Such a high prevalence makes it clear that dieting is not a sufficient factor to account for the development of an eating disorder, since the majority of children and adolescents who engage in dieting behavior will never develop an eating disorder. Thus researchers have shifted to focusing on identifying factors that interact with dieting to predict eating disorder onset, so as to identify the subgroup of dieters who are at greatest risk of developing an eating disorder. A study of 2,992 young women endorsing current dieting behaviors identified the following eating-related features as best discriminating future eating disorder cases from future noncases: frequency of self-reported binge eating, eating in secret, low body mass index (i.e., ≤19), preoccupation with food and eating, desire to have an empty stomach, frequency of purging, fear of losing control over eating, and preoccupation with shape or weight (Fairburn, Cooper, Doll, & Davies, 2005). Other research with adolescents has indicated that dieting to change one's appearance and for health reasons associated with being overweight may be a benign behavior, whereas dieting because of psychological distress (including either depressed mood or emotional problems, or a diffuse feeling of being fat despite objectively normal-weight or underweight status) indicates significant risk for developing an eating disorder (Isomaa, Isomaa, Marttunen, Kaltiala-Heino, & Bjorkqvist, 2010).

The association between dieting and increased risk for development of an eating disorder has been accounted for in part by "restraint theory." Restraint theory suggests that prolonged dietary restraint creates physiological and psychological deprivation that contributes to the eventual counterregulation of appetite via binge eating (Herman & Polivy, 1988; Polivy, Herman, Olmsted, & Jazwinski, 1984). The association between elevated dietary restraint and subsequent binge eating has been supported by both experimental (Agras & Telch, 1998) and naturalistic (Steiger, Lehoux, & Gauvin, 1999) studies. As noted previously, the Minnesota Semi-Starvation Experiment demonstrated that prolonged dietary restraint can also have a significant impact on behavioral, emotional, and cognitive functioning, often triggering symptoms characteristic of eating disorders. Changes observed during the study included significant preoccupation with food, to the extent that the men found it increasingly difficult to concentrate on their usual activities and were consumed by incessant thoughts about food and eating. Emotional deterioration was prevalent, and was perceived to be severe and to interfere with functioning in almost 20% of the men. The men were frequently irritable and angry, experienced increased anxiety, and demonstrated increased apathy. In addition, the men became increasingly withdrawn and isolated, and experienced significant strain on their relationships. They reported impaired concentration, alertness, comprehension, and judgment. Finally, several men were unable to adhere to the strict dietary rules and reported engaging in binge-eating episodes, which were typically followed by self-deprecatory feelings. These results clearly demonstrate

the powerful impact of dietary restraint on overall functioning, and on both the development and maintenance of eating disorder symptomatology. Such symptoms accrue in part through significant changes in neural activity and other physiological processes that result from such dietary restraint, and are critical to consider in understanding, preventing, and treating eating disorders (Ioakimidis et al., 2011; Treasure et al., 2012).

The dual-pathway model of eating pathology (Stice, 2001; see also "Sociocultural Influences," above) builds in part on restraint theory, and postulates both a dietary restraint pathway and a negative affect pathway in the development of eating pathology. According to this model, dieting behaviors characteristic of the dietary restraint pathway can promote binge eating for reasons similar to those postulated via restraint theory, as well as by providing comfort and distraction from negative affect. Such negative affect may develop as a result of the impact of caloric deprivation on mood, as well as the experience of failures often associated with weight control efforts. Several studies have provided empirical support for this model (Allen, Byrne, & McLean, 2012; Stice, 2001), although conflicting findings have also emerged (Evans et al., 2013). In particular, conflicting findings have questioned the temporal sequence of dieting and binge eating (Brewerton, Dansky, Kilpatrick, & O'Neil, 2000; Reas & Grilo, 2007). Overall, research suggests that dieting is more likely to precede binge eating, but binge eating precedes dieting in a substantial number of cases and may be particularly common among overweight children. Among a sample of 105 non-treatment-seeking overweight children ages 6–13 years, 65% of children reported engaging in loss-of-control eating before having dieted (Tanofsky-Kraff, Faden, Yanovski, Wilfley, & Yanovski, 2005). Most children additionally reported becoming overweight before having engaged in either dieting or loss-of-control eating. The few children who reported engaging in dieting before becoming overweight demonstrated significantly higher scores on measures of negative mood and eating pathology. Thus dietary restraint may characterize one pathway to eating pathology that may be particularly common among normal-weight children, whereas overweight may serve as a risk factor along another pathway (Tanofsky-Kraff et al., 2005). More longitudinal research with child samples is needed.

Alongside increasing recognition of the association between dieting and risk of developing an eating disorder, increasing concern has developed regarding overweight as a serious health problem among children and adolescents. As a result, debate has emerged between those who dissuade dieting to reduce risk for eating disorders and those who encourage dieting to reduce overweight (Neumark-Sztainer, 2009a, 2009b). A review of a small number of studies concluded that professionally administered weight loss programs that encourage healthy (not extreme) dieting pose minimal risks of increasing symptoms of eating disorders in overweight children and adolescents (Butryn & Wadden, 2005). The review noted that such programs often demonstrate significant improvements in children and adolescents' psychological health. Nonetheless, experts from various health fields have maintained that caution should be used when providing such programs, and have warned that health professionals should inform clients of unintentional negative effects that can be associated with weight loss messages (McLaren et al., 2009). Likewise, researchers have suggested that encouraging weight control among children and adolescents via exercise, rather than via dietary restraint, may pose less risk for the development of an eating disorder (Patton et al., 1999), although it may be less effective at reducing weight.

Genetic Influences

Although eating disorders theorists initially focused on environmental, sociocultural, and personality factors involved in the development of eating pathology, genes are now recognized as an important part of the story. Genetic influences have been identified in risk for specific eating disorder diagnoses, including both full-threshold and subthreshold presentations (Campbell, Mill, Uher, & Schmidt, 2011; Strober, Freeman, Lampert, Diamond, & Kaye, 2000; Thornton, Mazzeo, & Bulik, 2011), as well as specific disordered eating symptomatology, such as self-induced vomiting and dietary restraint (e.g., Mazzeo et al., 2009). More recent research has sought to better define the specific contribution of genetics in eating disorders, to determine specific genes that are involved, and to identify interactions with other environmental and biological factors that serve to enhance and/or mitigate genetic risk. Despite continuing research advances, much remains to be understood.

The role of genes in the development of eating disorders is complex. Genetic contributions to eating disorders tend to be subtle and of small effect, and are often only observed following interactions with environmen-

tal risk factors. Genetic studies of eating disorders are also challenged by the low prevalence of the disorders, as well as the significant overlap and crossover within eating disorder diagnoses. Such overlap suggests that genetic risk may not be specific to a particular eating disorder diagnosis. Moreover, with high rates of psychiatric comorbidity observed among individuals with eating disorders, some genetic risk may not be specific to eating disorders but shared with other psychopathology, such as depression, anxiety, and substance misuse.

Overall, research suggests that eating disorders are familial and that they aggregate in families as a broad spectrum of disordered eating symptomatology, with some common, shared liability across specific eating disorder diagnoses and subclinical eating pathology (Strober et al., 2000; Thornton et al., 2011). Specifically, female relatives of probands with AN are 11 times more likely to develop AN and 4 times more likely to develop BN in comparison to female relatives of unaffected individuals, and female relatives of probands with BN are 12 times more likely to develop AN and 4 times more likely to develop BN in comparison to relatives of unaffected individuals (Strober et al., 2000). In regard to BED, available data suggest that relatives of probands with BED are approximately twice as likely to develop BED as relatives of unaffected individuals are (Hudson et al., 2006; Javaras et al., 2008). Some liability factors appear to be shared across eating disorder diagnoses (Thornton et al., 2011).

However, increased familial risk does not necessarily indicate a genetic contribution, as families also share environment, which may contribute to increased risk of the disorder as well. Using twin studies, we can discern the relative contribution of genetic and environmental factors via a comparison of concordance rates between monozygotic twins, who share 100% of their genes, and dizygotic twins, who share approximately 50% of their genes. Thus a concordance rate for an eating disorder between monozygotic twins that is twice as high as the concordance rate between dizygotic twins indicates an additive genetic effect. Twin studies have confirmed that AN and BN are both substantially heritable, with heritability estimates ranging from approximately 33 to 84% for AN and from 28 to 83% for BN (Bulik, 2005; Thornton et al., 2011). Recent twin research suggests that genetic and unique environmental factors overlap moderately in influencing liability to AN and BN (Bulik et al., 2010). Research on genetic contributions to BED lags behind that on AN and BN, but preliminary research suggests that heritability is likely to be approximately 31–50% (Reichborn-Kjennerud, Bulik, Tambs, & Harris, 2004). Recent findings comparing twins and singletons suggest that results from twin studies regarding eating pathology generalize to singleton samples (Munn-Chernoff et al., 2013).

Recognizing the significant contribution of genetics in the development of eating disorders, research has progressed to examining specific genes hypothesized to be involved in the pathophysiology of eating disorders. Unfortunately, few candidate gene association studies have replicated findings, although some results appear promising. For example, associations have been observed between eating pathology and the serotonergic system, including the serotonin transporter gene and various serotonin receptors (Bulik, 2005). In addition, a susceptibility locus for BN on chromosome 10p has been observed (Bulik et al., 2003), as well as a susceptibility gene for AN on chromosome 1 (Grice et al., 2002). However, the task of identifying specific genes involved in the pathogenesis of eating disorders remains difficult, particularly as eating disorders are likely to be caused by the interaction of many common, low-risk variants, with the effect size of each variant possibly too small to discern. Genome-wide association studies of eating disorder phenotypes continue to be conducted, with the aim of identifying genetic variants associated with eating disorder symptoms (Boraska et al., 2012).

Genetic contributions to eating pathology appear to vary across development. For females, puberty has a significant impact on genetic influence, with genetic factors accounting for 0% of eating pathology prior to puberty and approximately 50% of eating pathology after puberty (Klump et al., 2012) and into middle adulthood (Klump, Burt, et al., 2010). This effect has not been observed among males, suggesting the importance of interactions with biological factors such as ovarian hormones and/or other female-specific factors (Klump et al., 2012). Research continues to consider other variables that may interact with genetic liability to contribute to the development of eating pathology. Recently, researchers have considered how epigenetics (i.e., the reversible regulation of various genomic functions, mediated principally through changes in DNA methylation and chromatic structure, without changing the classical DNA sequence) may be relevant to the pathogenesis of eating pathology. Nutrition and dieting— two variables that are significantly influenced by, and influence, eating pathology—are interesting and important areas for further research that may be important to epigenetic processes in eating pathology.

Biological Mechanisms

There are numerous biological mechanisms implicated in the pathology of eating disorders. Initially, researchers believed that biological mechanisms were most relevant to the maintenance and perpetuation of disordered eating (Kaplan & Woodside, 1987); however, more recent research advances have also implicated biological factors in the predisposition to and precipitation of disordered eating. In particular, there is increasing evidence that individuals with eating disorders have disturbances of hypothalamic activity; alterations of serotonin, dopamine, and other neuromodulatory systems; and dysregulation of higher cortical functions (Kaye, Fudge, & Paulus, 2009). Many of these abnormalities are considered to have substantial impact on the pathogenesis of disordered eating.

However, determining to what degree biological symptoms and neural changes are causes or consequences of disordered eating remains a major methodological challenge. As eating disorders (in particular, AN) involve dietary restriction that can lead to malnutrition, the development and persistence of eating disorders can lead to widespread alterations of brain and peripheral organ functions (Kaye & Bailer, 2011). To determine causality, it must be demonstrated that a biological factor exists prior to the onset of the disorder (Jacobi et al., 2004). For many biological factors, further research is needed to substantiate a causal relationship. However, researchers are increasingly recognizing the significance of premorbid symptoms of eating disorders (e.g., anxiety, obsessionality, and inhibition in AN, and impulsiveness and sensation seeking in BN) and considering the possibility that the biological abnormalities observed in individuals with eating disorders may reflect trait-related premorbid dispositions.

Anorexia Nervosa

A growing body of research (e.g., Connan, Campbell, Katzman, Lightman, & Treasure, 2003; Lo Sauro, Ravaldi, Cabras, Faravelli, & Ricca, 2008; Misra et al., 2004) implicates hyperactivity of hypothalamic–pituitary–adrenocortical (HPA) axis functioning in AN, including among adolescents (Oskis, Loveday, Hucklebridge, Thorn, & Clow, 2012). In particular, evidence suggests that individuals with AN hypersecrete cerebrospinal fluid corticotropin-releasing hormone, plasma cortisol, and dehydroepiandrosterone. As such, HPA hyperactivity is speculated to arise from increased amounts of secretory bursts (Misra et al., 2004) and dysregulated feedback inhibition in the hypothalamus and/or higher brain centers (Connan et al., 2003). Notably, higher levels of cortisol have been associated with disordered eating psychopathology in women with widely varying body mass (Lawson et al., 2011); this finding implicates increased cortisol and HPA hyperactivity in the development of a variety of eating disorders, including AN, rather than simply being a consequence of starvation and malnutrition (Oskis et al., 2012).

Neurotransmitters have been strongly implicated in the biological mechanisms of AN as well. In particular, findings from genetic, pharmacological, and physiological research all indicate altered striatal dopamine function in AN (Kaye, 2008). For example, research indicates an altered frequency of functional polymorphisms of dopamine D2 receptor genes in individuals with AN (Bergen et al., 2005), and reduced cerebrospinal fluid dopamine metabolites in individuals with AN (Kaye, Ebert, Raleigh, & Lake, 1984) as well as individuals who have recovered from AN and obtained normal weight, nutritional intake, and menses (Kaye, Frank, & McConaha, 1999). This altered striatal dopamine function may contribute to a range of AN symptomatology, including altered feeding behavior; impaired decision making and executive control; increased stereotypic motor activity; and dysphoric mood and anhedonia (Bailer et al., 2012; Haber, Kim, Mailly, & Calzavara, 2006; Kaye, 2008). In particular, recent research has uncovered a positive association between endogenous dopamine release and anxiety in the precommisural dorsal caudate of individuals who have recovered from AN (Bailer et al., 2012). This association could in part account for the fact that eating (and the food-related release of dopamine) produces anxiety in individuals with AN (Bailer et al., 2012; Kaye et al., 2003), which is unlike the pleasurable experience that feeding typically provides for nonafflicted individuals. Thus, if individuals with AN experience endogenous dopamine release as anxiogenic rather than hedonic, dietary restraint may be an "effective" means of anxiety reduction (Bailer et al., 2012). In sum, growing evidence suggests that dopamine disturbances may represent traits that contribute to a vulnerability to the development of AN.

Serotonin is another neurotransmitter implicated in the AN disease process (Steiger, 2004), and it has specifically been proposed to play a role in the altered satiety, dysphoric mood, and impulse control observed

in AN (Kaye, 2008; Kaye et al., 2009; Kaye, Wierenga, Bailer, Simmons, & Bischoff-Grethe, 2013). For example, brain imaging studies have shown disturbances of serotonin function that persist after recovery in individuals with AN, including increased serotonin-1A binding and reduced serotonin-2A binding (Kaye, 2008; Kaye et al., 2013). Differences in serotonin functioning may contribute to differences in impulse control and differentiate individuals who develop restricting AN and those who develop binge-eating/purging AN (Kaye et al., 2013).

Further support for the role of serotonin in the AN disease process emerges from studies of tryptophan, an essential amino acid that is only available via one's diet and is the precursor of serotonin. Via dietary restriction, plasma tryptophan is lowered, resulting in a decreased plasma ratio of tryptophan to neutral amino acids, and a consequent reduction in the availability of tryptophan to the brain. This sequence in turn has an impact on serotonin function (Goodwin, Fairburn, & Cowen, 1987; Huether, Zhou, & Rüther, 1997). A limited body of research has indicated that malnourished, underweight women with AN have decreased availability of plasma tryptophan (Schweiger, Warnhoff, Pahl, & Pirke, 1986). Thus it has been postulated that a trait-related disturbance of serotonin neuronal modulation may predate the onset of AN and contribute to a vulnerability for restricted eating and dysphoric mood (Kaye, 2008). These individuals may learn that dietary restraint reduces anxious mood, via reducing plasma tryptophan availability and modulating serotonin functional activity (Kaye et al., 2003). This may in turn set the stage for the maintenance and chronicity of the disorder, as dietary restraint is reinforced by providing a reprieve from dysphoric mood (Herpertz-Dahlmann, Seitz, & Konrad, 2011; Kaye, 2008).

Bulimia Nervosa

Mounting evidence supports the substantial impact of biological mechanisms in both the development and maintenance of BN. A recent study indicated that individual differences in proneness to binge eating emerged during puberty in female rats (Klump, Suisman, Culbert, Kashy, & Sisk, 2011). As animals do not experience psychosocial risk factors for eating disorders, these findings place particular emphasis on the role of biology in the development of bulimic pathology, particularly during puberty. One biological factor that has received increasing research attention is ovarian hormones; a growing body of research indicates significant associations between levels of ovarian hormones and disordered eating, particularly bulimic symptomatology. For example, data indicate significant associations between changes in ovarian hormones (i.e., increases in progesterone and decreases in estradiol levels) and binge eating across the menstrual cycle in both clinical (Edler, Lipson, & Keel, 2007) and nonclinical (Klump, Keel, Culbert, & Edler, 2008) females. Likewise, more recent findings have indicated differential associations across the menstrual cycle between ovarian hormones and other specific disordered eating symptoms (e.g., body dissatisfaction and drive for thinness demonstrated stronger associations with ovarian hormones and greater variation across the menstrual cycle than dietary restraint; Racine et al., 2012), highlighting potentially distinct etiological biological processes for various eating symptomatology. As ovarian hormones regulate gene transcription in neurotransmitter systems implicated in eating disorders (e.g., serotonin; Klump & Culbert, 2007), associations between binge eating and ovarian hormones may reflect genomic effects on the production of neurotransmitters, their receptors, or their signal transduction mechanisms (Klump et al., 2008).

As in individuals with AN, altered functioning of the HPA axis has been observed in individuals with BN. However, findings concerning the directionality of these relationships have been mixed, suggesting heterogeneous stress response profiles and HPA functioning (Fichter, Pirke, Pöllinger, Wolfram, & Brunner, 1990; Koo-Loeb, Costello, Light, & Girdler, 2000; Monteleone et al., 2001; Neudeck, Jacoby, & Florin, 2001; Steiger et al., 2001). A recent study of women with a bulimia spectrum disorder indicated less cortisol suppression, as compared to healthy controls, in response to the dexamethasone suppression test (Bruce et al., 2012). Nonsuppression was also associated with elevated depression and anxiety symptoms. This response may reflect a trait-like, genetically determined disposition toward down-regulation of glucocorticoid receptor sensitivity, which may contribute to the development of comorbid bulimic and mood disorders (Bruce et al., 2012).

Alterations in striatal dopamine have additionally been implicated in BN, although the specific role that dopamine plays in the etiology and maintenance of BN remains less clear (Broft, Berner, Martinez, & Walsh, 2011). Notably, the binge-eating behavior characteristic of BN is a complex behavior that parallels the etiology

and biology of addictive behaviors (e.g., substance use), and a large body of research suggests that dopamine plays a role in the rewarding properties of food intake and addiction (Broft et al., 2011). For example, eating palatable foods activates dopaminergic neurons within the nucleus accumbens and other reward centers; repeated stimulation of this system as a means to relieve negative affect is associated with the development of both binge eating and substance abuse (Koob & Le Moal, 2008). Alterations in the functioning of these natural reward pathways, including dopamine and endogenous opioid systems, have been observed in individuals with binge eating, including altered dopamine receptor and dopamine transporter gene expression (Shinohara et al., 2003) and decreased opioid receptor binding within the insular cortex (Bencherif et al., 2005).

Altered serotonin neurotransmitter activity may also contribute to susceptibility to BN symptomatology (Kaye, Strober, Stein, & Gendall, 1999; Kaye et al., 2009; Pichika et al., 2012). Research with women with BN has indicated a moderating effect of the serotonin system on binge antecedents and outcomes. Specifically, lower platelet paroxetine-binding density in bulimic women predicted poorer prebinge mood and self-esteem, and larger postbinge decreases in mood and self-esteem and increases in cognitive dietary restraint (Steiger et al., 2005). These findings suggest that the serotonin system is involved in bulimic pathology via creating a susceptibility to mood dysregulation and affecting the proposed affect-mediated pathway to binge eating. Notably, individuals who recover from bulimic pathology continue to demonstrate serotonin alterations (Kaye et al., 1998, 2001), suggesting that such alterations may be trait-related and contribute to the development of bulimic pathology (Pichika et al., 2012).

Binge-Eating Disorder

Research examining biological mechanisms implicated in BED lags behind that on AN and BN. However, the defining feature of binge eating that characterizes both BED and BN suggests that research examining biological mechanisms involved in binge eating in individuals with BN may generalize to individuals with BED. However, notable differences in clinical presentation are evident between the two disorders (e.g., the high prevalence of overweight and obesity, and the absence of compensatory behavior, among individuals with BED), which emphasize that caution should be taken in generalizing findings across disorders. Further research of biological mechanisms with BED samples is needed.

Childhood Experiences

Eating pathology has been associated with various adverse life events experienced in childhood. In particular, adverse life events have been observed to precipitate the onset of eating pathology, suggesting that such adverse experiences increase risk of developing an eating disorder. For example, a retrospective comparison of 102 women with BN and 204 age-matched control women without an eating disorder indicated that women with BN reported more life events occurring throughout the year before the onset of disordered eating than reported by control women of the same age (Welch, Doll, & Fairburn, 1997). Specifically, women with BN more commonly reported a major house move, a major episode of illness, pregnancy, a change in family structure, sexual abuse, and/or physical abuse during the year before onset of pathology. Furthermore, a dose–response effect was observed: A greater number of events experienced was associated with an increased likelihood of having BN. In addition, longitudinal research has identified unique associations between particular childhood adverse life events and particular eating and weight problems (Johnson, Cohen, Kasen, & Brook, 2002), indicating that certain disordered eating symptoms (e.g., self-induced vomiting) may be more likely to follow certain adverse childhood experiences (e.g., sexual abuse) than others.

However, the strength of this association has been questioned. The authors of a comprehensive review of risk factors for eating disorders (Jacobi et al., 2004) cautioned that the potency of adverse life events on eating pathology is small; that the evidence for an association with adverse life events in general is less consistent than for specific life events; and that more prospective research in this area is needed. Critically, the association with general adverse experiences may lack specificity to the development of eating pathology, as adverse life events may increase risk for the development of psychopathology in general (Jacobi et al., 2004; Wade, Gillespie, & Martin, 2007). More research is needed to determine specific mechanisms that may lead to the development of eating pathology, rather than symptoms of other psychopathology, following adverse life experiences.

In regard to particular adverse life events associated with the development of eating disorders, associations

between childhood trauma and eating pathology have been often researched and frequently observed. An examination of participants from the NCS-R indicated that 100%, 100%, and 93.3% of women with lifetime AN, BN, and BED, respectively, had previously experienced at least one type of trauma (Mitchell, Mazzeo, Schlesinger, Brewerton, & Smith, 2012). Interpersonal trauma (i.e., kidnapped or held captive, beaten by parents/guardians as a child, beaten by a spouse or romantic partner, beaten by anyone else, mugged or threatened with a weapon, raped, experienced sexual assault other than rape, stalked, or witnessed serious physical fights at home as a child) was particularly prevalent: 71.2%, 78.2%, and 63.7% of women with lifetime AN, BN, and BED, respectively, endorsed experiencing at least one type of interpersonal trauma. Likewise, 100%, 100%, and 98.40% of men with lifetime AN, BN, and BED, respectively, had experienced at least one trauma—including 68.2%, 100%, and 74.3% of men with lifetime AN, BN, and BED, respectively, who had experienced at least one interpersonal trauma. Rates of lifetime PTSD were also elevated among individuals with eating disorders, particularly among individuals with BN (see "Common Comorbidities"), although the majority of individuals with eating disorders did not endorse comorbid PTSD (Mitchell et al., 2012). Thus childhood trauma—in particular, trauma involving a threat to one's interpersonal safety and/or security—may be associated with eating pathology. However, it is likely to be only one of several possible pathways to the development of an eating disorder, and may not be specific to the development of eating pathology versus other psychopathology.

The role of childhood abuse, especially childhood sexual abuse, has been particularly widely examined as a type of childhood trauma associated with eating pathology (Jacobi et al., 2004). Unfortunately, the majority of research has been cross-sectional, limiting conclusions regarding causality and the direction of effects. However, one community-based longitudinal study of 782 mothers and their offspring indicated that children who had experienced sexual abuse or physical neglect were at increased risk of developing subsequent eating problems (e.g., recurrent fluctuations in weight, strict dieting, and self-induced vomiting) and/or an eating disorder during adolescence or early adulthood (Johnson et al., 2002). Similar to associations with adverse life events in general, associations between eating pathology and childhood abuse appear to be largely nonspecific, with similar associations observed between childhood abuse and other psychopathology (Fairburn, Welch, Doll, Davies, & O'Connor, 1997; Welch & Fairburn, 1996). For example, a survey of 7,403 randomly selected English adults examined associations between childhood sexual abuse and multiple psychiatric disorders: depressive episode, mixed anxiety and depression, generalized anxiety disorder, panic disorder, OCD, drug dependence, alcohol dependence, and eating disorders. Results indicated that the association between childhood sexual abuse and psychopathology was nonspecific (Jonas et al., 2011).

Beyond various types of adverse life events, poor attachment to caregivers—a process that begins in infancy—has also been associated with the development of eating disorders. According to the interpersonal theory of eating disorders (Sullivan, 1953; Wilfley, Pike, & Streigel-Moore, 1997), attachment plays a fundamental role in the development and maintenance of eating pathology, particularly binge eating. Specifically, insecure attachment with significant caregivers is theorized to contribute to low self-esteem and the use of binge eating as an alternative, yet maladaptive, means to regulate negative emotions. Numerous empirical studies have supported the theorized associations between attachment and eating pathology. Individuals with eating disorders report more attachment concerns than individuals without eating disorders (Illing, Tasca, Balfour, & Bissada, 2010). Associations have been reported between attachment and overall severity of eating pathology (Eggert, Levendosky, & Klump, 2007), as well as specific disordered eating symptoms such as dietary restraint (Turner, Bryant-Waugh, & Peveler, 2009) and body dissatisfaction (Abbate-Daga, Gramaglia, Amianto, Marzola, & Fassino, 2010; Troisi et al., 2006). Among a sample of 555 children ages 8–11 years, insecure attachment was associated with loss-of-control eating, and it mediated the association between self-esteem and loss-of-control eating (Goossens, Braet, Bosmans, & Decaluwé, 2011). Likewise, a 1-year longitudinal study with 601 children ages 8–11 indicated that after adjustments for gender and baseline eating pathology and weight, insecure attachment to one's mother prospectively predicted increased dietary restraint, eating concerns, weight concerns, shape concerns, and adjusted body mass index (Goossens, Braet, Van Durme, Decaluwé, & Bosmans, 2012). Insecure attachment to one's father prospectively predicted persistence in subjective binge-eating episodes (Goossens et al., 2012), highlighting the differential impact of attachment to mother and father on eating pathology.

In addition, a recent examination indicated that both emotion dysregulation and social comparison mediated the association between insecure attachment and eating pathology (Ty & Francis, 2013).

Unfortunately, the majority of research that explores the role of adverse childhood experiences—including stressful and traumatic events, as well as poor attachment to caregivers—in the development of eating pathology has failed to control for parental psychopathology, which may affect children's psychopathology via environmental effects, genetic effects, and/or gene–environment interactions. More genetically informed research examining adverse childhood experiences and eating pathology is needed to parse their interrelationship.

Adolescent Development

Across adolescence, many developmental challenges and transitions are encountered that have been theorized to increase risk for eating pathology, particularly among females. In particular, significant physical maturation, further development of self-identity, and shifting importance of interpersonal relationships have been considered to contribute to risk for eating pathology.

Physical Maturation

Adolescence is associated with numerous physical changes associated with puberty that may heighten adolescents' awareness of their bodies. For boys, physical maturation typically involves the development of muscle and lean tissue. For girls, such maturation includes onset of menarche, breast development, and increased adiposity (Stang & Story, 2005). Whereas boys may view their physical changes positively, some girls may perceive their own physical changes as leading them further away from the cultural ideal of a thin physique, and this perception may trigger elevated body dissatisfaction, increased dietary restraint, and use of other weight control behaviors. Thus these differences in girls' and boys' physical maturation during adolescence may partially explain the disproportionate increase in eating pathology among girls during this period of development. Furthermore, elevated levels of reproductive hormones among girls during this time have been hypothesized to activate genes responsible for eating pathology (Klump et al., 2006; Klump, Keel, Sisk, & Burt, 2010). Indeed, while puberty has been found to affect genetic risk for disordered eating among females, no such effect has been observed among males (Klump et al., 2012), emphasizing the importance of this period in the development of eating disorders among females.

Following onset of puberty and the associated physical changes, increased prevalences of dieting and other forms of eating pathology have consistently been observed among girls (Attie & Brooks-Gunn, 1989; Bulik, 2002; Killen et al., 1992). Females who undergo puberty at an earlier age than their peers are at particularly increased risk for eating pathology (Jacobi et al., 2004), and such pathology is more strongly associated with pubertal stage than with chronological age during the peripubertal period (Killen et al., 1992). Recently, the genes that predispose girls to early pubertal timing have also been determined to increase risk for dieting (Harden, Mendle, & Kretsch, 2012), suggesting a common genetic vulnerability. However, early menarche has also been associated with a range of psychiatric disorders, psychological symptoms, and adjustment problems beyond those associated with eating disorders (Graber, Lewinsohn, Seeley, & Brooks-Gunn, 1997).

Despite the strong associations demonstrated between pubertal development and eating pathology among girls, recent research suggests that this association is limited to the adolescent period, regardless of pubertal timing. Specifically, a longitudinal study of 1,964 twins from the Swedish Twin Study of Child and Adolescent Development indicated that significant associations between pubertal development and eating pathology in early to middle adolescence were no longer significant in young adulthood (Baker, Thornton, Lichtenstein, & Bulik, 2012). Thus it appears that timing of puberty is an important risk factor for eating pathology, but that progression through puberty likewise increases risk, regardless of pubertal timing.

Self-Identity

Beyond changes to one's physical body, adolescence is associated with changes to one's psychological identity for both girls and boys, including critical development of one's sense of self. During early adolescence, the ability to reflect on one's thoughts and behaviors increases, and self-perceptions often become increasingly unstable (Rosenberg, 1986). As a result, new self-awareness emerges, as well as increasing concern about how one is perceived by others. Moreover, physical appearance (including weight and shape) becomes an increasingly salient aspect of perceived self-worth

(Lunde & Frisén, 2011), and the adolescent years are often considered the most influential period in shaping one's body image (Levine & Smolak, 2002). Thus this developmental period sets the stage for eating pathology to occur, as some individuals begin attempting to change their shape and weight in order to improve their self-concept.

Since the early psychodynamic theories of eating disorders were developed, eating pathology has often been construed as a disorder of the self. One of the earliest theorists, Hilde Bruch, theorized that AN is caused by impairments in identity development. According to Bruch (1981, 1982), in order to compensate for a lack of clear identity, adolescents may focus on their body shape and weight as a personally controllable self-domain that is highly salient and culturally valued. More recent theoretical models of eating disorders have greatly evolved, yet still often emphasize that disturbed self-image and low self-worth are fundamental to eating pathology (Fairburn, Cooper, et al., 2003), and that individuals attempt to resolve such self-perceptions by controlling their eating and focusing on the pursuit of thinness (Polivy & Herman, 2002). For some adolescents, an excessive focus on dietary control and weight loss may provide a means to channel identity concerns and to avoid recognizing and managing other issues. Mounting empirical evidence has supported these assertions. For example, a study of 5,287 adolescent girls indicated that girls who had high levels of eating pathology were characterized by unstable self-perceptions and low self-esteem (Kansi, Wichstrøm, & Bergman, 2003). Likewise, core low self-esteem has prospectively predicted eating symptomatology (Button, Sonuga-Barke, Davies, & Thompson, 1996; Leon, Keel, Klump, & Fulkerson, 1997) and poor response to eating disorder treatment (Fairburn, Cooper, et al., 2003).

Interpersonal Relationships

The increasing importance of peer relationships during adolescence can also have an impact on the development of eating pathology. Adolescence is a period of development characterized in part by increasing concern about social acceptance (Harter, 2012). During this period, adolescents seek greater independence from their families, and place greater importance on interpersonal relationships with peers (McCabe, Ricciardelli, & Finemore, 2002; Steinberg, 2001). In comparison to perceived parental approval, perceived peer approval is more strongly associated with perceived physical attractiveness (Harter, 2012), further contributing to adolescents' concerns about their weight, shape, and overall appearance, and ultimately to risk of developing an eating disorder. According to one interpersonal model of eating disorders (Rieger et al., 2010), changing social contexts and associated shifts in determination of self-worth during adolescence can result in negative self-evaluation, which in turn promotes eating pathology in some individuals. This model states that adolescence is a period of increased risk for eating disorders because it is a period of development wherein self-esteem is particularly influenced by social evaluation; peer acceptance is increasingly important for self-esteem; and appearance is increasingly perceived as important for peer acceptance. Relatedly, an interpersonal model specific to binge eating was evaluated in a sample of 219 non-treatment-seeking girls and boys ages 8–17 years. The model proposes that social problems lead to negative affect, and in turn to binge-eating episodes as a means to cope with such affect (Elliott et al., 2010). Results supported the model.

In addition, adolescence involves an increasing interest in romantic relationships, and many adolescents begin dating during this period. Romantic and/or sexual involvement may heighten awareness of one's physical appearance, including one's weight and shape, due to the centrality of physical appearance in partner selection and attraction. Some adolescents may become dissatisfied with their body image because they are concerned that they do not meet cultural ideals, and so may attempt to control their eating, shape, and weight. Previous research indicated increased dieting and eating pathology among adolescent girls involved in social and sexual activities with boys, as compared to adolescent girls not thus involved. The association was particularly strong among postmenarcheal girls (Cauffman & Steinberg, 1996). In addition, adolescent girls who place greater importance on popularity with boys have reported increasing body dissatisfaction, with this association fully mediated by the belief that boys perceive thinness to be important to girls' attractiveness (Paxton, Norris, Wertheim, Durkin, & Anderson, 2005). Overall, adolescent romantic and/or sexual activity has been associated with a range of disordered eating symptoms; however, it has also been associated with symptoms extending beyond eating pathology, including depressive, anxiety, and externalizing symptoms, calling into question the specificity of this effect (Starr et al., 2012).

Personal and Family Weight History

The development of eating pathology has also been associated with a history of personal and parental overweight and obesity. Overweight children report more severe disordered eating cognitions and behaviors, including higher frequency of loss-of-control eating, than normal-weight children do (Tanofsky-Kraff et al., 2004). In addition, the majority of overweight children report becoming overweight before the onset of dieting or loss-of-control eating (Tanofsky-Kraff et al., 2005). Community-based case–control studies have also indicated that retrospectively reported childhood obesity is elevated among women with BN (Fairburn et al., 1997) and BED (Fairburn et al., 1998), in comparison to both healthy control participants and general psychiatric control participants. Unfortunately, the majority of research in this area is retrospective and/or cross-sectional, limiting the inferences that can be drawn. However, a prospective study of 153 girls indicated that girls who were at risk for overweight at age 5 years (i.e., body mass index ≥ 85th percentile), relative to girls who were not at such risk, reported significantly higher levels of body dissatisfaction, weight concern, dietary restraint, and disinhibited eating at age 9 years. Furthermore, a prospective study of 1,597 children demonstrated that parents' perceptions of their children's weight may be a stronger predictor of the development of eating disorders than the children's objective weight (Allen, Byrne, Forbes, & Oddy, 2009). Such parental perceptions at ages 8 and 10 years not only predicted eating disorder caseness at age 14 years, but also differentiated between adolescents with an eating disorder and psychiatric control participants, suggesting that parents' perceptions of their children's weight is a specific risk factor for the development of eating pathology.

The latter study also indicated prospective associations between parental weight status and subsequent development of an eating disorder (Allen et al., 2009). Specifically, elevated maternal body mass index at 16 weeks of gestation predicted eating disorder caseness at age 14 years, relative to general control participants. However, this association was not specific to eating pathology compared to other psychopathology, indicating that maternal weight status was associated with risk for psychiatric disturbances in general. Other prospective research indicates that girls whose parents are both overweight demonstrate greater increases in disinhibited eating from the ages of 5 to 13 years than girls whose parents are not both overweight (Francis, Ventura, Marini, & Birch, 2007). Cross-sectional research has also indicated that daughters of overweight mothers endorse greater dietary restraint and body dissatisfaction than daughters of normal-weight mothers do (Jacobi, Schmitz, & Agras, 2008). Finally, individuals with a personal and/or paternal history of obesity have also demonstrated a poorer response to treatment for eating disorders and a greater likelihood of perpetuation of eating pathology (Fairburn et al., 1995).

Are Eating Disorders Addictions?

Eating disorders and substance use disorders, as well as other addictive behaviors including DSM-IV pathological gambling/DSM-5 gambling disorder, often co-occur at higher than expected rates (see, e.g., Baker, Mitchell, Neale, & Kendler, 2010; Petry, Stinson, & Grant, 2005; von Ranson, Wallace, Holub, & Hodgins, 2013). In particular, recurrent binge eating, with or without compensatory behaviors, is frequently comorbid with substance use disorders and other addictive behaviors (Holderness, Brooks-Gunn, & Warren, 1994; Sinha & O'Malley, 2000; Umberg, Shader, Hsu, & Greenblatt, 2012; von Ranson et al., 2013). These associations have spurred a great deal of interest in the theory that BN and BED, as well as obesity, might be addictive disorders akin to substance addictions (e.g., Cassin & von Ranson, 2007; Davis et al., 2011; Speranza et al., 2012; Umberg et al., 2012). Some have observed that substance and behavioral addictions share such hallmark features as loss of control and craving (e.g., Davis & Carter, 2009; Gearhardt, White, & Potenza, 2011), and that both involve attempts to regulate one's emotions (Haylett, Stephenson, & Lefever, 2004). It has been proposed that behavioral addictions and substance use disorders may both be maintained via altered neurobiological self-control and reward pathways (e.g., Davis & Carter, 2009; Gold, Frost-Pineda, & Jacobs, 2003; Umberg et al., 2012). Animal models of "food addiction" have been developed and tested, with some findings indicating that neurochemical responses to binge intake of sugar are similar to those observed in response to intake of some drugs (e.g., Avena, 2010). The argument has been made that knowledge about substance addiction may assist in the treatment of obesity (Volkow & Wise, 2005). However, a crucial difference exists between eating disorders or obesity considered as ad-

dictive behaviors, and other forms of substance or behavioral addictions: One can abstain from taking drugs or from gambling, but one cannot abstain from eating, which makes treatment more complicated for eating-related problems.

Others believe that arguments emphasizing similarities between eating disorders and addictive behaviors overlook important differences between them, and selectively attend to confirmatory and not disconfirmatory evidence (Wilson, 2010). For example, although rates of substance use disorders are high among those with eating disorders, depression and anxiety disorders are even more common comorbid conditions (see "Common Comorbidities," above). As a result, the theory that eating disorders are forms of addiction remains somewhat contentious (von Ranson & Cassin, 2007; Wilson, 2010).

With gambling disorder recently having joined substance use disorders in DSM-5 in a new diagnostic category—substance-related and addictive disorders—suddenly behavioral addictions have taken a leap toward legitimacy (APA, 2013a). There is a brief explanation in the introductory text to the DSM-5 feeding and eating disorders chapter justifying the exclusion of eating disorders from the addictive disorders category, on the basis of inadequate comprehension of the shared and distinct etiological and maintaining factors in these two types of problems (APA, 2013a). The boundaries among BED, obesity, and food addiction are not yet clear (Gearhardt et al., 2011) but remain avidly studied.

Personality

Personality traits have long been theorized to play a key role in both the onset and maintenance of eating disorder symptoms, and a great many studies have examined a wide range of personality characteristics among those with eating disorders. Most research efforts have focused on examining a handful of selected personality traits at a time, although a few studies have used broader measures of personality. In summary, traits that have been consistently observed in both AN and BN include perfectionism, obsessive–compulsive symptoms, neuroticism, negative emotionality, harm avoidance, low self-directedness, low cooperativeness, and traits associated with avoidant personality disorder (Cassin & von Ranson, 2005). However, distinct personality traits are also observed in specific eating disorders. Specifically, AN has been linked with high levels of constraint and persistence, and low levels of novelty seeking; in contrast, BN has been linked with high levels of impulsivity, sensation seeking, novelty seeking, and traits associated with borderline personality disorder (Cassin & von Ranson, 2005). Research on personality traits in BED remains limited.

Despite these trends related to eating disorder diagnosis, it is worth noting that there is considerable heterogeneity in personality traits across eating disorder types. Nevertheless, a replicated finding is that most individuals with AN and BN can be categorized into one of three personality types: high-functioning/perfectionistic, constricted/overcontrolled, and emotionally dysregulated/undercontrolled (Westen & Harnden-Fischer, 2001; Wildes et al., 2011; Wonderlich, Joiner, Keel, Williamson, & Crosby, 2007). These personality groups have shown the ability to predict eating disorder symptoms, adaptive functioning, and sexual abuse history. Those who adapt the best tend to exhibit high-functioning/perfectionistic personality characteristics; those with prominent anorexic symptoms tend to exhibit constricted/overcontrolled personality characteristics; and those with prominent bulimic symptoms tend to exhibit emotionally dysregulated/undercontrolled personality pathology (Westen & Harnden-Fischer, 2001). Among people with AN, the undercontrolled type has been associated with worse outcome at treatment discharge than the other types, including higher rates of discharge against medical advice and readmission (Wildes et al., 2011).

Personality research has important implications for our understanding of the etiology of eating disorders. The heritability of personality characteristics is approximately 50%, suggesting that our personalities are shaped about equally by genes and environment (Tellegen et al., 1988). Thus one plausible means by which genes may influence individuals' risk of developing eating disorders may be through heritable personality traits (Klump et al., 2004).

Evidence has been accumulating that impulsivity is a key predictor of the liability to develop binge-eating symptoms (Anestis, Selby, & Joiner, 2007; Claes, Vandereycken, & Vertommen, 2005; Fischer & Smith, 2008). A particular type of impulsivity, negative urgency—or the tendency to act rashly in response to negative affect—appears to be especially important. A recent study of 222 female same-sex twin pairs found that negative urgency was related to binge eating even after the investigators controlled for elevated negative

affect, and that genetic factors accounted for about two-thirds of this association (Racine et al., 2013). Thus genetically mediated tendencies to experience negative emotions, and to act rashly in response to such affect, are linked to risk for binge eating.

The role of perfectionism in eating disorders is a popular area of study. Perfectionism appears to be important, although its precise role with respect to eating disorders continues to be investigated. For example, a study of daily fluctuations in perfectionism and eating disorder symptoms found that these symptoms covaried among women across the day, which provides strong evidence of a direct association (Boone et al., 2012). It has been proposed that perfectionism serves as an etiological and maintaining mechanism for eating disorders as well as for anxiety disorders and depression, and thus merits targeting in treatment (Egan, Wade, & Shafran, 2011). Theorists have argued that the tendencies to prioritize attaining and maintaining social status or rank, to hide mistakes and imperfections, and to ruminate over perceived mistakes are particularly problematic for individuals with eating disorders (Bardone-Cone et al., 2007; Nolen-Hoeksema, Stice, Wade, & Bohon, 2007). Among recent findings are that perfectionism mediates the relationship between eating disorder and obsessive–compulsive symptoms among women with BN or subthreshold BN, and so may help to explain comorbidity between these sets of symptoms (Bernert et al., 2013). Also, degree of perfectionism may differ according to stage of illness of the eating disorder: In one study, recovered women had comparable levels of perfectionism as healthy controls, whereas those who were partially recovered and women with an acute eating disorder had comparable levels, which were greater than those of women who had recovered (Bardone-Cone, Sturm, Lawson, Robinson, & Smith, 2010).

The Role of the Family

Although this line of thought has been controversial, families have historically been theorized to be a primary cause of the development of eating disorders in children and adolescents. For example, Minuchin, Rosman, and Baker (1978) theorized that certain pathological interactive familial processes were fundamental to the pathogenesis of AN, including enmeshment, overprotectiveness, rigidity, and conflict avoidance. They maintained that families of adolescents with AN are "psychosomatic," in that they transform emotional conflicts into somatic symptoms. Minuchin and colleagues' view of the family as a necessary context for the development of AN has subsequently been supported by cross-sectional research showing that family dysfunction is associated with disordered eating in children and adolescents.

A large-scale review of putative risk factors for eating disorders (Jacobi et al., 2004) indicated that individuals with AN and BN report various aspects of their family structure (e.g., interaction, communication, cohesion, and affective expression) to be more disturbed, conflictual, pathological, and/or dysfunctional than those of healthy controls are reported to be. Four specific family factors that have garnered increasing research attention include (1) parental overprotection and high control; (2) family weight-related teasing and critical comments; (3) family focus on appearance; and (4) maternal eating pathology. Parental overprotection and high control have been suggested to hinder adolescents' ability to self-regulate emotions and behaviors, and to act competently and independently. In turn, adolescents may develop lowered perceptions of self-competence and seek to experience a sense of independence and self-control via changing their bodies or eating habits. Such pursuits may lead adolescents to become preoccupied with body image, and later to engage in weight loss strategies such as dietary restriction and binge–purge cycles (Salafia, Gondoli, Corning, Bucchianeri, & Godinez, 2009). Across numerous studies, family weight-, food-, and appearance- related teasing have been associated with the development of eating pathology, including body dissatisfaction, thin-ideal internalization, binge eating and purging, use of extreme weight control behaviors, and overweight status (Annus, Smith, Fischer, Hendricks, & Williams, 2007; Eisenberg, Berge, Fulkerson, & Neumark-Sztainer, 2012; Keery, Boutelle, van den Berg, & Thompson, 2005; Neumark-Sztainer et al., 2007; Wade et al., 2007; Wojtowicz & von Ranson, 2012). Preliminary evidence has indicated that the association of teasing with eating pathology is mediated by increased expectancies for reinforcement from eating and thinness (Annus et al., 2007). A family focus on appearance has also been associated with disordered eating behaviors, which may be partially mediated by increased body dissatisfaction (Kluck, 2010). Researchers have speculated that individuals raised in appearance-focused families may be more aware of and concerned about their physical appearance and how it fits with familial and societal standards (Kluck, 2010). Older rather than younger children (i.e.,

ages 9–10 years vs. ages 7–8 years; Anschutz, Kanters, Van Strien, Vermulst, & Engels, 2009) and individuals with high neuroticism (Davis, Shuster, Blackmore, & Fox, 2004) may be particularly at risk of developing eating pathology within the context of an appearance-focused family. Finally, symptoms of maternal eating pathology—including maternal body dissatisfaction, drive for thinness, and eating disorder diagnosis—and maternal overweight status have all been associated with child and/or adolescent eating pathology (Anschutz et al., 2009; Canals, Sancho, & Arija, 2009; Jacobi et al., 2008; Stein et al., 2006). This link between parent and child eating pathology may be attributable to shared genetic risk, as well as modeling and/or reinforcement of pathological symptoms and behaviors.

However, methodological limitations have limited the strength of conclusions that can be drawn from the available research in this area. Critically, the majority of studies in this area are cross-sectional and/or rely on retrospective recall. Of the prospective studies that have examined the effects of family factors on predicting later onset of disordered eating, some studies have found such factors to be significant predictors (Beato-Fernandez, Rodriguez-Cano, Belmonte-Llario, & Martinez-Delgado, 2004; Johnson et al., 2002; Neumark-Sztainer et al., 2007; Salafia et al., 2009), whereas others have not (Attie & Brooks-Gunn, 1989; Graber, Brooks-Gunn, Paikoff, & Warren, 1994; McKnight Investigators, 2003; Nicholls & Viner, 2009). Such conflicting findings emphasize that family-related influences are likely to be complex and interactive. Furthermore, conclusions from longitudinal studies are at times limited by not beginning assessment early enough in the lifespan, not continuing assessment late enough in the lifespan, and/or not controlling for initial eating disturbances (Jacobi et al., 2004). Most longitudinal studies have not been genetically informed and hence have failed to account for the moderate to large heritability of eating pathology.

In addition, research has inconsistently discriminated between risk factors and early symptoms and/or correlates of eating disorders (Jacobi et al., 2004). Increasingly, researchers are examining the possibility that negative family dynamics are *outcomes* of the development of an eating disorder. Indeed, the lack of longitudinal research showing that family factors significantly predict the development of eating pathology has led to a recent conceptual shift away from emphasizing family etiological factors and toward emphasizing family maintenance mechanisms. Many researchers have hypothesized that high levels of family distress and dysfunction are likely to be the *outcomes* of living with a child with a medically dangerous and chronic condition (Nilsson, Engstrom, & Hagglof, 2012; Sim et al., 2009; Ward, Tiller, Treasure, & Russell, 2000). A recent longitudinal, population-based study that used cross-lagged structural models to control for preexisting and within-age associations indicated that parent–child conflict is a consequence of disordered eating (in particular, weight preoccupation), rather than a precipitant of such eating (Spanos, Klump, Burt, McGue, & Iacono, 2010). This study's analytic approach provided a particularly rigorous test of causality, as well as strong support for the aforementioned hypothesis. In addition, prospective research designs have demonstrated that improvements in family functioning (e.g., increased closeness and decreased distance in family climate) are associated with recovery from adolescent-onset eating disorders; these changes in family function are observed subsequent to improvement in eating pathology (Nilsson et al., 2012). Thus more recent study designs and findings reinforce family context as a consequence or maintaining variable rather than a causal one.

Another limitation of available research is that studies have often lacked psychiatric control groups, and this lack has led to questions about the specificity of effects. Identified family factors may be associated with risk for psychopathology in general (e.g., depression, anxiety), rather than with disordered eating specifically. Overall, very few specific, replicated family risk factors have emerged, with further research in this area needed. Authors of a recent authoritative review have suggested that family factors preceding the onset of eating disorders are likely to increase risk for psychopathology in general (Le Grange, Lock, Loeb, & Nicholls, 2010). They postulate that this general risk may subsequently interact with genetic and biological vulnerabilities to trigger particular phenotypes of disordered eating.

On the other hand, it is also important to consider that family factors may serve as *protective factors* against the development of eating disorders, maintenance of these disorders, or both. For example, frequent family meals and a positive atmosphere at family meals (Neumark-Sztainer et al., 2007), high levels of family support and connectedness (Croll et al., 2002; Perkins, Luster, & Jank, 2002), and positive family communication (Fonseca, Ireland, & Resnick, 2002) have all been observed to protect against the development of eating disorders.

Overall, minimal evidence supports the theory that family factors play a primary and specific causal role in the development of eating disorders. Experts have speculated that family factors are probably among several groups of factors that play a role in the genesis and maintenance of eating disorders, and that they can also serve a protective function against and facilitate recovery from such pathology (Le Grange et al., 2010). Further research in this area is necessary to determine specific family factors that contribute to the development of eating pathology, trigger genetic susceptibility for eating pathology, and/or protect against the development and perpetuation of eating pathology.

FUTURE DIRECTIONS

Several areas of research stand out as potentially fruitful to consider in the coming years. Research is clearly needed on the diagnostic categories revised in, added to, or proposed for further study in DSM-5, particularly ARFID and the various forms of OSFED (low-frequency AN, BN, and BED; purging disorder; and night eating syndrome). With clear definitions, research on these syndromes can proceed apace. Primary questions pertain to their validity, reliability, and clinical utility. Further work is required to describe these problems and their interrelationships, and to examine the appropriateness of the boundaries we have drawn between them. The relationship of feeding and eating disorders with obesity also deserves continued scrutiny. Now that feeding disorders and eating disorders have been combined into a single category, the stage is set for the study of developmental aspects of all these disorders to come to the fore—including research on their epidemiology, symptom expression, developmental course, correlates, and outcome among people of all ages.

Other topics in need of further evaluation relate to the validity of various models of the development and maintenance of feeding and eating disorders, including the construct of food addiction, as well as research into biological and genetic underpinnings of these common and often disabling problems. As is always the case, attention to methodological issues remains critical, such as examining the specificity of relationships through the use of appropriate control groups, and using longitudinal, prospective designs to study such questions as the temporal order of symptom onset. For example, starting longitudinal studies in childhood, before many symptoms have already started to develop, is optimal; adolescence or adulthood is often too late. Careful attention to study design is of paramount importance in the identification and study of risk factors, as described aptly by Kraemer, Stice, Kazdin, Offord, and Kupfer (2001). The study of interactions, including epigenetics and gene–environment interactions, may hold particular promise for the development and refinement of treatment and prevention programs, as we identify important mediators and moderators of change and continue to build our knowledge base regarding eating disorders.

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CHAPTER 18

Personality Disorders in Children and Adolescents

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Children and adolescents differ strikingly in their emerging personalities. Already by childhood, youth vary in their typical positive and negative emotions; capacities for self-control and positive relationships with others; feelings of empathy and warmth versus hostility and alienation; and views of themselves, others, and their life experiences. For some youth, their typical personality patterns may begin to cause them difficulties in life; for example, their problematic personality patterns may lead them to experience high levels of distress or serious impairment in their daily lives, particularly in their relationships or self-development. These difficulties may become severe enough for some youth to be diagnosed with a personality disorder (PD); for others, the problems may not reach clinical significance, yet may still bear negative consequences. Both the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV; American Psychiatric Association [APA], 1994) and DSM-5 (APA, 2013) acknowledge that youth may experience PDs warranting treatment. The diagnostic manuals define PDs in terms of problematic cognition, affectivity, interpersonal functioning, and impulse control—all personality differences that vary in children and adolescents and that may become disturbed well before adulthood.

The present chapter surveys the existing state of knowledge about PDs in the first two decades of life. Although there is far less research on PDs in childhood and adolescence than on other early-emerging disorders, the research that does exist has made it clear that personality pathology does occur in childhood and adolescence and poses significant risks for mental health problems and impairment both concurrently and later in life (Cohen, Crawford, Johnson, & Kasen, 2005; De Fruyt & De Clercq, 2012; Freeman & Reinecke, 2007; Hill, 2008; Johnson et al., 2012; Mervielde, De Clercq, De Fruyt, & van Leeuwen, 2005; Shiner, 2007, 2009; Tackett, 2010; Tackett, Balsis, Oltmanns, & Krueger, 2009; Westen & Chang, 2000). This is an exciting time for research on PDs because researchers are finally turning their attention to the early manifestations of personality pathology and to the antecedents of adult PDs (see, e.g., the recent special issues of *Clinical Psychology: Science and Practice*, DeFife & Ritschel, 2013; *Development and Psychopathology*, Cicchetti & Crick, 2009; *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, Biskin & Paris, 2013; *Journal of Personality Disorders*, Tackett & Sharp, 2014; *Journal of Psychopathology and Behavioral Assessment*, Tackett, 2010). Borderline PD (BPD) in youth and the childhood antecedents of antisocial PD (ASPD—e.g., conduct disorder and psychopathy) have received considerable attention, but researchers have begun to explore many of the other PDs and broader personality pathology domains in youth as well.

Throughout the chapter, we adopt a developmental psychopathology perspective on PD (Cicchetti, 1993, 2013). In particular, we draw on two especially impor-

tant tenets of developmental psychopathology. First, the study of normal development is critical for understanding pathological development. The same basic biological, psychological, and contextual processes underlie both normal and abnormal development, and therefore findings and theories from the study of normal development are relevant for explaining the development of psychological disorders. The converse is true as well (i.e., the study of pathological development has the potential to inform research on normal development), but at this point, far more is known about normal than about pathological personality development. Thus we draw on current research on personality development to explain patterns and fill gaps in the literature on PDs in youth.

Second, it is not possible to achieve a complete understanding of psychological disorders without charting the pathways both leading to and following from the development of those disorders (Cicchetti, 1993, 2013). These pathways are often complex (Cicchetti & Rogosch, 1996); different pathways and sets of processes may lead to similar outcomes (known as *equifinality*), and similar origins may yield a broad range of outcomes (known as *multifinality*). The developmental pathways leading to PD in adolescence and adulthood remain poorly understood. At present, there is only one large-scale longitudinal study that has examined the pathways leading to the full set of PDs included in DSM-IV and DSM-5—the Children in the Community study (Cohen, Crawford, et al., 2005). This study began with approximately 800 children ages 1–10 years living in upstate New York and has followed the participants at multiple time points, approximating ages 14, 16, 22, and 33; PDs were assessed at all four time points, as were a variety of other psychiatric disorders, risk factors, and outcomes. This study has provided a wealth of information about the prevalence, development, and course of PDs. Because other large-scale, longitudinal studies of all the PDs are lacking, we sometimes review findings from the literature on PDs in adults to supplement the relatively more scant developmental data.

This chapter proceeds in seven sections. The first section reviews the history of PDs in the DSM system, summarizes the nature of the PD diagnoses in DSM-IV and in DSM-5 Section II, and addresses the still-controversial status of PDs in youth. In its main section (Section II), DSM-5 retains the categorical PD diagnoses in exactly the same form as found in DSM-IV. The second section of the present chapter offers a conceptual framework for describing and explaining the nature of personality pathology in youth; this framework takes into account the ways that personality traits, mental representations, coping strategies, and life narratives may become disturbed in PDs earlier in life. The third section presents several dimensional personality models as diagnostic alternatives to the categorical model of PDs. This section also reviews the trait-based dimensional model for PD offered in Section III of DSM-5; this new section in DSM-5 addresses conditions requiring further research, including a proposed dimensional model of PD. The fourth section of this chapter provides a synopsis of recent research on the epidemiology of PDs, comorbidity among PDs, and links between PDs and other psychiatric disorders (previously called Axis I disorders). The fifth section charts what is known about the stability of early personality pathology and associated life outcomes. The sixth section surveys what is known about the etiology of PDs in general in the first two decades of life and addresses the etiology of specific PDs: Cluster A PDs (paranoid, schizoid, and schizotypal); BPD, ASPD, psychopathy, and narcissism; and the Cluster C PDs (avoidant, dependent, and obsessive–compulsive). The seventh section concludes the chapter with suggestions for future research on PDs in youth.

PDs IN YOUTH IN THE DSM SYSTEMS

A History of PDs from DSM-I to DSM-5

Although PDs have been present in every DSM from the beginning, their formulation has varied over time. The present section reviews the changing structure of PDs across all of the DSM systems, including the decision to retain the DSM-IV PD diagnoses in DSM-5, against the recommendation of the DSM-5 Personality and PDs Work Group. Millon (2012), Oldham (2005), and Widiger (2012) offer more complete reviews of the DSM history, and this history is drawn from their reviews.

DSM-I (APA, 1952) differentiated among three main types of disorders: psychoses, neuroses, and character disorders. The character disorders consisted of "personality disturbances," the name given in the first manual to PDs. Neuroses were seen as being milder and treatable through psychoanalysis, whereas personality disturbances were viewed as patterns that were essentially permanent by early adulthood, and thus difficult (if not impossible) to treat. The manual

recognized that these personality disturbances varied in severity, with some being highly impairing and others being only significantly impairing if patients faced high levels of stress. As for the causes of these disturbances, in DSM-I "personality disorders were generally viewed as deficit conditions reflecting partial developmental arrests or distortions in development secondary to inadequate or pathological early caretaking" (Oldham, 2005, p. 6). DSM-II (APA, 1968) attempted to shift from more theory-based diagnoses to diagnoses describing conditions that could be easily observed and measured; however, many of the specific PDs were retained, and they were still conceptualized as being enduring over time.

DSM-III (APA, 1980) involved a significant overhaul of the entire manual, and it was this manual that had the greatest impact on current conceptualizations of PDs. The first two manuals had presented narrative descriptions of the disorders, whereas DSM-III listed specific criteria to be met for each diagnosis; these criterion lists were added to increase the reliability of the diagnoses. The descriptions of the PDs thus included lists of specific symptoms for each disorder. In addition, DSM-III introduced a multiaxial system, with disorders seen as more episodic placed on Axis I and disorders seen as more enduring placed on Axis II. The Axis II disorders included mental retardation and the PDs. The manual itself suggested that the PDs were placed on Axis II for another reason—to ensure that "consideration is given to the possible presence of disorders that are frequently overlooked when attention is directed to the usually more florid Axis I disorder" (APA, 1980, p. 23).

DSM-III retained several PD diagnoses that had been present in some form in the previous two manuals: paranoid, schizoid, histrionic, passive–aggressive, compulsive, and antisocial. Two previous PD diagnoses were moved to Axis I: intermittent explosive disorder and cyclothymic disorder. In addition, several new PDs were added that are still present in the newest manual: BPD and schizotypal, narcissistic, avoidant, and dependent PDs. Millon (2012) describes the rationale for adding these new PDs in this way: "A major goal of the newly appointed *DSM-III* Task Force was to include as many clinically useful personality syndromes as could be justified. Despite objections from certain quarters, a decision was made to incorporate categories that had not been fully validated by systematic research but nevertheless had much to commend them in terms of their everyday clinical applicability" (p. 11). Another important addition to the manual was the cluster system for the PDs, which has been retained in later manuals; this clustering is described more fully in the next section.

It is interesting to note that DSM-III included five childhood disorders that were seen as potential antecedents to adult PDs: avoidant disorder, schizoid disorder, identity disorder, oppositional disorder, and conduct disorder (Widiger, De Clercq, & De Fruyt, 2009). These were described as possible precursors to adult avoidant PD, schizoid PD, BPD, passive–aggressive PD, and ASPD, respectively. This explicit focus on possible childhood precursors of adult PDs was lost in later editions of the DSM because schizoid disorder and identity disorder in childhood were deleted; childhood avoidant disorder was merged with social phobia in DSM-IV; and the adult counterpart to oppositional disorder (passive–aggressive PD) was eliminated. Only ASPD continued to have an explicit childhood antecedent in the form of conduct disorder. Because conduct disorder and its related conditions (e.g., oppositional defiant disorder, childhood aggression) have been widely studied in the intervening years, much more is known about the developmental pathways leading to ASPD than the pathways leading to other PDs.

As hoped, the amount of research and clinical attention devoted to the PDs did increase significantly following the publication of DSM-III. DSM-III-R (APA, 1987) involved relatively few changes to the PDs. Likewise, DSM-IV (APA, 1994) retained almost all of the PD diagnoses and the cluster system of DSM-III; the continuity from DSM-III to DSM-IV was not surprising because DSM-IV was designed to take a conservative stance to making changes to the diagnoses (Frances & Widiger, 2012). Passive–aggressive PD was moved to Appendix B of DSM-IV, and a set of general diagnostic criteria for a PD was added to the chapter on PDs. DSM-IV-TR (APA, 2000) changed only the narrative text, not the diagnostic criteria, but even the changes to the narrative text for PDs were minimal.

The APA considered making major changes to the PD diagnoses for DSM-5. As more research was conducted on the PDs following the publication of DSM-III, DSM-III-R, and DSM-IV, it became clear that there were some significant flaws in the PD diagnostic system; these are described in more detail in this chapter's section on dimensional models. As a result of these concerns about the PD diagnoses, the APA opted to focus the first of a series of international conferences, held in 2004, on psychiatric classification on dimensional models of PDs (Widiger, Simonsen, Sirovatka, & Regi-

er, 2005). The Personality and PDs Work Group for DSM-5 thus undertook the task of revising the PD diagnoses, with an eye toward implementing a dimensional system for these diagnoses; this process is described in detail in Skodol (2012). It is interesting to note that although all of the DSM-5 Work Groups were initially encouraged to consider making substantial changes to the conceptualization and operationalization of the disorders, all of these groups except for the Personality and PDs Work Group eventually took a conservative stance toward revision and focused on making minor modifications instead of sweeping changes (Skodol, 2012; Widiger, 2013).

The Personality and PDs Work Group eventually submitted a final proposal that retained six of the PD diagnoses—ASPD, BPD, and avoidant, narcissistic, obsessive–compulsive, and schizotypal PDs—and proposed new diagnostic criteria for them (Skodol, 2012; Skodol, Bender, et al., 2011). These diagnoses were retained based on some combination of prevalence in community and clinical samples, associated psychosocial impairment, and evidence for the validity and clinical utility of the disorders. The proposal also included a new diagnosis of PD—Trait Specified, which was defined by the presence of significant impairment and specified by each individual's most prominent personality difficulties on a set pathological personality trait dimensions. This model is described more fully in the section on dimensional models.

Ultimately, the APA Board of Trustees rejected the proposal from the Personality and PDs Work Group (APA, 2012; Krueger, 2013). Instead, the board opted to retain the categorical PD classification system presented in DSM-IV and the 10 PD diagnoses in their exact form from DSM-IV. Thus, although the text has been updated in DSM-5, the PD diagnoses in Section II are identical to the ones presented in DSM-IV. The Board of Trustees also voted to eliminate the multiaxial system, so the PDs now appear in Section II, along with all of the other categorical psychiatric disorders. Two PDs are now cross-referenced in other chapters; in each case, the PD has close ties to non-PD disorders. Specifically, schizotypal PD is also listed in the chapter on schizophrenia spectrum and other psychotic disorders, and ASPD is also listed in the chapter on disruptive, impulse-control, and conduct disorders. The proposed pathological personality dimensional system is presented as the "alternative DSM-5 model for PDs" in Section III, "Emerging Measures and Models," which includes measures and diagnoses requiring further study before potential inclusion in future diagnostic manuals (similar to, e.g., Appendix B in DSM-IV). At this point, the plan is to update DSM-5 as more research is conducted, with future updates being numbered in decimals (e.g., DSM-5.1, DSM-5.2), so it is possible that the alternative model will be moved into Section II if more research substantiates this model.

Several themes stand out in this history of the PDs in the DSM system. First, the PDs have been conceptualized consistently as long-lasting conditions that start at least by early adulthood. The presumed chronic nature of PDs has been part of their conceptualization from DSM-I onward, and it was this nature that was thought to set them apart from more episodic disorders. Second, the PD diagnoses included in the manuals were chosen for inclusion based on experts' clinical experience with "types" of personalities that tend to be accompanied by significant impairment, not based on empirical research on how best to define the nature of personality pathology. Third, some of the current PD diagnoses have been included in similar forms since the original 1952 manual (ASPD and paranoid, schizoid, histrionic, and obsessive–compulsive PDs), and others have been included since 1980 (BPD and schizotypal, narcissistic, avoidant, and dependent PDs). Thus all of the diagnoses have been in use for 30–60 years, and it is not surprising that there would be resistance to removing any of them, regardless of whether there is research supporting their validity. Taken together, it is striking how relatively consistent the PD framework has been throughout the DSM systems; yet, as we review elsewhere in this chapter, newer research has called into question some of the most basic assumptions about the PDs as defined in these systems.

PDs in DSM-IV and DSM-5 Section II

This section describes in more detail the nature of PD diagnoses in DSM-IV and DSM-5. (We focus here on the PD chapter in Section II of DSM-5; we review the Section III alternative DSM-5 model for PDs in this chapter's later section on alternative dimensional models of PDs.) These manuals provide an overarching framework for what constitutes a PD. According to this general framework, PDs consist of deviant patterns of inner experience and behavior in at least two of the following four areas: "(1) cognition (i.e., ways of perceiving and interpreting self, other people, and events); (2) affectivity (i.e., the range, intensity, lability, and appropriateness of emotional response); (3) interpersonal

functioning; (4) impulse control" (APA, 1994, p. 633; APA, 2013, p. 646).

Skodol (2005) has fleshed out what these four areas often include. Cognition typically manifests as disturbances in how patients view themselves and others—for example, overinflated self-views or unduly negative views of the self, profound mistrust or alienation toward others, or tendencies to idealize or devalue others. Cognition also includes deviant thinking about the world, such as expectations for perfectionism or odd, delusional beliefs. Affectivity involves a wide range of disturbances in patients' typical emotions, including disrupted mean levels of emotions (e.g., restricted emotional experience), as well as problems with emotion regulation (e.g., excessively intense and labile emotions). The emotions that are disturbed include the full gamut of human emotions: sadness, anxiety, anger and irritation, joy and pleasure, and love and affection. Difficulties in interpersonal functioning typically involve problems with one or both of the two main dimensions of interpersonal behavior: agency (ranging from dominance and self-assuredness to submission) and communion (ranging from affiliation and warmth to detachment and cold-heartedness) (Pincus & Hopwood, 2012). Finally, several PDs involve problems with impulse control—either deficits in self-control (poor planning, thinking without acting, poor self-regulation of behavior and emotions) or excessive levels of self-restraint and inhibition of healthy impulses.

These deviant personality patterns are further defined by DSM-IV and Section II of DSM-5 in several ways (APA, 1994, pp. 630–631; APA, 2013, pp. 646–647). Consistent with the definition of PDs in all of the DSM systems to date, the patterns must be enduring, inflexible, and pervasive across many contexts in the person's life. The patterns are expected to have started at least by adolescence or early adulthood. The personality patterns must be distressing to the person or must cause impairment in important arenas of daily life, such as social relationships, school, or work. Finally, the pattern must not be better accounted for as a consequence of another disorder, a medical condition, or the use of some substance.

The diagnostic manuals present the PDs as personality "types" made up of combinations of pathological personality tendencies. DSM-IV and DSM-5 outline diagnostic criteria for 10 specific PDs, which are grouped into three clusters: Cluster A, odd or eccentric (paranoid PD, schizoid PD, and schizotypal PD); Cluster B, dramatic, emotional, or erratic (ASPD, BPD, histrionic PD, and narcissistic PD); and Cluster C, anxious or fearful (avoidant PD, dependent PD, and obsessive–compulsive PD) (APA, 1994, pp. 629–630; APA, 2013, p. 646). The essential features of these 10 PD diagnoses are presented in Table 18.1. DSM-5 acknowledges: "It should be noted that this clustering system, although useful in some research and educational situations, has serious limitations and has not been consistently validated" (p. 646).

DSM-IV provided the option of diagnosing PD not otherwise specified (NOS), for those cases in which the general criteria for a PD are met and PD symptoms are present, but in which the person does not fulfill the criteria for any specific PD in the manual. However, DSM-5 has eliminated all NOS diagnoses. Instead, there are two options for Section II diagnoses for patients who exhibit a PD but don't meet criteria for a specific PD: other specified PD (when the clinician wants to note why the patient fails to meet criteria for a specific PD) and unspecified PD (when the clinician does not want to specify why the patient fails to meet such criteria). DSM-5 also offers the option of diagnosing personality change due to another medical condition, for instances in which a patient displays "a persistent personality disturbance that represents a change from the individual's previous characteristic personality pattern" (p. 682) as a result of a neurological or other medical condition.

PDs in Youth in the DSM Systems

Like DSM-IV, DSM-5 offers some directives that are specific to diagnosing PDs in children and adolescents under the age of 18. DSM-5 Section II cautions clinicians to be careful about diagnosing children and adolescents with a personality disorder, except in "those relatively unusual instances in which the individual's particular maladaptive personality traits appear to be pervasive, persistent, and unlikely to be limited to a particular developmental stage or another mental disorder" (APA, 2013, p. 647). For all of the PD diagnoses except for ASPD, the diagnostic criteria for children and adolescents are the same as those used for adults, but for youth under age 18, the patterns must have been present for at least a year. Youth under 18 may not be diagnosed with ASPD. Typically, youth with antisocial behavior are diagnosed with conduct disorder instead, and conduct disorder with onset before age 15 is required for an adult diagnosis of ASPD. Interestingly, the Section III alternative DSM-5 model for PDs does

TABLE 18.1. DSM-5 Personality Disorders (Section II)

- **Paranoid personality disorder** is a pattern of distrust and suspiciousness such that others' motives are interpreted as malevolent.
- **Schizoid personality disorder** is a pattern of detachment from social relationships and a restricted range of emotional expression.
- **Schizotypal personality disorder** is a pattern of acute discomfort in close relationships, cognitive or perceptual distortions, and eccentricities of behavior.
- **Antisocial personality disorder** is a pattern of disregard for, and violation of, the rights of others.
- **Borderline personality disorder** is a pattern of instability in interpersonal relationships, self-image, and affects, and marked impulsivity.
- **Histrionic personality disorder** is a pattern of excessive emotionality and attention seeking.
- **Narcissistic personality disorder** is a pattern of grandiosity, need for admiration, and lack of empathy.
- **Avoidant personality disorder** is a pattern of social inhibition, feelings of inadequacy, and hypersensitivity to negative evaluation.
- **Dependent personality disorder** is a pattern of submissive and clinging behavior related to an excessive need to be taken care of.
- **Obsessive–compulsive personality disorder** is a pattern of preoccupation with orderliness, perfectionism, and control.
- **Personality change due to another medical condition** is a persistent personality disturbance that is judged to be due to the direct physiological effects of a medical condition (e.g., frontal lobe lesion).
- **Other specified personality disorder and unspecified personality disorder** is a category provided for two situations: 1) the individual's personality pattern meets the general criteria for a personality disorder, and traits of several different personality disorders are present, but the criteria for any specific personality disorder are not met; or 2) the individual's personality pattern meets the general criteria for a personality disorder, but the individual is considered to have a personality disorder that is not included in the DSM-5 classification (e.g., passive–aggressive personality disorder).

Note. Reprinted with permission from *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (pp. 645–646). Copyright 2013 by the American Psychiatric Association.

not include any cautions about diagnosing PDs before the age of 18; this model also does not require that the symptoms have lasted for a specific period of time, but rather simply requires that they be "relatively stable across time, with onsets that can be traced back to at least adolescence or early adulthood" (APA, 2013, p. 761). The alternative system thus does not appear to discourage diagnosis of PDs in children and adolescence.

Unfortunately, some clinicians and researchers have misinterpreted the DSM-IV guidelines to mean that PDs may never be diagnosed in childhood or adolescence. A recent study of Dutch and Belgian psychologists found that one-quarter of the psychologists wrongly believed that diagnostic manuals do not permit PD diagnosis in adolescents (Laurenssen, Hutsebaut, Feenstra, Van Busschbach, & Luyten, 2013). This explicit hesitance to diagnose PDs in youth may arise from several sources (Chanen & McCutcheon, 2008; Freeman & Rigby, 2003; Miller, Muehlenkamp, & Jacobson, 2008; Shiner, 2007; Westen & Chang, 2000). First, because PD has been conceptualized as long-lasting, difficult to treat, and severe, especially compared to many Axis I disorders, clinicians and researchers may have concerns about stigmatizing youth by giving them a PD diagnosis. Second, for centuries Western thinkers have suggested that adolescence is a tumultuous period characterized by erratic moods and impulsive behavior (Arnett, 1999), termed famously the "storm and stress" of adolescence (Hall, 1904). Perhaps a certain amount of personality "pathology" is seen as being normative during the adolescent period, and thus not worthy of clinical attention. Finally, youth's personalities are often viewed as being "under construction" during childhood and adolescence, and therefore too unstable to have lasting significance (Elliott, Tyrer, Horwood, & Fergusson, 2011). There is empirical evidence that all three of these reasons may prevent clinicians from making a PD diagnosis in adolescent patients (Laurenssen et al., 2013). This hesitance to diagnose PDs in youth has had a significant negative impact on researchers' interest in studying the development of PDs,

though fortunately this is changing as more work focuses on this topic.

The hesitance about diagnosing PDs may also lead clinicians to overlook the presence of personality pathology in their young patients. Westen, Shedler, Durrett, Glass, and Martens (2003) conducted a study in which they asked practicing psychologists and psychiatrists to report on a particular adolescent patient in their practices. Although only 28.4% of patients were assigned a PD diagnosis by their clinicians, 75.3% of the patients met criteria for a PD, based on their clinicians' reports of PD symptoms. Similarly, among a sample of practicing European psychologists, only 9% of clinicians reported diagnosing PDs in adolescence, and even fewer offered specialized treatments for adolescent PDs (Laurenssen et al., 2013). In short, misconceptions about the nature of PD in youth may prevent some clinicians from recognizing that their adolescent patients meet criteria for PDs. This is a serious problem, especially given the evidence reviewed in this chapter that PDs in youth are potentially serious and impairing, and certainly worthy of assessment and treatment.

THEORETICAL FRAMEWORK

As research on normal-range personality traits and their development in childhood and adolescence grows, the relevance of normal personality development for the emergence of personality pathology becomes ever more salient (Shiner, 2009; Tackett & Kushner, in press). Although the DSM PD system is largely nondevelopmental, it is possible to draw from the existing literature on normal personality development to provide a more truly developmental perspective on the development of personality pathology. As noted earlier, the developmental psychopathology perspective emphasizes the importance of normal-range and adaptive development for understanding the development of psychopathology (Cicchetti, 1993, 2013), providing a framework for integration of normal and abnormal phenomena. In this section, we review theory and research on normal personality constructs in youth, highlighting the relevance of this work for early-life personality pathology. Specifically, we use a very rich and comprehensive personality model developed by McAdams and colleagues (McAdams, 2013; McAdams & Olsen, 2010; McAdams & Pals, 2006). This model differentiates three levels of individual differences in personality. First, we discuss personality *traits*, which McAdams and Pals call the "dispositional signature" of personality. Next, we discuss "characteristic adaptations"—"a wide range of motivational, social-cognitive, and developmental adaptations, contextualized in time, place, and/or social role" (McAdams & Pals, 2006, p. 208). We focus on two specific characteristic adaptations that hold particular relevance for youth PDs: attachment/social cognition and emotion regulation/coping (Shiner, 2009). Finally, we discuss the third level of "personal narratives"—stories that individuals begin to develop in adolescence to help them make sense of their identities over time. We believe that personality pathology in youth may involve disruptions at all of these levels of analysis.

Temperament and Personality Traits

A predominant theoretical and conceptual approach to personality across the lifespan focuses on personality traits as constructs that summarize characteristic patterns of thinking, feeling, and behaving that are pervasive across situations and stable across time. In particular, the "Big Five" model defines five broadly defined traits that capture salient features across persons: Extraversion (tendencies such as sociability, gregariousness, and experiencing positive emotions); Neuroticism (tendencies to experience negative emotions, such as sadness, anxiety, and distress); Conscientiousness (tendencies toward persistence, responsibility, and organization); Agreeableness (tendencies toward empathy and communion vs. hostility and aggression); and Openness to Experience/Intellect (tendencies toward intellectual engagement and exploration/enjoyment of stimulating experiences; John, Naumann, & Soto, 2008). These traits characterize the personalities of children as early as the preschool period (De Pauw, Mervielde, & Van Leeuwen, 2009), and they robustly characterize children's traits in later childhood and adolescence as well (Shiner & DeYoung, 2013). Table 18.2 illustrates the nature of the Big Five traits by presenting components of each trait; these components are taken from measures of temperament and personality traits in childhood and adolescence.

These traits are linked to early-emerging temperament traits, which have historically represented the primary constructs of interest for individual difference researchers focusing on infancy and early childhood (Rothbart & Bates, 2006; Shiner & Caspi, 2012). Early in life, children manifest individual differences in their experiences and expressions of positive and negative

TABLE 18.2. Child Temperament and Personality Facets Constituting the Big Five Higher-Order Traits in Childhood and Adolescence

Big Five higher-order domains	Child temperament facets	Child and adolescent personality facets
Neuroticism	Frustration[a] (CBQ/EATQ-R) Discomfort (CBQ) Fear (CBQ; EATQ-R) Sadness (CBQ)	Fearful/insecure (ICID) Anxiety (HiPIC) Negative affect (ICID) Self-confidence—rev. (HiPIC)
Extraversion	Activity level (CBQ; EATQ-R) Approach (CBQ) High-intensity pleasure (CBQ; EATQ-R) Shyness—rev. (CBQ; EATQ-R) Smiling and laughter (CBQ)	Positive emotions (ICID) Sociability (ICID); Shyness—rev.[a] (HiPIC) Activity level (ICID); Energy (HiPIC) Expressiveness (HiPIC) Optimism (HiPIC)
Agreeableness	Affiliation[a] (EATQ-R)	Antagonism—rev. (ICID); Altruism (HiPIC) Strong-willed—rev. (ICID) Dominance—rev. (HiPIC) Egocentrism—rev. (HiPIC) Compliance (HiPIC); Irritability—rev. (HiPIC)
Conscientiousness	Attention (CBQ; EATQ-R) Impulsivity—rev. (CBQ) Inhibitory control (CBQ; EATQ-R) Activation control (EATQ-R)	Organized (ICID); Order (HiPIC) Achievement orientation (ICID); Achievement Motivation (HiPIC) Distractible—rev. (ICID); Concentration (HiPIC) Perseverance (HiPIC)
Openness to Experience/Intellect	Low-intensity pleasure (CBQ) Pleasure sensitivity (EATQ-R) Perceptual sensitivity (CBQ; EATQ-R)	Intellect (ICID; HiPIC) Creativity (HiPIC) Curiosity (HiPIC)

Note. Rev., reversed (meaning that the facet loads negatively on the higher-order trait).

CBQ, Children's Behavior Questionnaire (Rothbart, Ahadi, Hershey, & Fisher, 2001); EATQ-R, Early Adolescent Temperament Questionnaire—Revised (Ellis & Rothbart, 2001); ICID, Inventory of Child Individual Differences (Halverson et al., 2003); HiPIC, Hierarchical Personality Inventory for Children (Mervielde & De Fruyt, 2002).

[a]Facets potentially loading on more than one higher-order Big Five domain.

emotions, as well as in their ability to regulate their emotions and behavior. Temperament trait models typically converge on three higher-order traits (rather than the five traits of the Big Five): Surgency or Positive Emotionality (akin to Extraversion); Negative Emotionality (akin to Neuroticism); and Effortful Control (most clearly linked with Conscientiousness, but with some association with Agreeableness as well). Recent efforts have focused on merging our understanding of three- and five-factor trait models, and have offered evidence of empirical links among these traits in both childhood and adulthood (Markon, Krueger, & Watson, 2005; Tackett et al., 2012). Thus temperament and personality traits are now linked both theoretically and empirically (De Pauw et al., 2009; Shiner, 2010; Shiner & DeYoung, 2013), and greater merging of these literatures is expected to increase as the field moves forward.

Although advancing research in the domain of child personality traits has provided increasing evidence for connections with adult models such as the Big Five (e.g., Digman & Shmelyov, 1996; Goldberg, 2001), differences across development have emerged as well. For example, some studies have suggested that Neuroticism, compared to other traits, may be more difficult to measure in early life (Tackett, Krueger, Iacono, & McGue, 2008; Tackett et al., 2012). This challenge potentially reflects the restricted access that standard informants (e.g., parents, teachers) have to the type of internalized affect that defines trait Neuroticism (Grills & Ollendick, 2002; Tackett, 2011; Vazire, 2010). It is also unclear how distinct Agreeableness and Consci-

entiousness traits emerge across development from the broad Effortful Control trait defined in temperament models (Rothbart, Ahadi, & Evans, 2000; Tackett et al., 2012). The content of child personality traits is typically analogous, but not identical, to adult personality traits (De Pauw et al., 2009); researchers therefore need to maintain a developmentally sensitive perspective in such work and to guard against atheoretical top-down approaches, often seen in the application of adult personality theory and research to younger age groups.

Children's early personalities shape their experiences of the environment through a number of important processes (Caspi & Shiner, 2006; Shiner & Caspi, 2012): the ways that children are conditioned by their environments, the responses children evoke from the people in their lives, the ways that children interpret their experiences, the ways children evaluate themselves and form a sense of identity, the environments that children "select" themselves into, and the ways that children modify and manipulate their environments. The personalities of young people can help explain why children who are exposed to relatively similar environments do not have the same outcomes—an excellent example of the principle of multifinality. For example, a child who is intensely anxious and irritable, and who lacks good self-control, is going to have a very different experience of parental divorce than a child who is emotionally stable and behaviorally restrained; these differences in the experience of divorce could then lead to differing outcomes for the children.

Personality traits represent an important focus in understanding the emergence and development of PD in youth because traits show similar levels of heritability (or genetic influence; Saudino & Wang, 2012) to PD constructs; they are salient and measurable from early life (Rothbart & Bates, 2006); and they reach moderate levels of stability by early childhood (Roberts & DelVecchio, 2000). We elaborate on these points later in this chapter. Work on adults suggests that PD symptom-level change *follows* change in normal personality traits (Warner et al., 2004), highlighting their importance as early core components of personality pathology; we return to this point as well later in the chapter. In addition, early efforts at utilizing personality traits as selection factors for indicated prevention efforts (i.e., prevention efforts delivered to a group defined as high-risk on the basis of some key vulnerability feature) have already shown great promise in reducing the emergence and severity of adolescent personality pathology (e.g., Chanen, Jovev, Djaja, et al., 2008).

Characteristic Adaptations: Attachment and Social Cognition

McAdams and Pals (2006) describe characteristic adaptations as those components of individual personality that are more closely tied to situations, contextual factors, and personal roles. One such aspect of individual functioning that holds great relevance for youth PDs is attachment to a primary caregiver and social-cognitive functioning more broadly. Attachment reflects a specific type of mental representation; mental representations are defined by children's perceptions of themselves, their experiences, their relationships, and their environments (Shiner, 2010). These perceptions hold predictive value in understanding later behavior and play an important role in shaping adaptive and maladaptive developmental trajectories. Attachment theory has played a central role in the conceptualization and theoretical underpinnings of a number of PDs, with empirical support for the importance of attachment in PD development (e.g., Crawford et al., 2006; Sroufe, Carlson, Levy, & Egeland, 1999; Weston & Riolo, 2007). Development from infancy to early childhood has been identified as a critical developmental period for PDs because of its relevance for adaptive attachment (Tackett et al., 2009), when patterns of security and insecurity form in response to the child's relationship with a primary caregiver (Mikulincer & Shaver, 2007). In this way, the central role played by attachment in PD conceptualization has anchored PD developmental origins to infancy and early childhood, underscoring the idea that PD emergence begins early in the lifespan (Paris, 2003).

The mental representation of this early relationship is thought to provide a context for the children's future relationships and responses to the world around them (Sroufe, 2005; Sroufe et al., 1999). Modern models of attachment define two key dimensions of attachment styles: the first reflecting the extent to which a person worries versus feels secure about the availability of a partner (or caregiver), and the second reflecting the extent to which a person prefers independence and detachment versus affiliation and intimacy (Fraley & Shaver, 2008). Disrupted and maladaptive attachment patterns have been a long-standing component of the theoretical background behind multiple PDs, but have played a particularly important role in the conceptualization of BPD (Levy, 2005). Empirical data indicate a higher prevalence of disrupted attachment styles (e.g., attachment styles characterized by fears of rejec-

tion and abandonment) among adolescents with BPD (Westen, Nakash, Thomas, & Bradley, 2006).

Although the transition from infancy to early childhood has been the key critical developmental period in attachment theory and is thus highly relevant for early PDs, two other critical developmental periods for PD development are also closely tied to interpersonal relationships (Tackett et al., 2009). Specifically, the transition from middle childhood to adolescence is marked by the increasing salience of the peer group, whereas the transition from late adolescence to adulthood is marked by the shift toward intimate partners as the primary relational context. Certainly, mental representations formed during the early years in the context of attachment to a primary caregiver may serve as risk or resiliency factors when youth are faced with these new relational tasks across development. Theory and research at these later stages has focused on broader definitions of social-cognitive factors that play a role in PD emergence. For example, children's sense of alienation from their peer group, perceptions of their self-competence, perceptions of the hostile intentions of other people, and beliefs about the malleability of their own behavior are all mental representations with implications for adjustment and maladjustment (Shiner, 2009; Tackett et al., 2009).

Three specific categories of youth's social cognition have been highlighted as especially relevant for personality pathology: emotion recognition, theory of mind (also called "mentalizing"), and trust (Sharp, 2012b). The relevance of emotion recognition for PD may emerge either via biases in emotion recognition, or via dampened/heightened emotion recognition. For example, BPD in adolescents has been associated with a negativity bias, as well as with potentially heightened recognition of one's own and others' emotions (Sharp, in press). Areas of social cognition show relevance across diverse forms of personality pathology, although sometimes in divergent directions. For example, hypermentalizing (i.e., overinterpreting the thoughts and behaviors of others) is associated with BPD, whereas hypomentalizing (i.e., impoverished interpretations of others' thoughts and behaviors) is associated with ASPD in youth (Sharp, 2012). Social-cognitive tendencies may also play a role in shaping adaptive versus maladaptive functioning. For example, "agentic" motives (meaning goals focused on achieving power, mastery, and assertion over others) differentiate children with narcissistic tendencies from children with adaptive high self-esteem, who are primarily motivated by communal motives (goals focused on achieving intimacy and affiliation; Thomaes, Stegge, Bushman, Olthof, & Denissen, 2008).

Characteristic Adaptations: Emotion Regulation and Coping

Another aspect of personality that is highly relevant for youth PDs and is best defined as a characteristic adaptation consists of emotion regulation and coping. The manner by which children learn to respond to and cope with stressors falls under the domain of characteristic adaptations, as this aspect of functioning is closely linked with those specific environments that an individual might encounter (Shiner, 2010). Coping strategies can be both adaptive and maladaptive, and have been closely linked to the development of personality pathology over time. Coping strategies have been broadly categorized into two domains: strategies reflecting engagement (or approach-motivated behaviors) and those reflecting disengagement (or avoidance-motivated behaviors; Skinner & Zimmer-Gembeck, 2007). In addition, coping strategies may include both conscious processes (e.g., active distraction from a negative stimuli) and unconscious processes (e.g., the use of defense mechanisms; Cramer, 2008).

Predominant coping strategies in childhood include problem solving, escape, distraction, and support seeking (Skinner & Zimmer-Gembeck, 2007). Adolescents develop a more complex repertoire of coping strategies, including adaptive strategies such as cognitive restructuring, as well as less adaptive strategies such as rumination and externalization of blame. Adolescence in particular may be viewed as a developmental stage of skill attainment and experimentation, as youth begin to discover new coping strategies and examine their effectiveness at goal attainment. Emotion regulation is an important aspect of coping, and it refers specifically to an individual's self-regulatory responses to emotions, rather than to the status or content of emotions themselves (Gratz et al., 2009). Deficits in emotion regulation include poor behavioral control in the context of emotional distress, as well as difficulties with the modulation of emotion arousal.

Youth PDs may be differentially associated with problems in emotional regulation and ineffective coping. Cluster B PDs seem likely to be associated with maladaptive emotion regulation strategies, whereas Cluster C PDs are likely to reflect maladaptive overreliance on disengagement coping approaches. Research-

ers may also differentiate these categories of personality pathology as defined by emotional underregulation (Cluster B) versus emotional overregulation (Cluster C), whereas Cluster A PDs are more likely to reflect general problems in the actual nature or quality of emotions (specifically, their absence). BPD in particular has been both theoretically and empirically associated with problematic emotion regulation approaches. A recent investigation by Gratz and colleagues (2009) highlights the nature of emotion regulation as a characteristic adaptation. Specifically, in this study the influence of a vulnerability trait (affective dysfunction) on child BPD symptoms was mediated by dysfunctional emotion regulation. In other words, this study supported the idea that an existing trait vulnerability may increase risk for later BPD, but showed that it did so (at least partly) through its impact on maladaptive emotion regulation processes. However, other aspects of maladaptive coping may cut across PDs and PD clusters. For example, experiential avoidance (a maladaptive coping technique defined by attempts to avoid internal distress) is present in BPD and has been historically associated with anxiety problems, and thus is probably connected to Cluster C PDs as well (Gratz, Tull, & Gunderson, 2008). Future research in this area should focus on core underlying components of maladaptive coping and emotion regulation, which are likely to be relevant for a variety of PD manifestations.

Narrative Identity

The final level in McAdams and Pals's (2006) model is that of personal narratives, or life stories. This level is of fundamental importance for youth PD, as a key function provided by personal narratives is identity development (McAdams & McLean, 2013; McLean & Pasupathi, 2012)—a process that may be disturbed in the development of certain types of personality pathology (Fonagy & Bateman, 2008). Thus considering this level is essential for a full understanding of how normal personality development influences the development and manifestation of PDs. Narrative identity development is a particularly important task for adolescence, when youth gain the cognitive and social skills to think about their lives in more coherent and complex ways (Habermas & de Silveira, 2008; Shiner, 2010).

The development of life narratives is firmly embedded in an individual's social context (McLean & Pasupathi, 2012; Shiner, 2009). Children begin co-constructing their narratives, primarily with their parents, from an early age, and these experiences appear to influence narrative complexity (e.g., Fivush, Haden, & Reese, 2006). The social context of the peer group becomes an active part of narrative construction in adolescence. Thus the cross-cutting theme of interpersonal relationships for personality pathology in general highlights the potential relevance of life narratives for the development of personality disorder. Identity functioning is specifically embedded in the conceptualization of BPD, but it is likely to be relevant to many other PDs as well.

Shiner (2009) highlights two particularly problematic pathways in identity development with relevance for PD emergence. The first is problems with integrating negative experiences into the life narrative in constructive and adaptive ways, and the second is difficulties with progressive coherence of the life narrative. Regarding the first pathway, there are positive and adaptive ways of integrating negative experiences into a life narrative, such as utilizing positive explanatory frameworks and coping (Pals, 2006). A construct frequently studied by narrative psychologists is that of meaning making, or an individual's ability to develop positive meaning out of a potentially challenging or negative experience (McLean & Pasupathi, 2012). Meaning making is frequently associated with more adaptive functioning and life narratives. In contrast to narratives that construct positive meanings out of negative experiences, some life narratives contain a high number of "contamination sequences," in which descriptions of positive experiences are followed by descriptions of subsequent negative experience (McAdams, 2009); the negative experience spoils the rewards of the positive one. The presence of more frequent contamination sequences is associated with a variety of maladaptive psychological outcomes (McAdams, 2009). A second maladaptive pathway in identity development may involve problems in developing a coherent and integrated life narrative (Shiner, 2009). Specifically, some adolescents may struggle with committing to a specific pathway of identity development, and others may tend to recall few specific memories and instead focus only on diffuse or general memories; both of these problems with developing a coherent life story may result in negative or maladaptive consequences. Indeed, identity integration is a fundamental way in which personality-disordered youth differ from normal controls (Feenstra, Hutsebaut, Verheul, & van Limbeek, 2014). Furthermore, in this study by Feenstra and colleagues (2014), the majority of youth with a PD diagnosis showed in-

creasing levels of identity integration across the experience of inpatient psychotherapy, suggesting that this domain also represents an important target for treatment. As we describe later in this chapter, the alternative dimensional system for PDs in DSM-5 explicitly moves toward a more central role for problematic identity development and identity functioning in its definition of PDs.

Thus all three levels of normal personality development as described by McAdams and Pals (2006) are highly relevant for the development of PD in youth. Personality traits (Level 1) are likely to serve as both risk and resilience factors for the development of personality pathology. Characteristic adaptations (Level 2) show both general and specific connections to emerging PD, particularly via social-cognitive processes such as attachment and emotion regulation/coping strategies. The content and structure of adolescents' life narratives (Level 3) hold particular relevance for adaptive identity development and adjustment. We now turn from an examination of general constructs reflecting normal personality development to discussion of dimensional models of personality pathology.

ALTERNATIVE DIMENSIONAL MODELS OF PDs

In this section, we review dimensional alternatives to the categorical *DSM* PD system. First, we discuss the rationale for adopting a dimensional model for PDs. Second, we review research on a set of higher-order pathological personality traits obtained across studies of normal-range and pathological traits, in both youth and adults. Third, we present the alternative DSM-5 model for PDs, which includes a dimensional system for pathological personality traits. A move toward dimensional trait models of personality pathology is of great relevance for developmental research, as traits offer greater opportunity to investigate the development of these problems across the lifespan (Tackett et al., 2009). There is increasing evidence that some childhood conditions are best conceptualized as dimensions rather than categories (Coghill & Sonuga-Barke, 2012)—including attention-deficit/hyperactivity disorder (ADHD), posttraumatic stress disorder (PTSD), some forms of depression, and aggression—so dimensional models of personality pathology are worthy of further attention by researchers and clinicians working with children and adolescents.

The Rationale for Dimensional Models of PDs

A key issue in conceptualizing personality pathology is whether it is most validly described as categorical patterns or quantitative variations on dimensional traits. The model of PDs adopted in DSM-IV and now DSM-5 is a categorical one: The PDs are each seen as distinct patterns that differ qualitatively both from normal personality functioning and from each other. However, even within DSM-IV-TR, there is some recognition of the possibility of a dimensional approach: "An alternative to the categorical approach is the dimensional perspective that Personality Disorders represent maladaptive variants of personality traits that merge imperceptibly into normality and into one another" (APA, 2000, p. 689). As noted earlier, when the DSM-5 revision process first started, serious consideration was given to dimensional models of psychopathology across the diagnostic manual as a whole (Krueger, Watson, & Barlow, 2005; Rounsaville et al., 2002), but particularly within the PDs (Widiger et al., 2005).

The validity of the DSM PD categorical system has been challenged on a number of fronts (reviewed in Clark, 2007; Clark, Livesley, & Morey, 1997; Simonsen & Widiger, 2005; Trull & Durrett, 2005; Widiger & Trull, 2007). The PDs co-occur within patients at a rate that is much higher than would be expected if the disorders are truly distinct, categorical entities with distinct etiologies (Clark, 2007; Trull, Scheiderer, & Tomko, 2012); this is probably true for youth as well as adults, as we discuss later in the chapter. The cutoffs for the number of criteria needed for a PD diagnosis are arbitrary. The existing PD diagnoses include heterogeneous groups of patients within each category because of the polythetic criteria sets that are used. Despite the long list of PDs included in the DSMs, the existing PDs do not provide adequate coverage of the range of personality pathology that patients exhibit. As a result, PD-NOS has turned out to be the most common PD diagnosis used in actual practice with adults (Verheul & Widiger, 2004), and it is highly prevalent in psychotherapy outpatients (Verheul, Bartak, & Widiger, 2007) when the DSM-IV system is used. PD-NOS may also be the most prevalent DSM-IV PD in both adolescents and adults (Johnson, First, et al., 2005).

It seems, then, that personality pathology may be more validly conceptualized within a dimensional framework than via a number of discrete categories. In a dimensional taxonomy, it is recognized that psychopathology involves variation in underlying dimen-

sions of cognition, affect, and behavior. Implicit in such a model is the recognition that there is no clear-cut boundary between normal and abnormal functioning; in other words, in a dimensional model, PDs differ from normal-range personality quantitatively rather than qualitatively. Dimensional models of personality pathology address the problems with the current categorical model. The high comorbidity of PDs makes sense if personality pathology is an expression of extreme standing on pathological trait dimensions because similar PD traits may be present across PD diagnoses. In addition, diagnostic heterogeneity within diagnoses probably results from a mixture of pathological traits in individuals within a PD category. Dimensional models should be able to describe the full range of individuals with PDs.

Evidence for a Set of Pathological Personality Traits

Research on dimensional approaches to PDs has relied on two key sources of evidence: research linking normal-range personality traits such as the Big Five traits with PDs, and research delineating the structure of pathological personality trait dimensions. In both lines of research, most of the focus has been on adult PDs, but the patterns observed for adult PD dimensions have been explored in youth as well.

The DSM-IV and DSM-5 PD diagnoses may be described in terms of variation of normal-range personality traits. In particular, extensive research has demonstrated that the Big Five traits described previously (Extraversion, Neuroticism, Conscientiousness, Agreeableness, and Openness to Experience/Intellect) may be used to characterize DSM-defined personality pathology (Widiger & Costa, 2013). Each of the broad, higher-order Big Five dimensions includes a number of more narrow, lower-order dimensions, or "facets" (e.g., Extraversion involves components such as activity level, gregariousness, and positive emotions). These facets are used to describe personality pathology in a more nuanced way than is possible with the Big Five traits alone. For example, BPD in adults can be characterized by specific facets of Neuroticism (emotional lability, anxiousness, separation anxiety, hostility) and low Conscientiousness (impulsivity, risk taking) (Trull, 2012). As with adults, there is some evidence that PDs in adolescence can be described by using Big Five personality and temperament measures (De Clercq & De Fruyt, 2003; De Clercq, De Fruyt, & Van Leeuwen, 2004; Decuyper, De Clercq, De Bolle, & De Fruyt, 2009; De Fruyt & De Clercq, 2013; Tackett & Kushner, in press). The findings of these studies with adolescents suggest that although patterns of links between Big Five facet scores and PD symptoms reasonably replicate patterns seen in adults, unexpected associations of personality traits and PD symptoms also occur, indicating possible developmental differences (De Fruyt & De Clercq, 2013). Another implication of this work is that some domains of PD in youth are not well captured by existing normative trait models (e.g., the role of identity disturbance in BPD; Tackett & Kushner, in press).

In addition to the work linking PDs with normal-range personality traits, many different pathological personality trait models have been proposed (Widiger & Simonsen, 2005). Several lines of research point to the evidence that personality pathology may be defined along four overarching dimensions (Clark, Simms, Wu, & Casillas, 2011; Livesley & Jackson, 2009; Markon et al., 2005; Trull & Durrett, 2005; Widiger & Mullins-Sweatt, 2005; Widiger & Simonsen, 2005). First, Extraversion versus Introversion/Detachment measures how outgoing, active, energetic, expressive, and emotionally positive a person is. At the pathological extremes, this dimension taps exhibitionism (high end) and detachment, social avoidance, and excessive shyness (low end). Second, Negative Affectivity versus Emotional Stability measures individual differences in the experience of negative emotions. At the pathological high end, this dimension taps anxiousness, insecure attachment, identity problems, affective lability, feelings of worthlessness, and poor coping with stress. It is not clear whether there is a pathological low end, but it is possible that it may involve an excessive lack of fear and anxiety (as in psychopathy). Third, Conscientiousness versus Disinhibition measures tendencies to be responsible, attentive, persistent, orderly, high-achieving, and planful versus irresponsible, unreliable, careless, and quitting easily. At the pathological extremes, this dimension taps compulsivity and workaholism (high end) and impulsiveness, irresponsibility, and excessive risk taking (low end). Fourth, Antagonism versus Agreeableness measures tendencies toward being hostile and cynical versus kind, modest, empathic, honest, and trusting. At the pathological high end, this dimension taps mistrust and alienation, aggression, entitlement, and callousness. Less often represented is a fifth factor reflecting Cluster A characteristics and sometimes labeled Psychoticism or Peculiarity versus

Lucidity (Harkness & McNulty, 1994; Tackett, Silberschmidt, Krueger, & Sponheim, 2008). Psychoticism, which is conceptualized as a pathological trait, reflects the tendency to experience cognitive or perceptual aberrations. Psychoticism is particularly notable for its relative lack of attention in the developmental literature and its absence from commonly used dimensional measures of personality pathology in youth (Tackett et al., 2009). Thus, although it is clearly relevant as a core component of personality pathology, much more work is needed to understand approaches to assessment of this trait and its utility in early life.

Although most of the research on pathological personality dimensions has focused on adults, there is newer evidence suggesting that the same pathological personality traits describe early PD manifestations in youth. PD trait questionnaire measures created for adults have been adapted for use with adolescents, and findings suggest that the same higher-order pathological traits validly represent the structure of personality pathology in adolescents (Linde, Stringer, Simms, & Clark, 2013; Ro, Stringer, & Clark, 2012; Tromp & Koot, 2008, 2010). In contrast to the "top-down" evidence from adult measures adapted for adolescents, "bottom-up" data on pathological personality traits in youth come from a questionnaire designed to measure maladaptive extreme variants of normal-range personality traits in youth (De Clercq, De Fruyt, Van Leeuwen, & Mervielde, 2006; De Clercq, De Fruyt, & Widiger, 2009; De Fruyt & De Clercq, 2013). This measure yields four higher-order traits comparable to those found in the adult research: Introversion, Disagreeableness, Compulsivity, and Emotional Instability. An attempt is currently being made to develop a measure of the Peculiarity dimension in youth (De Clercq & De Fruyt, 2012).

Despite similarities in the findings for the hierarchical structure of pathological personality traits in adults and youth, it is important to note that some differences are found in youth, much like the differences found for the structure of normal personality traits in youth (Kushner, Tackett, & De Clercq, 2013). For example, a robust pathological Introversion trait does not appear to be as salient in youth as in adults; this finding may be analogous to the difficulties in measuring "pure" Neuroticism in early life, when access to children's early experiences of sadness, anxiety, and anger may be more difficult to obtain. The use of dimensional measures of personality pathology in youth is becoming increasingly feasible with the advent of such measures, but it will be important to remain sensitive to potential developmental differences in early personality pathology. For example, Westen and colleagues have obtained evidence for a larger number of PD-relevant dimensions in their work on clinician assessment of adolescent PD traits (Westen et al., 2003; Westen, Dutra, & Shedler, 2005). More work will be needed to identify early maladaptive personality traits in a developmentally sensitive manner.

Proposed Alternative DSM-5 Model for Personality Disorders

DSM-5 acknowledges the importance of dimensional models of PDs by its inclusion of the alternative DSM-5 model for PDs in Section III of the manual. This system is based on the research on the higher-order domains of pathological personality traits described in the preceding section. DSM-5 states the rationale for including both the categorical PD diagnoses and the alternative dimensional model thus: "The inclusion of both models in DSM-5 reflects the decision of the APA Board of Trustees to preserve continuity with current clinical practice, while also introducing a new approach that aims to address numerous shortcomings of the current approach to personality disorders" (APA, 2013, p. 761). In other words, the alternative model is designed to address the previously described limitations of the categorical PD approach.

Like the categorical formulation of PDs in Section II, the alternative model for PDs in Section III presents a set of general criteria for PDs (APA, 2013, p. 761). There are two key features to PDs in this new formulation: (1) impairment and (2) pathological personality traits. (See Table 18.3 for a general overview of these proposed diagnostic criteria for impairment in the elements of personality functioning and the presence of pathological personality traits.) As in the Section II PD diagnoses, the PD condition must be impairing; however, here "impairment" is defined in terms of moderate or greater impairment in self and interpersonal functioning. The person must also display one or more pathological personality traits. These two main features—impairment and pathological personality traits—are qualified in a number of ways: They must be relatively stable over time, present since adolescence or early adulthood, not better explained by another mental disorder, not merely the result of a substance or medical condition, and not normative for the person's age or sociocultural environment (APA, 2013, p. 761). This

TABLE 18.3. DSM-5 Proposed Diagnostic Criteria for Personality Disorder—Trait Specified (Alternative DSM-5 Model for Personality Disorders)

A. Moderate or greater impairment in personality functioning, manifested by difficulties in two or more of the following four areas:
   1. ***Identity***
   2. ***Self-direction***
   3. ***Empathy***
   4. ***Intimacy***

B. One or more pathological personality trait domains OR specific trait facets within domains, considering ALL of the following domains:
   1. **Negative Affectivity** (vs. Emotional Stability): Frequent and intense experiences of high levels of a wide range of negative emotions (e.g., anxiety, depression, guilt/shame, worry, anger), and their behavioral (e.g., self-harm) and interpersonal (e.g., dependency) manifestations.
   2. **Detachment** (vs. Extraversion): Avoidance of socioemotional experience, including both withdrawal from interpersonal interactions, ranging from casual, daily interactions to friendships to intimate relationships, as well as restricted affective experience and expression, particularly limited hedonic capacity.
   3. **Antagonism** (vs. Agreeableness): Behaviors that put the individual at odds with other people, including an exaggerated sense of self-importance and a concomitant expectation of special treatment, as well as a callous antipathy toward others, encompassing both unawareness of others' needs and feelings, and a readiness to use others in the service of self-enhancement.
   4. **Disinhibition** (vs. Conscientiousness): Orientation toward immediate gratification, leading to impulsive behavior driven by current thoughts, feelings, and external stimuli, without regard for past learning or consideration of future consequences.
   5. **Psychoticism** (vs. Lucidity): Exhibiting a wide range of culturally incongruent odd, eccentric, or unusual behaviors and cognitions, including both process (e.g., perception, dissociation) and content (e.g., beliefs).

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new framework acknowledges that PDs may be only relatively stable (unlike the Section II model, which describes PDs as enduring and inflexible), consistent with research described later in this chapter indicating that PDs may change over time. The dimensional framework does not specify exactly how long the condition needs to have persisted, also unlike the Section II framework. As noted earlier, the new formulation also does not suggest that PDs are relatively rare in childhood and adolescence, but instead asks the clinician or researcher to determine whether a patient is displaying traits and impairment that are not normative for the youth's developmental phase of life.

The first of the two key components required for a PD diagnosis in the dimensional system is impairment in the areas of self (including the elements of identity and self-direction) and interpersonal functioning (including the elements of empathy and intimacy). The DSM-5 definitions of these four elements are provided in Table 18.4. These elements are viewed as existing on a continuum and should be rated by researchers or clinicians on a scale with these four levels (APA, 2013, pp. 775–778): 0, little or no impairment; 1, some impairment; 2, moderate impairment; 3, severe impairment; and 4, extreme impairment. DSM-5 defines each scale point for each of the four elements of potential impairment. For example, a person displaying Level 3 (severe impairment) in the element of self-direction would exhibit this pattern: "Has difficulty establishing and/or achieving personal goals. Internal standards for behavior are unclear or contradictory. Life is experienced as meaningless or dangerous. Has significantly compromised ability to reflect on and understand own mental processes" (p. 777). A person must manifest Level 2 (moderate or greater impairment) in two or more elements to receive a PD diagnosis.

The DSM-5 Personality and PDs Work Group decided to include impairment as a key feature of PDs

TABLE 18.4. DSM-5 Proposed Elements of Personality Functioning

Self:

1. ***Identity:*** Experience of oneself as unique, with clear boundaries between self and others; stability of self-esteem and accuracy of self-appraisal; capacity for, and ability to regulate, a range of emotional experience.
2. ***Self-direction:*** Pursuit of coherent and meaningful short-term and life goals; utilization of constructive and prosocial internal standards of behavior; ability to self-reflect productively.

Interpersonal:

1. ***Empathy:*** Comprehension and appreciation of others' experiences and motivations; tolerance of differing perspectives; understanding the effects of one's own behavior on others.
2. ***Intimacy:*** Depth and duration of connection with others; desire and capacity for closeness; mutuality of regard reflected in interpersonal behavior.

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because substantial theoretical and empirical literatures point to the importance of problematic self and interpersonal functioning as a manifestation of personality pathology, separate from deviant personality traits (Bender, Morey, & Skodol, 2011; Livesley, 2007; Skodol, 2012; Skodol, Clark, et al., 2011; Tackett et al., 2009). Severity of dysfunction in self and interpersonal domains predicts PD outcomes in both adults (Hopwood et al., 2011) and adolescents (DeFife, Goldberg, & Westen, in press), and there is some preliminary support for the structure of the levels of personality functioning (Morey et al., 2011).

The second of the two key components required for a PD diagnosis is the presence of one or more pathological personality traits. These pathological traits are organized into five domains, and these five broad domains include between three and nine specific, narrowband facets. The five personality trait domains and their specific trait facets are as follows (see APA, 2013, pp. 779–781):

1. Negative Affectivity (vs. Emotional Stability): emotional lability, anxiousness, separation insecurity, submissiveness, hostility, perseveration, depressivity, suspiciousness, and restricted affectivity (lack of).
2. Detachment (vs. Extraversion): withdrawal, intimacy avoidance, anhedonia, depressivity, restricted affectivity, suspiciousness.
3. Antagonism (vs. Agreeableness): manipulativeness, deceitfulness, grandiosity, attention seeking, callousness, hostility.
4. Disinhibition (vs. Conscientiousness): irresponsibility, impulsivity, distractibility, risk taking, and rigid perfectionism (lack of).
5. Psychoticism (vs. Lucidity): unusual beliefs and experiences, eccentricity, and cognitive and perceptual dysregulation.

The DSM-5 definitions for the five pathological personality trait domains are presented in Part B of Table 18.3. Some facets are included for more than one domain because, empirically, they are components of multiple domains.

The choice of these five PD trait domains was based on the research on pathological personality traits described in the previous section (Krueger, Eaton, Clark, et al., 2011; Skodol, 2012), and the domains clearly overlap with much previous work on normal and abnormal trait structure (Markon et al., 2005; Widiger, 2013). The primary domain names all focus on the more negative end of the trait dimension, however. The DSM-5 Personality and PDs Work Group opted to frame the domains in terms of pathological traits, rather than in terms of the normal-range personality models like the Big Five, in part because normal-range personality models do not adequately capture the full range of personality pathology (Krueger, Eaton, Clark, et al., 2011). A particular challenge that faced the work group was that although there is general consensus among researchers about the nature of the five domains, research has not clearly specified the facets that make up those domains (Clark, 2007; Krueger, Eaton, Clark, et al., 2011). The work group generated a set of facets based on the clinical relevance of the facets and based on current research on the ways that personality trait pathology may manifest itself, and then refined the list of facets based on research using a new questionnaire inventory of the DSM-5 facets—the Personality Inventory for DSM-5 (PID-5; Krueger, Derringer, Markon, Watson, & Skodol, 2011; Krueger, Eaton, Derringer, et al., 2011). Preliminary research on the PID-5 in adult samples suggests that it is structured in terms of the

five broad trait domains (Wright, Thomas, et al., 2012) and recovers much of the information obtained through use of the PD symptom lists in DSM-IV (Hopwood, Thomas, Markon, Wright, & Krueger, 2012).

Once a clinician or researcher has determined that a patient meets the general criteria for impairment and pathological personality traits, there are two possible routes to specifying the nature of the PD: (1) providing a specific PD diagnosis, or (2) providing a diagnosis of personality disorder—trait specified. To address the first route, there are six specific PD diagnoses retained from *DSM-IV*—ASPD, BPD, and avoidant, narcissistic, obsessive–compulsive, and schizotypal PDs—but the diagnoses are defined by new diagnostic criteria framed in terms of specific impairments and pathological personality traits, consistent with the general Section III framework. The typical features of these six diagnoses are presented in Table 18.5. As noted earlier, these diagnoses were retained based on some combination of prevalence in community and clinical samples, associated psychosocial impairment, and evidence for the validity and clinical utility of the disorders (Skodol, 2012; Skodol, Bender, et al., 2011). To address the second route to PD diagnosis, for people who do not display a pattern of impairment and pathological traits consistent with one of these six diagnoses, the diagnosis of personality disorder—trait specified is used instead; the nature of the diagnosis is made clear by noting the specific aspects of impairment and pathological personality traits exhibited by a particular patient. This new diagnosis is designed to provide more detail and nuance for what may have previously been a diagnosis of PD-NOS.

At this point, it is not clear to what extent this Section III model for the PDs will be used in both clinical and research settings. Obviously, the model was not unanimously well received by the APA Board; otherwise, the DSM-IV PD diagnoses would not have been retained in DSM-5's Section II. The model has been criticized for lacking adequate empirical support and breaking away too radically from the previous model (Frances & Widiger, 2012; Leising & Zimmerman, 2011). Other criticisms have been leveled against it as well: It deletes numerous PD diagnoses that have been useful for decades; it is unduly complex; and it does not adequately cover the full range of normal personality traits (Widiger, 2011). However, the model has much to commend it, especially in light of the research described in this section of the chapter, and future research will help refine it further.

TABLE 18.5. DSM-5 Proposed Specific Personality Disorders

Section III [of DSM-5, Emerging Measures and Models,] includes diagnostic criteria for antisocial, avoidant, borderline, narcissistic, obsessive–compulsive, and schizotypal personality disorders. Each personality disorder is defined by typical impairments in personality functioning (Criterion A) and characteristic pathological personality traits (Criterion B):

- Typical features of **antisocial personality disorder** are a failure to conform to lawful and ethical behavior, and an egocentric, callous lack of concern for others, accompanied by deceitfulness, irresponsibility, manipulativeness, and/or risk taking.
- Typical features of **avoidant personality disorder** are avoidance of social situations and inhibition in interpersonal relationships related to feelings of ineptitude and inadequacy, anxious preoccupation with negative evaluation and rejection, and fears of ridicule or embarrassment.
- Typical features of **borderline personality disorder** are instability of self-image, personal goals, interpersonal relationships, and affects, accompanied by impulsivity, risk taking, and/or hostility.
- Typical features of **narcissistic personality disorder** are variable and vulnerable self-esteem, with attempts at regulation through attention and approval seeking, and either overt or covert grandiosity.
- Typical features of **obsessive–compulsive personality disorder** are difficulties in establishing and sustaining close relationships, associated with rigid perfectionism, inflexibility, and restricted emotional expression.
- Typical features of **schizotypal personality disorder** are impairments in the capacity for social and close relationships, and eccentricities in cognition, perception, and behavior that are associated with distorted self-image and incoherent personal goals and accompanied by suspiciousness and restricted emotional expression.

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EPIDEMIOLOGY AND COMORBIDITY

Epidemiology

It is important to estimate the prevalence of PDs across the lifespan, in order to obtain a clearer developmental perspective on the emergence and course of PDs. At this point, far more prevalence studies have been conducted in adult samples than in samples of youth.

In community samples of adults assessed with a structured or semistructured clinical interview, the average current prevalence of any PD is between 10.5 and 12% (Lenzenweger, 2008; Torgersen, 2012), and the current prevalence for any specific PD is around 1–2% (Torgersen, 2012). The most common PDs in adult samples appear to be avoidant PD and obsessive–compulsive PD; consistent with this finding, the Cluster C PDs appear to be more prevalent than the Cluster A and B PDs (Torgersen, 2012). The prevalence studies in adults are limited in several ways (relatively small, mostly urban, and mostly American samples), but the consistency of the findings across studies lends support to the idea that approximately 1 in 10 adults has at least one PD at any one point in time. The lifetime prevalence rates are of course higher, with estimates of at least 30% for any PD and 3–4% for specific PDs (Torgersen, 2012). Clinical samples of adults display high current rates of PDs, with an estimate range of 46–81%, and with estimates as high as 51–88% when PD-NOS is included (Torgersen, 2012).

The data on prevalence in youth are more limited, but they point to the likelihood that PDs may be slightly more prevalent earlier in life than in adulthood. Several studies with youth suggest that the rates of PDs may be higher in early and middle adolescence (Bernstein et al., 1993; Johnson, Cohen, Dohrenwend, Link, & Brook, 1999; Zaider, Johnson, & Cockell, 2000) than is typical in later adolescence and adulthood, although one unusual study found very low rates of PDs in a community sample of adolescents ages 14–18 (Lewinsohn, Rohde, Seeley, & Klein, 1997). The Children in the Community study has particularly helpful data on this issue because it has tracked the prevalence of PDs assessed by interviews in the same sample across time (Johnson, Cohen, Kasen, Skodol, & Oldham, 2008). The study obtained the following point prevalence rates: age 14, 14.6%; age 16, 12.7%; age 22, 13.9%; and age 33, 12.7%. The finding of slightly higher PD prevalence rates earlier in adolescence in several samples is consistent with findings that pathological personality traits are at highest levels during adolescence, as described later in this chapter. In adulthood, Cluster B PDs are more prevalent earlier in adulthood than later in adulthood (Torgersen, 2012). Interestingly, the Children in the Community study found that the Cluster B PDs were the most common PDs in adolescence (Johnson, Cohen, Kasen, Skodol, et al., 2000); this suggests that the Cluster B PDs may be most prevalent earlier in life, particularly adolescence. Two studies of PDs in clinical samples of adolescents indicate that, as in adult samples, rates of PDs are high, with estimates falling between 41 and 64% (Feenstra, Busschbach, Verheul, & Hutsebaut, 2011; Grilo et al., 1998). Taken together, the more limited data on youth indicate that (1) PDs are at least as common in adolescence as in adulthood; (2) the Cluster B PDs may be more prevalent in adolescence than in adulthood; (3) the Cluster C PDs may be more prevalent in adulthood than in adolescence; and (4) PDs are extremely common in clinical samples of youth.

As with general prevalence rates for PDs, much more is known about gender differences in PD rates in adults than in adolescents. Although the overall prevalence rates for PDs appear to be roughly equal for adult males and females, some specific PDs may be more prevalent in one gender or the other (Oltmanns & Powers, 2012; Paris, 2007; Torgersen, 2012). In adult community samples, ASPD is much more common in men (Torgersen, 2012), with rates five times as high in men than in women (Magnavita, Powers, Barber, & Oltmanns, 2013; Oltmanns & Powers, 2012). Dependent PD is more common in women (Torgersen, 2012). Other differences are less certain: Narcissistic PD and obsessive–compulsive PD may be more common in men, and histrionic PD and avoidant PD may be more common in women (Torgersen, 2012), but most gender differences in prevalence are nonexistent, small, or inconsistent across studies (Oltmanns & Powers, 2012). It is especially notable that rates of BPD do not appear to differ consistently by gender. The few cases where there are gender differences appear to reflect gender differences in related personality traits (Oltmanns & Powers, 2012; Paris, 2007); on average, men tend to be higher in assertiveness and excitement seeking, whereas women tend to be higher on facets of the higher-order factors Neuroticism and Agreeableness. In short, gender differences in adult PDs are not as common or as large in community samples of adults as often assumed.

The limited available information on community samples of PDs and PD traits in youth suggests that gender differences in prevalence rates or levels of symptoms are likewise small or nonexistent (Bernstein et al., 1993; see the review for BPD traits in Belsky et al., 2012), other than the consistent finding that conduct problems are more prevalent in samples of males (Moffitt, Caspi, Rutter, & Silva, 2001). Although gender differences in prevalence rates are typically small in adults and potentially small in youth, gender still seems to have an important impact on the manifestations of

specific PDs in adults (Oltmanns & Powers, 2012), and the same is likely to be true for youth as well. For example, although adolescent girls with BPD show correlates similar to those of adults with BPD, boys with BPD tend to be more disruptive and antisocial (Bradley, Conklin, & Westen, 2005). Clearly, this is an issue requiring more research in samples of youth.

Unfortunately, even less is known about variability in prevalence rates of PDs by ethnicity, race, or culture in adults and youth (Magnavita et al., 2013; Mulder, 2012). A recent meta-analysis compared rates of adult PDs across racial groups and found slightly lower rates among black than white populations, but no differences among white, Asian, and Hispanic populations (McGilloway, Hall, Lee, & Ghui, 2010); however, the studies included in the meta-analysis had significant limitations. There are no epidemiological studies of prevalence rates for PDs across cultures (Mulder, 2012). However, the existing evidence suggests that ASPD is found in all cultures studied, though the prevalence rates vary (Mulder, 2012); other PDs have been identified in most cultures, but again, prevalence rates vary. More work is needed to understand the validity of the use of PD diagnoses across cultures and to determine prevalence rates, if PDs are valid diagnostic categories in those cultures.

Comorbidity among PDs and between PDs and Other Psychiatric Disorders

Comorbidity appears to be the rule rather than the exception among PDs in both adolescents and adults. There tends to be a high level of comorbidity among PDs in epidemiological samples of adults (Skodol, 2005; Trull et al., 2012); in fact, it is relatively uncommon for an adult to have only one PD, and this is even rarer in clinical samples (Trull et al., 2012). In adult samples, BPD, paranoid PD, and dependent PD show the highest rates of co-morbidity with other PDs, and ASPD and obsessive–compulsive PD show the lowest rates (Trull et al., 2012). In contrast to the substantial literature on comorbidity among PDs in adults, there are surprisingly few studies of such comorbidity in youth. The Children in the Community study has not reported specific rates of PD comorbidity, but Cohen, Crawford, and colleagues (2005) noted that in this sample, "There is relatively high comorbidity and correlation among the criteria counts for the PDs" (p. 470). Becker, Grilo, Edell, and McGlashan (2000) reported that a sample of hospitalized adolescents with BPD showed unusually high rates of comorbidity with Cluster A and Cluster C PDs, compared to a comparison sample of adults. Similarly, De Clercq and colleagues (2004) found unusually high rates of overlap among PD symptoms in their adolescent sample. Future work should address the question of whether comorbidity among PDs is especially high in youth.

There is also a high rate of concurrent comorbidity between PDs and other psychiatric disorders in both adults (Links, Ansari, Fazalullash, & Shah, 2012) and adolescents (Cohen, Crawford, et al., 2005; Feenstra et al., 2011; Grilo et al., 1998). All three clusters of PDs in adolescence show high rates of comorbidity with other psychiatric disorders, including depressive, anxiety, and disruptive behavior disorders (Cohen, Crawford, et al., 2005), and PDs are associated with substance use problems as well (Serman, Johnson, Geller, Kanost, & Zacharapoulou, 2002). Adolescent PD-NOS also shows high comorbidity with non-PD conditions (Johnson et al., 2005). Furthermore, earlier disorders, including anxiety, depression, and disruptive behavior disorders, predict heightened risk for later emergence and continuation of PDs into adulthood (Cohen, Crawford, et al., 2005; Goodwin, Brook, & Cohen, 2005; Lewinsohn et al., 1997). The reverse is true as well: Earlier PDs predict greater risk for other early adult psychiatric disorders, including depressive, anxiety, and substance use disorders (Cohen, Chen, Crawford, Brook, & Gordon, 2007; Cohen, Crawford, et al., 2005; Daley et al., 1999; Levy et al., 1999), sometimes even after the presence of earlier PDs and other disorders is taken into account. In addition, when PDs co-occur with other psychiatric disorders in adolescence, the likelihood of the PDs' continuing into adulthood is increased (Cohen, Crawford, et al., 2005). It appears that there is often a transaction between PDs and other disorders across the years from adolescence to adulthood, with other psychiatric disorders contributing to the expression of PDs and vice versa.

Some patterns of associations between PDs and other disorders seem to be especially common for particular clusters of PDs. First, not surprisingly, Cluster A PDs seem especially associated with psychotic disorders, but they are associated with other disorders as well. Adolescents who exhibit schizotypal PD and who meet prodromal criteria for psychotic disorders show higher rates of transition to disorders with psychotic features (Correll et al., 2008); this finding is consistent with the idea that genetic risk for schizophrenia predisposes individuals to develop schizotypal PD (Fanous et

al., 2007). We discuss research supporting the idea that shared genetic factors underlie vulnerability to Cluster A PDs and psychotic disorders in the section on the etiology of the Cluster A PDs. Adolescent disruptive behavior disorders predict heightened risk of schizoid PD, and adolescent anxiety disorders predict risk of paranoid PD (Kasen et al., 2001). The persistence of Cluster A PDs from adolescence to adulthood is much greater in the presence of anxiety disorders than the persistence of Cluster B and C PDs' co-occurring with anxiety (Cohen, Crawford, et al., 2005).

Second, several lines of evidence indicate that Cluster B PDs show especially strong links with disruptive behavior, substance abuse, and depression. Cluster B PDs are substantially more stable when they co-occur in adolescence with disruptive behavior disorders or depression (Kasen, Cohen, Skodol, Johnson, & Brook, 1999); adolescent Cluster B PDs predict higher risks of substance abuse in adulthood (Cohen et al., 2007); and disruptive behavior disorders predict increased risks for Cluster B disorders (Cohen, Crawford, et al., 2005). Young adolescents with high levels of BPD traits also display heightened rates of other disorders—particularly depression, but also conduct disorder, psychosis, and anxiety disorders (Belsky et al., 2012). Childhood ADHD and oppositional defiant disorder predict heightened risks for BPD symptoms in early adulthood (Burke & Stepp, 2012; Stepp, Olino, Klein, Seeley, & Lewinsohn, 2013), and conduct disorder and anxiety disorders sometimes do as well (Stepp et al., 2013). A recent longitudinal twin study of adolescents found that although shared/familywide environmental influences accounted for an association between BPD and substance use at age 14, the association was accounted for by shared genetic factors at age 18 (Bornovalova, Hicks, Iacono, & McGue, 2013). Taken together, the findings across these studies suggest that the Cluster B disorders, particularly BPD, show strong links with externalizing and internalizing disorders both concurrently and across time.

Third, the more limited research on the Cluster C PDs suggests that they seem to show fewer specific links with other psychiatric disorders, but rather exhibit various associations with disruptive behavior disorders, depressive disorders, and anxiety disorders over time (Cohen, Crawford, et al., 2005). Major depression in adolescence predicts adult dependent PD (Kasen et al., 2001). Although the Cluster C PDs show strong co-occurrence with anxiety disorders in adolescence, they do not predict later anxiety disorders after controls for earlier ones, although they do predict later disruptive behavior disorders (Johnson, Cohen, Skodol, et al., 1999).

Numerous researchers have suggested that the high rates of comorbidity among the PDs, and between the PDs and other disorders, indicate that genetic factors and personality traits are likely to underlie these co-occurrences (Clark, 2005, 2007; De Fruyt & De Clercq, 2012; Krueger, 2005; Krueger & Markon, 2008). Other psychiatric disorders probably include a strong component of personality functioning; these disorders would be better understood by considering their associations with personality functioning. There is evidence that symptoms of other psychiatric disorders are linked with PD traits in childhood (Mervielde et al., 2005): Antagonism and Disinhibition with externalizing symptoms, and Negative Affectivity and Detachment with internalizing symptoms. As we have discussed in the section on the trait models of PDs, disorders may co-occur because they arise from shared genetic sources and personality traits. For example, an adult twin study found evidence for a common genetic liability influencing the co-occurrence of major depression and dimensional representations of paranoid PD, BPD, and avoidant PD (Reichborn-Kjennerud et al., 2010); it seems possible that the genes influencing all of these conditions do so by shaping propensities toward Negative Affectivity.

The high rates of overlap between PDs and other psychiatric disorders suggest that the two types of disorders are not nearly as distinct as originally conceived. Empirical research on this topic almost certainly played some part in the decision to remove Axis II from DSM-5 and to put the categorical PDs in Section II with the rest of the disorders. Although PDs and other disorders show significant overlap in many respects, it is important to recognize that they may still differ somewhat, with PD traits being more stable and the symptoms of other disorders being more episodic. Improvement in PDs is typically more likely to lead to improvement in other conditions than the reverse (Clark, 2005). An adult twin study of the genetic and environmental structure of PDs and other psychiatric disorders in DSM-IV provided further evidence for the distinction between these two groups of disorders (Kendler et al., 2011). The results indicated four genetic factors that accounted for the observed covariation among disorders: Axis I internalizing (somatoform disorder, panic disorder, major depression, agoraphobia, specific phobia, generalized anxiety disorder, eating disorders); Axis

II internalizing (dysthymia, schizoid PD, schizotypal PD, avoidant PD, social phobia); Axis I externalizing (ASPD, drug abuse/dependence, conduct disorder, alcohol abuse/dependence); and Axis II externalizing (histrionic PD, narcissistic PD, obsessive–compulsive PD). Paranoid PD and dependent PD were related to the genetic factors for both internalizing and externalizing Axis II, and BPD was related to the genetic factors underlying Axis I and II externalizing disorders and an environmental factor underlying Axis I internalizing disorders. These results suggest that different genetic factors may underlie many of the PDs versus the other psychiatric disorders. The relationships among PDs, other psychiatric disorders, and personality traits in childhood and adolescence will be an especially exciting direction for future research.

COURSE: STABILITY AND LIFE OUTCOMES

Stability of PD Diagnoses/Traits and Pathological Personality Traits

Embedded in the DSM-IV and DSM-5 Section II PD diagnoses are some explicit claims about the stability and course of PDs. Specifically, in these diagnostic models, the PDs are described as *enduring* patterns that start by adolescence or early adulthood, and the patterns need to have existed for at least a year to warrant diagnosis in youth under age 18. These older views of PD have been challenged by a number of longitudinal studies that have examined the stability and course of PD diagnoses and symptoms in both youth and adults. These more recent studies have demonstrated that although PD symptoms show moderate rank-order stability by adolescence, PD diagnoses themselves are less stable than previously assumed. The findings for PD diagnoses and symptoms can be understood in light of recent research on the stability of normal-range personality traits over time. The newer view of PDs is reflected in the DSM-5 Section III requirement that PDs be only *relatively* stable over time.

Rank-Order Stability

Personality stability is itself a complex notion because there are many different kinds of continuity and change (Caspi & Shiner, 2006). First, "rank-order stability" refers to the degree to which the relative ordering of individuals on a given trait is maintained over time. Rank-order stability is high if people in a group maintain their position on a trait relative to each other over time, even if the group as a whole increases or decreases on that trait over time. It is typically indexed by correlations between scores on the same trait measured across two points in time (i.e., test–retest correlations). PD symptoms in adolescents and young adults display moderate to strong levels of rank-order stability across time, often in the range of .40–.65 (Bornovalova et al., 2013; Cohen, Crawford, et al., 2005; Crawford et al., 2005; Daley et al., 1999; Ferguson, 2010; Frick & White, 2008; Johnson, Cohen, Kasen, et al., 2000; Winograd, Cohen, & Chen, 2008); these are similar to the levels of PD symptom stability observed in adulthood (Clark, 2007, 2009; Ferguson, 2010; Grilo & McGlashan, 2005). Less is known about the rank-order stability of PD symptoms in childhood, but two studies suggest that PD symptoms and pathological traits may show similar levels of moderate to strong rank-order stability over periods of 1 and 2 years in childhood (Crick, Murray-Close, & Woods, 2005; De Clercq, Van Leeuwen, Van Den Noortgate, De Bolle, & De Fruyt, 2009). The De Clercq, Van Leeuwen, and colleagues (2009) study of pathological traits also found high within-person stability, meaning that the absolute levels of PD traits of each individual in the study tended to remain high.

The results for the rank-order stability of PD symptoms in youth parallel those found for normal-range personality traits. Personality traits are already moderately stable by childhood (Roberts & DelVecchio, 2000), but become increasingly stable from childhood through adolescence (Ferguson, 2010; Shiner, 2014). A recent meta-analysis demonstrated that the same is true for normal and pathological personality traits in adulthood, in that both kinds of traits show high levels of stability (Ferguson, 2010). The findings for rank-order stability of PD symptoms, pathological traits, and normal-range traits converge on a shared conclusion: There is nothing transformative about the age of 18 with regard to stability of PDs measured dimensionally. Moderate to strong stability is already apparent by adolescence and may already be in place by late childhood and early adolescence.

Mean-Level Stability

Second, "mean-level change" refers to increases or decreases in the average trait level of a population as a whole. In other words, investigations of mean-level

change address the question of whether people, on average, tend to increase or decrease on particular trait or symptom measures during different periods of life. In terms of mean-level change, findings from the Children in the Community study suggest that levels of PD symptoms may peak in adolescence and then decline across the years of later adolescence and early adulthood (Cohen, Crawford, et al., 2005; Johnson, Cohen, Kasen, et al. 2000). Narcissistic symptoms showed the greatest decline from adolescence to adulthood (Cohen, Crawford, et al., 2005; see also Carlson & Gjerde, 2009), whereas obsessive–compulsive symptoms did not decline at all (Cohen, Crawford, et al., 2005). A short-term study of pathological personality traits in childhood found slight mean-level decreases in such traits (except for Introversion) across 1 and 2 years in later childhood (De Clercq, Van Leeuwen, et al., 2009). BPD traits have been found to decline modestly from ages 14 to 18 (Bornovalova et al., 2013). Findings from longitudinal studies of adults suggest that PD symptom levels and pathological trait levels continue to decline in adulthood as well (Clark, 2007). Recent research in older adults, however, has called this finding somewhat into question (Cooper, Balsis, & Oltmanns, 2014). Specifically, Cooper and colleagues found that the pattern of declining PD symptoms over time only held when self-reports were examined; informant reports of PD symptoms actually showed slight increases over time. This study raises interesting questions about potentially confounding measurement factors in such studies, and challenges the general notion that PD symptoms decline across adulthood.

These findings for mean-level change are generally consistent with results for mean-level change of normal personality traits from childhood through adulthood, and these mean-level changes in normal-range traits may help to explain changes in the prevalence rates of PDs over time. In fact, a recent study demonstrated that mean-level changes in aspects of the Big Five traits from adolescence through later adulthood could explain parallel mean-level changes in psychopathy (a construct discussed later in this chapter) and its prevalence in forensic samples (Vachon et al., 2013). The studies on mean-level trait changes in childhood and early adolescence are not entirely consistent, but there is some evidence that although children develop better emotional self-regulation and greater Conscientiousness and Agreeableness across the childhood years (Shiner, in press), youth may show mean-level decreases in these positive traits in the transition from childhood to adolescence, followed by increases in those traits later in adolescence (Shiner, 2014; see, e.g., Soto, John, Gosling, & Potter, 2011). Across the late adolescent and early adult years, there is a movement toward greater personality maturity on average. Neuroticism decreases in young adulthood, and Agreeableness and Conscientiousness increase in young adulthood and middle age (Roberts, Walton, & Viechtbauer, 2006). Given that many PDs are characterized by high Neuroticism and low Agreeableness and Conscientiousness, it is not surprising that on average, PD symptoms may peak in early or mid-adolescence and later decline.

The positive growth in personality traits from late adolescence through adulthood is accounted for in part by young adults' greater investment in socially important roles as spouses or partners, workers, and parents (Lodi-Smith & Roberts, 2007). However, it is important to recognize that not all people benefit from increased personality maturity as they enter adulthood (Roberts, Wood, & Caspi, 2008). Rather, some people show changes in their personality traits in more negative directions. People who lack normative experiences with adult roles may be particularly vulnerable to such negative changes in personality (Roberts et al., 2008). Given that PDs in adolescence put youth at risk for problems with developmental tasks in the transition to adulthood, it is likely that youth struggling with personality pathology may sometimes miss out on the beneficial effects of adopting more adult roles. This is consistent with evidence that the transition from late adolescence to early adulthood represents a critical developmental period for PDs, and a time when individuals with PD diagnoses grow increasingly deviant from their peer group (Clark, 2005; Tackett et al., 2009).

Stability of PD Diagnoses

Finally, the stability of PD diagnoses over time is important for understanding the nature of PDs. If a person meets criteria for a particular PD, is it likely that the person will still warrant that diagnosis over time? Contrary to what might be expected from the classic view of PDs represented in all of the previous DSMs, the stability of particular PD diagnoses appears to be relatively modest in samples of adolescents (Bernstein et al., 1993; Chanen et al., 2004; Cohen, Crawford, et al., 2005; Daley et al., 1999; Mattanah, Becker, Levy, Edell, & McGlashan, 1995) and adults (Clark, 2007, 2009; Grilo & McGlashan, 2005; Skodol et al., 2005; Zanarini, Frankenburg, Hennen, Reich, & Silk, 2005).

This relatively modest stability is probably due to several causes. First, it may result in part from the categorical system used for diagnosis; patients can switch from having a PD to not having one, simply because they exhibit one or two symptoms fewer for a particular PD. Second, the instability in diagnoses also reflects the mean-level changes in PD symptoms and traits; as mean levels of PD symptoms and traits decline, these mean-level changes lead to changes in PD diagnoses over time as well (Clark, 2009). Third, the surprising remission rates also reflect the nature of PDs, in that there are more and less stable aspects to PDs (Clark, 2007; Skodol et al., 2005; Zanarini et al., 2005). The less stable aspects typically involve more acute behaviors, such as odd behavior, self-harm, or avoidance of particular situations; in contrast, the more stable aspects involve personality traits underlying the condition, such as the paranoid ideation seen in schizotypal PD or the feelings of inadequacy and social ineptness in avoidant PD (McGlashan et al., 2005). BPD similarly includes more acute aspects (substance abuse, chaotic relationships) and more temperamental, chronic aspects (anger and odd thinking) (Hopwood, Donnellan, & Zanarini, 2010). As the more acute aspects of PDs resolve over time, people may no longer qualify for PD diagnoses, even if the more chronic aspects remain in place.

It is important to note that despite the general improvements that typically occur in personality functioning, there may be some individuals whose PD symptoms worsen in adolescence and adulthood and become a more persistent pattern. In the Children in the Community study, adolescents with PD diagnoses frequently continued to display high PD traits in early adulthood (Johnson, Cohen, Kasen, et al., 2000), and a fifth of the youth showed an increase in PD symptoms over the decade from midadolescence through early adulthood (Cohen, Crawford, et al., 2005). In the short-term longitudinal study of older children's pathological personality traits described previously, the children who started with the highest levels of pathological traits exhibited less pronounced declines in those traits than the rest of the sample (De Clercq, Van Leeuwen, et al., 2009). And although rates of continuity may be low for specific PD diagnoses, there is some evidence that adolescent patients with a PD diagnosis may still be at higher risk of having *any* PD diagnosis over time (Chanen et al., 2004; Cohen, Crawford, et al., 2005). These youth with non-normative development in PD symptoms may be the ones who especially need research and clinical attention.

Life Outcomes Associated with PDs

Although data on some aspects of PDs in youth are sparse, there is a convincing literature about the negative life outcomes predicted by PDs earlier in life. In a previous section, we have described research indicating that an adolescent PD heightens the chances that a youth will develop a non-PD condition in adulthood. Youth PDs increase vulnerability for the development of a wide variety of other harmful and potentially risky behaviors as well. PDs from Clusters A and B in adolescence predict risks for adolescent and adult violence—including acts such as "arson, assault, breaking and entering, initiating physical fights, robbery, and threats to injure others" (Johnson, Cohen, Smailes, et al., 2000, p. 1406)—and for violence against romantic partners (Ehrensaft, Cohen, & Johnson, 2006), even when possible confounding variables are taken into account. Paranoid and narcissistic symptoms in particular are associated with later violence and criminality, perhaps because they fuel the suspiciousness and entitlement that often precipitate aggression (Cohen, Crawford, et al., 2005). Adolescents with PDs are also at heightened risk for having high numbers of sexual partners and for high-risk sexual behaviors more generally (Lavan & Johnson, 2002). Adolescent PDs from all three clusters are predictive of heightened risk of suicidal ideation or attempts in early adulthood (Brent, Johnson, Perper, & Connolly 1994; Johnson, Cohen, Skodol, et al., 1999). Nonsuicidal self-injury (NSSI) may also be present in youths with PDs; NSSI may take the form of cutting, burning, or punching oneself (Nock, 2010; see Cha & Nock, Chapter 7, this volume). A study of adolescent inpatients found that two-thirds of the patients who had engaged in NSSI prior to admission met criteria for a PD (Nock, Joiner, Gordon, Lloyd-Richardson, & Prinstein, 2006). Suicide and NSSI seem to be particularly associated with BPD, in that adolescent suicide attempts and NSSI are associated with the number of borderline symptoms (Jacobson, Muehlenkamp, Miller, & Turner, 2008), and adolescent inpatients with BPD are more likely to have experienced suicidal ideation earlier in life and with more frequency than psychiatric controls (Venta, Ross, Schatte, & Sharp, 2012). A study of adult patients with BPD found that, among the patients who had engaged in self-mutilation, approximately one-third reported having started harming themselves as children, and another third reported having started as adolescents (Zanarini et al., 2006). Taken together, the evidence suggests that particular adolescent PDs pose

risks in terms of violence, criminality, high-risk sexual behaviors, suicide attempts, and NSSI.

Beyond the effects of PDs on symptomatology and risky behaviors, there is evidence that adolescent PDs are associated with risks for problems with adaptation, both concurrently and later in adulthood. Adolescent PDs put youth at risk for later overall impairment in adulthood (Skodol, Johnson, Cohen, Sneed, & Crawford, 2007) and are associated with high health care costs and reduced quality of life among patients, especially when accompanied by a non-PD condition (Feenstra et al., 2012). Some PDs in both adolescents and adults seem to be associated with higher risks of impairment (e.g., BPD and schizotypal PD), whereas others seem to be associated with relatively little overall impairment (e.g., histrionic PD, narcissistic PD, and obsessive–compulsive PD) (Chen et al., 2006; Torgersen, 2012). Adolescent PDs and traits pose heightened risks for later conflicts with family members (Johnson, Chen, & Cohen, 2004); difficulties with child rearing in middle adulthood (Johnson, Cohen, Kasen, & Brook, 2008); and problems with romantic relationships, including stressful relationships, conflicts, and low partner satisfaction (Chen et al., 2004; Daley, Hammen, Davila, & Burge, 1998; Johnson et al., 2005; Winograd et al., 2008). Adolescents with PDs also have heightened rates of problems in other domains of life, including difficulties in friendships, few social activities, poor educational achievement, and work difficulties (Bernstein et al., 1993; Johnson et al., 2005; Winograd et al., 2008).

The Children in the Community study has identified several patterns of outcomes for the three clusters of PDs. The adolescents with high levels of Cluster A symptoms displayed the greatest degree of impairment in the transition from adolescence to adulthood (Cohen, Chen, et al., 2005). This is probably attributable to the fact that Cluster A symptoms may reflect vulnerability to symptoms of schizophrenia for some people. The participants in the Children in the Community study were asked to provide life narratives describing themselves in various roles and social settings, and these narratives revealed worse trajectories in terms of education and achievement. In addition, Cluster A symptoms in adolescence predicted a greater likelihood of teenage parenting (Cohen, Chen, et al., 2005) and higher levels of partner conflict through age 23 (Chen et al., 2004). Fortunately, some of the adolescents with high Cluster A symptoms did better in terms of life adaptation in the transition to adulthood, and this then predicted a decline in Cluster A symptoms over time (Cohen, Crawford, et al., 2005). Cluster B symptoms showed particular relevance for romantic relationships because of their links with identity disturbance (Crawford, Cohen, Johnson, & Sneed, 2004); specifically, adolescent Cluster B symptoms were associated with lower well-being and intimacy in relationships in adolescence, and the negative association with intimacy became stronger in adulthood. Cluster A symptoms in adolescence predicted heightened partner conflict over the next decade (Chen et al., 2004). In contrast, although youth with high levels of Cluster C symptoms were less likely to develop romantic relationships, those in romantic relationships showed higher levels of conflict until age 23 only, and then later showed even lower levels of conflict than was typical (Cohen, Crawford, et al., 2005). Thus, although most PDs are associated with some degree of impairment, the patterns of problematic adaptation may vary according to the symptoms a youth displays.

All of the findings for PDs and adaptation are consistent with research on personality in childhood and adolescence more generally; youth's personalities are predictive of many important life outcomes, including peer relationships, formation of romantic relationships, academic attainment, effectiveness at work, and health (Caspi & Shiner, 2006; Zentner & Shiner, 2012). The effects of PDs on the critical developmental tasks of adolescence and young adulthood—developing friendships and romantic relationships, and developing skills for education and work—may be one of the most negative outcomes of PDs in youth. Impairment may be quite stable, even when PD symptoms change (Clark, 2007, 2009). The risks for later impairment well into adulthood are as high for PDs as for other psychiatric disorders in adolescence (Crawford et al., 2008); the combination of PDs and non-PD conditions in adolescence is even more problematic for adult outcomes. The more persistent PDs are in adolescence, the greater the adaptive impairment in adulthood is likely to be (Skodol, Johnson, et al., 2007).

Despite the seemingly gloomy picture for adolescent PDs, it is important to recognize that not all youth with PDs suffer clear-cut impairment (Cohen, Crawford, et al., 2005; Johnson et al., 2005). Fortunately, some youth with PDs improve in their functioning as they age (Cohen, Crawford, et al., 2005). There appear to be transactions between youth's PD symptoms and their adaptation. Positive adaptation in school and in relationships can lead to improvements in some PD

symptoms over time (Skodol, Bender, et al., 2007). As PD symptoms improve, youth's sense of well-being may correspondingly improve as well (Crawford et al., 2004). Conversely, problems with adaptation are likely to cause and perpetuate PD symptoms. Poor school achievement, being suspended from school, and repeating a grade all predict later adolescent PD symptoms (Cohen, Crawford, et al., 2005). Similarly, young adults who perpetrate partner violence are less likely to experience the positive declines in PD symptoms that occur normatively during this span of life (Ehrensaft et al., 2006). The interaction between personality pathology and impairment is likely to be complex.

ETIOLOGY

Genetic, Family, and Broader Contextual Influences

As is true for many other topics in the study of PDs in youth, empirical research on the developmental pathways leading to the development of PDs is more limited than would be desirable. Much of the early clinical interest in PDs in the 20th century arose from rich, complex psychodynamic theories about the origins of these conditions. Most of these etiological theories were based on clinicians' discussions with their patients about their early histories. Although these theories spurred interest in PDs and provided a basis for interventions, relatively little is known empirically about the developmental pathways leading to many of the PDs. Nonetheless, there are several promising leads for potential causes of PDs. Because we have provided an overview of the personality characteristics likely to be involved in the development of PDs earlier in this chapter (see our description of the research on temperament and personality traits, mental representations [including attachment and social-cognitive processes], emotion regulation and coping, and life narratives), we focus here instead on three other potential contributors: genetic influences, experiences within the family, and broader contextual factors (peers, schools, socioeconomic resources, and cultural influences). We focus in this section on a discussion of the etiology of PDs in youth in general. Following this section, we turn to a review of research on the etiology of Cluster A PDs, BPD, ASPD/psychopathy/narcissism, and Cluster C PDs.

There has been some research on the neurobiological correlates of many of the PDs in adults, as well as on the neurobiological basis of many of the dimensions associated with the different clusters of PDs (e.g., psychotic-like perceptual distortions in Cluster A and affective instability in Cluster B; Roussos & Siever, 2012). Relatively few studies have examined the neurobiological basis of most of the PDs in youth; however, we review briefly the existing neuroscience research on schizotypal PD, BPD, and psychopathy in the relevant sections.

Genetic Influences

Most people who experience adversity do not go on to develop PDs. This simple finding suggests that there are almost certainly genetic factors that shape vulnerability to developing personality pathology in the face of adverse experiences. Thus far, three twin studies have been conducted to examine the genetic and environmental contributions to individual differences in PD symptom counts for all 10 PDs listed in DSM-IV (South, Reichborn-Kjennerud, Eaton, & Krueger, 2012). One of these examined parent reports of PD symptoms in children (Coolidge, Thede, & Jang, 2001) and obtained heritability estimates ranging from .50 to .81, with no shared/familywide environmental effects and with moderate effects of the nonshared/child-specific environment on PD symptoms. The other two studies examined PD symptoms in adult twin samples (Kendler et al., 2006; Reichborn-Kjennerud et al., 2007; Torgersen et al., 2000, 2008). The average heritability of PD symptoms obtained across these three studies was .4–.5, indicating moderate heritability, and the studies have been consistent in finding only limited shared or familywide environmental effects (South et al., 2012). Estimates of heritability for PD traits in adults are roughly similar in magnitude to those for PD symptoms (Cloninger, 2005; Livesley, 2005). These behavior genetic findings for PD symptoms and traits are consistent with findings for temperament and personality traits in childhood (Saudino & Wang, 2012) and personality traits in adulthood (Krueger & Johnson, 2008; South et al., 2012). Although more research is needed before firm conclusions can be drawn, the existing data suggest that genetic influences on PD symptoms, PD traits, and normal-range personality traits are moderate in size, and that environmental differences account for a substantial portion of the variation as well. What environmental experiences tend to do, however, is to create differences in PD outcomes between children growing up in the same family, rather than to make siblings more alike.

An adult multivariate twin study by Kendler and colleagues (2008) examined the genetic and environmental influences on the co-occurrence of symptoms of the 10 DSM-IV PDs. Three genetic risk factors were identified: first, one accounting for the general risk for PDs (interpreted by the authors as most likely to be a propensity for Negative Affectivity); second, one influencing BPD and ASPD (interpreted as reflecting high Disinhibition and Antagonism); and, third, one influencing schizoid and avoidant PDs (interpreted as reflecting high Detachment). These three genetic risk factors appear likely to be linked with four of the five domain-level pathological personality traits in the DSM-5 Section III PD diagnoses. In addition, three nonshared/person-specific environmental factors accounted for the associations among the disorders within each of the three clusters of PDs (Clusters A, B, and C). In other words, similar nonshared/person-specific environmental factors influenced all of the disorders within each cluster. Finally, multiple genetic and nonshared/person-specific environmental factors contributed to each of the PDs. This study suggests that genetic factors do not contribute to the co-occurrence of PDs within clusters, but environmental experiences that shape PDs within clusters may do so. These results point to three important areas for future investigation: the developmental influences on the basic pathological personality dimensions; the environmental factors that shape disorders within the three clusters; and the specific genetic and environmental sources of variation in more narrowly defined aspects of personality pathology.

Finally, it is important to note that molecular genetic techniques have been used in an attempt to identify some of the specific genes responsible for genetic influences on PDs and normal-range personality traits. At this point, the results of molecular genetic research on these topics has been disappointing, in that replicable molecular genetic influences have not been identified, or only trivial amounts of variance in outcomes have been accounted for (South et al., 2012).

It is not clear yet which individual differences are the mediators through which genes influence the development of PDs. The personality differences described previously in this chapter may be one such mediator. Some other individual differences have been identified as risk factors for the development of PDs, including "low IQ, poor achievement, having been suspended or expelled from school, having repeated at least one grade, and not being goal directed" (Cohen, Crawford, et al., 2005, p. 471). These other individual differences, which may reflect different aspects of cognitive and executive functioning, are other individual differences beyond personality worthy of investigation as vulnerability factors for the development of PDs.

Family Influences

The behavior genetic research points to the importance of environmental experiences in the development of PD symptoms and traits. Among the most likely sources of environmental influence on PDs are youth's experiences within their families. Although there have been many theories about the ways that families influence the development of PDs, there were few data on this topic until the last 15 years. Many of the studies have focused on the role of the family in the development of particular PDs, and we address that research in the following sections. However, some studies have looked at the family effects across all of the PDs.

Maladaptive parenting generally poses risks for the development of PDs in early adulthood; such maladaptive parenting includes low parental affection or nurturing and aversive parental behavior (such as harsh punishment) (Johnson, Cohen, Chen, Kasen, & Brook, 2006). The greater the number of negative parental behaviors, the higher the risk for young adult PDs (Johnson et al., 2006). Other family risks for PD development include single parenthood, parental conflict, and parental psychiatric disorders (Cohen, Crawford, et al., 2005); separation from parents, particularly before the age of 5 (Lahti et al., 2012); and parental suicide attempts or completion, parental history of being jailed, and history of a battered mother (Afifi et al., 2011).

There is now longitudinal evidence that childhood abuse (including sexual, physical, and verbal abuse) and neglect predict heightened risk for the later development of PDs (Johnson, Cohen, Brown, Smailes, & Bernstein, 1999; Johnson et al., 2001; Johnson, Smailes, Cohen, Brown, & Bernstein, 2000). Retrospective reports also suggest that adults with PDs reported having been maltreated at higher rates than adults without PDs (see, e.g., Afifi et al., 2011; Battle et al., 2004). A recent study of a nationally representative sample of adults found that childhood adversity, defined broadly as childhood maltreatment and household dysfunction, was particularly associated with schizotypal PD and most of the Cluster B PDs (Afifi et al., 2011). Many of these analyses linking adverse family experiences with adolescent or young adult PDs have controlled for

a variety of potential confounds, which strengthens the evidence for a potential causal role for family adversity in the development of PDs.

Negative experiences in the family may shape youth's emerging personality pathology through a number of processes. Children facing these adverse experiences lack the socialization experiences that normally help children learn how to follow societal rules, inhibit impulses, and regulate emotions and behavior (Bradley et al., 2011; Kim, Cicchetti, Rogosch, & Manly, 2009). Maltreatment may also undermine the development of healthy, realistic, and positive views of the self, others, and the self in relationship to others (Bradley et al., 2011; Feiring, Cleland, & Simon, 2010). Recent research has shown that parenting predicts changes in children's emerging personality traits. When parents fail to provide an environment that helps children manage negative emotions—specifically, when parents create an insensitive, punitive, chaotic, and hostile environment—children's negative emotionality tends to increase over time (Bates, Schemerhorn, & Petersen, 2012; Lengua & Wachs, 2012; Shiner, 2014). In addition, youth with poorer self-control are particularly negatively affected by adverse family environments (e.g., low maternal responsiveness, high parental punitiveness, single parenting) (Shiner, 2014). Thus family adversity may tend to promote a number of negative personality outcomes, including high Negative Affectivity and Disinhibition, troubled attachment styles, and more negative social-cognitive functioning.

Given that the behavior genetic research conducted thus far indicates a role for person-specific environmental influences on PD but not familywide environmental effects, it is important to note that the family experiences likely to be most relevant to the development of PDs are those that are unique to each youth in a family. Person-specific experiences within the family could include family events that are encountered by only one child in the family (e.g., separation from parents at a specific time, a specific parent–child relationship) or family events that are experienced uniquely by each child (e.g., parental psychopathology or marital conflict that is experienced uniquely by each sibling). In most of the studies looking at family predictors of PD, family factors are measured in a child-specific way (e.g., maltreatment of a specific child, affection toward a specific child). Other family factors are measured as familywide variables that are not specific to each child (e.g., parental suicide, socioeconomic status [SES]). It is possible that some of the familywide variables, such as parental psychopathology, may predict the later development of youth PD not because the family factors are causing youth PD, but rather because the predictors (i.e., the familywide variables) and the outcomes (i.e., youth PD) are both the result of a third variable (e.g., genes shared between parents and offspring). As we note in the conclusion of this chapter, it will be important for future research to use sophisticated behavior genetic designs to tease apart these possibilities (the behavior genetic study by Belsky et al., 2012, described in the section on the etiology of BPD, provides an excellent example of such a study).

In addition, although family adversity poses significant risks for the development of personality pathology, it is crucial to recognize that early trauma and abuse are not present in the histories of all youths with PDs. In fact, in the Children in the Community Study, early trauma or abuse "do not account for all, or even most cases of PD observed in our longitudinal cohort" (Cohen, Crawford, et al., 2005, p. 482). Furthermore, even in cases of maltreatment, different children will be affected differently. In a recent study of adult PD, most of the participants who retrospectively reported a history of childhood maltreatment did not meet criteria for a PD (Afifi et al., 2011). These findings point to the importance of equifinality and multifinality in the links between family adversity and later PDs; we return to this topic in our final suggestions for future research on PDs.

Broader Contextual Influences

Beyond the family environment, there are also likely to be broader contextual factors influencing the development of PDs. First, peer relationships are an understudied potential contributor to the development of PDs in youth. Given that PDs involve difficulties in relationships, problematic peer relationships seem to be a likely influence on the emergence of PD symptoms. Peer relationships have been studied extensively in relation to the development of other disorders in childhood and adolescence (e.g., ADHD, conduct disorder, depression) (Deater-Deckard, 2013); aspects of peer relationships relevant to developmental psychopathology include social rejection/exclusion, lack of high-quality or the presence of poor-quality friendships, victimization/bullying, aggression, social withdrawal, peer contagion (adopting problematic behaviors from peers), and weaknesses in social skills. PD symptoms in early adulthood are predicted by a history of earlier social

isolation and low social competence (Cohen, Crawford, et al., 2005), and adolescent PDs are concurrently associated with shorter friendships, less enjoyment of others, lack of a confidant, and few social activities (Bernstein, Cohen, Skodol, Bezirganian, & Brook, 1996). Second, aspects of the school environment are likely to be relevant for the emergence and continuation of PD symptoms in childhood and adolescence. For example, students on average show declines in Cluster B PD symptoms in schools with a strong focus on learning (Kasen, Cohen, Chen, Johnson, & Crawford, 2009).

Third, the broader socioeconomic context (including family SES and poverty) seems likely to predict the development of PDs in youth. Adolescent PDs are associated with lesser parental education and lower occupational status and family income, even after researchers control for various potential confounds (Johnson, Cohen, Dohrenwend, et al., 1999), and adult PDs are linked with lower SES as well (Torgersen, 2012). Neighborhood-level characteristics may also influence PD symptoms (Hart & Marmorstein, 2009). There is considerable evidence linking poverty and low SES with difficulties in personality development and emotional and behavioral regulation more generally (Conger & Donnellan, 2007; Evans & Kim, 2013). Low SES, poverty, and risky neighborhoods are associated with declines in self-control in youth (Shiner, 2014). Fourth and finally, broader social forces (e.g., cultural values, customs, and mores accepted across societies or within societal subgroups) may be relevant to the development of PDs. For example, personality pathology characterized by poor constraint may be fostered in social contexts that do not provide structure or firm limits on the expression of impulsivity (Paris, 2005) or that offer lower levels of social cohesion (Millon, 2010). The very limited data on prevalence rates for Cluster B PDs indicate that ASPD and BPD may be more common in Western cultures, suggesting that there may indeed be significant cultural influences on these conditions (Mulder, 2012). Although there are good reasons to think that broader social contexts influence the development of PDs in youth, these potential contextual influences have received little attention in the literature on PDs and constitute an important direction for future research.

Etiology of Cluster A Disorders

The three Cluster A PDs—paranoid PD, schizoid PD, and schizotypal PD—are described in DSM-IV and DSM-5 as the "odd and eccentric" PDs. All three of these PDs involve a tendency to maintain distance in interpersonal relationships, although for different reasons in each case—distrust of and suspiciousness toward others in paranoid PD, emotional detachment from others in Schizoid PD, and discomfort with others in schizotypal PD (see Table 18.1 for more information). Although these three disorders do tend to co-occur frequently (Esterberg, Goulding, & Walker, 2010; Links et al., 2012; South et al., 2012), they also are frequently comorbid with avoidant PD in adolescents and adults (Esterberg et al., 2010; South et al., 2012); this is not surprising, given that avoidant PD is characterized by social inhibition and concerns about others' evaluations. Schizotypal PD and avoidant PD share genetic influences (Kendler et al., 2008). Thus avoidant PD is perhaps more appropriately studied in relation to the Cluster A PDs than in relation to the Cluster C PDs. At this point, there is far more research on schizotypal PD in both youth and adults than on the other two Cluster A PDs. Paranoid and schizoid PD are not included in the list of categorical PDs in DSM-5 Section III.

There is substantial evidence suggesting that the Cluster A PDs are schizophrenia spectrum disorders, meaning that they stem in part from the same genetic liabilities that predispose people to the development of psychotic disorders, including schizophrenia (South et al., 2012; see, e.g., Kendler et al., 2006). Schizotypal PD is the most closely and consistently linked with psychotic disorders, with paranoid PD and schizoid PD showing weaker and less consistent associations; schizotypal PD is even listed in the DSM-5 chapter on schizophrenia spectrum and other psychotic disorders, to indicate its close connection with this family of disorders. Schizotypal PD includes both positive symptoms (cognitive and perceptual abnormalities) and negative symptoms (social withdrawal, restricted emotions, lack of goal-directed behavior) seen in schizophrenia. Adolescent schizotypal PD that is accompanied by prodromal symptoms of schizophrenia heightens the risk of the later development of schizophrenia, schizoaffective disorder, or psychotic bipolar disorder (Correll et al., 2008), with one large-scale study indicating that approximately one-third of a sample of late adolescents with schizotypal PD developed schizophrenia within 2.5 years (Cannon et al., 2008). A small study of adolescents meeting criteria for schizotypal PD found that only about 40% of youth still met criteria for that disorder after a year; of those no longer meeting criteria for schizotypal PD, a third met criteria

for another PD, mostly paranoid or schizoid PD (Esterberg et al., 2010). This finding probably reflects the fact that the categorical diagnoses are unstable, but that the shared symptoms among the Cluster A disorders are more stable (Widiger, 2010). Taken together, the research on Cluster A disorders (especially schizotypal PD) and schizophrenia spectrum disorders suggests that these disorders have genetic influences and symptoms in common, but that numerous individuals who exhibit Cluster A PDs do not go on to develop clear-cut psychotic disorders.

Schizotypal PD in both adolescence and adulthood shares many of the cognitive, perceptual, and motor abnormalities seen in schizophrenia (Esterberg et al., 2010; Links et al., 2012). Schizotypal PD and schizotypy in adults are associated with a number of neurodevelopmental risk factors (Kwapil & Barrantes-Vidal, 2012): prenatal exposure to infection and malnutrition, obstetric complications, signs of prenatal androgen/estrogen disruptions (specifically, higher asymmetry in dermatoglyphic finger ridge counts), minor physical anomalies, and neurological "soft signs." Several neurodevelopmental risks have been identified in adolescents with schizotypal PD as well, including minor physical anomalies (Hans et al., 2009), neurological soft signs (Weinstein, Deforio, Schiffman, Walker, & Bonsall, 1999), and diminished gestural communication (Mittal et al., 2006). One large-scale prospective study found that signs of malnutrition at age 3 predicted lower performance IQ at age 11, which in turn predicted a heightened risk of schizotypal symptoms at age 23 (Venables & Raine, 2012). Although there have not yet been studies of brain anatomy and function in adolescents with schizotypal PD (to the best of our knowledge), research with adults points to several structural and functioning brain differences in adult schizotypal PD. Adults with schizotypal PD have been found to have structural abnormalities in the superior temporal gyrus, the posterior region of the fusiform gyrus, and the parahippocampus, whereas they seem to show fewer structural abnormalities than patients with schizophrenia in the frontal lobes and medial temporal lobes (Kwapil & Barrantes-Vidal, 2012). Adults with schizotypal PD likewise show diminished activation in the temporal lobes but more typical activation in the frontal lobes, perhaps accounting for the milder symptoms seen in schizotypal PD than in schizophrenia (Kwapil & Barrantes-Vidal, 2012). These findings have yet to be replicated in adolescents with schizotypal PD.

Several studies have examined a variety of nongenetic, experience-based contributors to schizotypal PD. Consistent with research linking early cannabis use with the development of schizophrenia, early cannabis use also predicts the development of schizotypal PD (Anglin et al., 2012). Early family predictors of schizotypal PD symptoms in adolescence and adulthood have also been identified; these include maternal separation in the first 2 years of life (Anglin, Cohen, & Chen, 2008) and high levels of family adversity, including abuse, neglect, and general household dysfunction (Afifi et al., 2011). Negative family experiences may potentially fuel the dissociation and interpersonal skill deficits observed in schizotypal PD. Low SES also predicts maintenance of schizotypal PD symptoms from adolescence through adulthood, in part through its effects on trauma, high stress, problematic parenting, and lower IQ (Cohen et al., 2008). Cluster A symptoms appear to decline more in schools that promote autonomy and minimize conflict and excessive informality among students and teachers (Kasen et al., 2009), and positive academic and social experiences in childhood or adolescence predict declines specifically in schizotypal symptoms (Skodol, Bender, et al., 2007). Thus, in addition to genetic influences on schizotypal PD, experiences that promote cognitive dysfunction (malnutrition and marijuana use) and that diminish positive social connections serve as risk factors for the development of schizotypal PD.

As noted, very little is known about the biological and contextual risk factors for paranoid and schizoid PDs, other than that the genetic and family risk factors for all PDs are relevant for these disorders as well. A prospective study examined childhood predictors of paranoid PD symptoms at age 15 (Natsuaki, Cicchetti, & Rogosch, 2009). Adolescent paranoid PD symptoms were predicted by an earlier history of maltreatment; by earlier increases in externalizing symptoms and in the youth's own bullying of other children (but not being bullied themselves); and by peer ratings of being less cooperative, less likely to be leaders, and more likely to start fights. These results are interesting, in that they suggest that early precursors of adolescent paranoid PD symptoms are expressions of interpersonal hostility and alienation, and the findings are consistent with previously described results indicating that adolescent paranoid PD predicts later violence and criminality. Schizoid PD may be related to experiences undermining the biologically based affiliative system that pro-

motes social interaction in most people (Lenzenweger, 2010), but there are not yet data testing this idea in youth. Because paranoid PD and schizoid PD have been dropped from the categorical diagnoses in DSM-5 Section III, they may not receive much research attention in the future. However, the alienation expressed in these conditions is important for understanding PDs more generally, so it should continue to be a focus of research.

Etiology of BPD

Within the limited research on the emergence and early development of most PDs, the predictors and processes underlying BPD have received significantly more attention. Several researchers have called for greater recognition of BPD in youth, in part because it is potentially associated with significant levels of impairment (Chanen, Jovev, McCutcheon, Jackson, & McGorry, 2008; Miller et al., 2008; Stepp, 2012).

Researchers have increasingly refined a trait-based conceptualization of BPD in youth, identifying several major dimensions: identity disturbance, affective instability, relationship difficulties, and impulsivity (Miller et al., 2008). These core dimensions map onto personality dimensions identified in child personality trait models, with best coverage for the impulsivity domain, followed by the dimensions of affective instability and relationship difficulties, and with the least coverage for the identity disturbance domain (Tackett & Kushner, in press). In other words, certain aspects of core youth BPD functioning are likely to be assessed with existing normal-range personality trait measures, whereas other aspects of the disorder (e.g., identity disturbance) are likely to call for supplemental assessment tools.

A number of the general risk factors described previously as predictors of PDs in youth have also been found specifically as risks for BPD, including genetics, family adversity, negative peer relationships, and problems with emotion regulation. There is evidence for a genetic basis for BPD symptoms; a recent twin study of 12-year-olds obtained a heritability of .66 for BPD characteristics (Belsky et al., 2012). Lower levels of executive functioning, IQ, and theory of mind at age 5 predict later BPD characteristics at age 12 (Belsky et al., 2012). Family risks include physical and sexual abuse, problematic parenting styles, and parental psychopathology (e.g., Cohen, Crawford, et al., 2005; Guzder, Paris, Zelkowitz, & Marchessault, 1996; Levy, 2005). Adolescent BPD symptoms are associated with maternal disrupted communication patterns and disrupted attachment as well (Levy, 2005; Ludolph, Westen, Misle, & Jackson, 1990). The experience of bullying in childhood predicts an increased risk of BPD symptoms by age 11 (Wolke, Schreier, Zanarini, & Winsper, 2012). Emotion dysregulation and social cognitive deficits are also linked with youth BPD (Reich & Zanarini, 2001; Sharp, in press). Research has identified ragefulness and overwhelming emotions as characteristics of adolescent BPD in particular, which may account for the previously described links between BPD and self-harm behaviors (Crowell et al., 2005; Reich & Zanarini, 2001). Taken together, there is good evidence for both genetic and environmental contributors to the development of BPD symptoms and personality processes in childhood and adolescence.

Personality traits are highly relevant for understanding the etiology of disorder, with multiple theoretical links proposed between these two domains (Nigg, 2006; Tackett, 2006). Personality traits may represent risk or vulnerability factors for disorder, or they may reflect common underlying causal factors influencing both personality and psychopathology. Although direct tests of such associations have been infrequent, modern research may support both types of associations between personality and youth BPD. For example, the biosocial development model that has emerged from work by Crowell, Beauchaine, and Linehan (2009) highlights potential transactional influences between youth BPD traits (such as negative affectivity and impulsivity) and environmental risk. Specifically, their theory suggests that early traits may represent true risk factors (to the extent that, e.g., high levels of Negative Affectivity promote the experience of environmental risks such as negative peer group responses), in addition to sharing underlying common causes across personality traits and youth BPD constructs.

Evidence for common causes—both biological and psychosocial—also emerges from a comparison of the literature on normal personality development and youth BPD. For example, dysfunction in the dopamine system has been identified as a biological vulnerability for youth BPD (Crowell et al., 2009) and has also been linked to the personality traits of Extraversion and Conscientiousness (Noble et al., 1998). Similarly, dysfunction in the serotonin system has also been identified as a biological vulnerability for youth BPD (Crowell et al., 2009) and has been connected to Neuroticism

and Disagreeableness (Greenberg et al., 2000; Hamer, Greenberg, Shabol, & Murphy, 1999). Such findings point to potential biological pathways resulting in the phenotypic correlations observed between youth BPD and these personality traits, in that BPD symptoms are typically associated with high Neuroticism, low Agreeableness, low Conscientiousness, and low Extraversion (Tackett & Kushner, in press). Similarly, research also points to potential shared psychosocial factors between youth BPD and normal personality. Early life experiences such as problematic attachment and maltreatment appear both to increase risk for youth BPD (e.g., Carlson, Egeland, & Sroufe, 2010; Gratz, Latzman, Tull, Reynolds, & Lejuez, 2011; Paris, Zweig-Frank, & Gudzer, 1994) and to alter the development of normal personality traits (e.g., Fabes, Poulin, Eisenberg, & Madden-Derdich, 2002; Rogosch & Cicchetti, 2004), again highlighting potential common pathways to normal and abnormal personality development.

Spectrum associations between personality–psychopathology constructs emphasize the potentially dimensional relationships between traits and disorders (Tackett, 2006). A spectrum association is consistent with a common-cause model, but can also be investigated by examining evidence for potentially quantitative (rather than qualitative) relationships at the phenotypic level. One recent study examined evidence for a spectrum association between youth BPD traits and more typical externalizing constructs in youth (aggression and rule breaking; Tackett, Herzhoff, Reardon, De Clercq, & Sharp, in press). This study found evidence that the antagonism traits at the core of youth BPD showed very high correlations with a general externalizing factor, supporting the argument that core aspects of youth BPD may be linked to both normal personality traits and DSM-IV Axis I psychopathology; this finding is consistent with the previously described research linking Cluster B PDs with numerous externalizing disorders (e.g., oppositional defiant disorder, substance abuse). This work points to a further need to examine underlying core components of normal personality, abnormal personality, and Axis I psychopathology in joint, multivariate investigations. As noted previously, BPD is also associated with internalizing psychopathology in adults (see also Eaton et al., 2011). This is corroborated by work in youth, which finds primary associations for antagonistic traits (more closely reflecting externalizing behaviors) as well as secondary associations for emotional instability (which typically reflects internalizing behaviors; Tackett et al., in press) relevant for the externalizing spectrum in youth. Thus BPD probably represents a more complex condition reflecting elements of both internalizing and externalizing problems across the lifespan.

Finally, in regard to brain differences in BPD, research with adults with BPD has pointed to several abnormalities in terms of brain structure, function, and neurochemistry (Hooley, Cole, & Gironde, 2012; Paris, 2012). In terms of structural differences, a meta-analysis of seven studies concluded that there are reductions in hippocampal and amygdalar volume in adults with BPD (Nunes et al., 2009); the hippocampus and amygdala are both part of the limbic system, which is involved in emotion processing and memory. Significant reductions in size have also been observed in the orbitofrontal cortex and anterior cingulate cortex, and alterations in the corpus callosum have been observed as well (Hooley et al., 2012); these are all areas that may be involved in the impulsivity and poor regulation seen in BPD. People with BPD also display reduced prefrontal regulation (Silbersweig et al., 2007) and dysregulation of the hypothalamic–pituitary–adrenocortical (HPA) system, which is an important component of stress response (Hooley et al., 2012). Hooley and colleagues (2012) have suggested, "It is reasonable to believe that BPD reflects stress-induced compromises in neural circuits that underlie regulatory processes" (p. 428), in light of the fact that the brain differences observed across studies of people with BPD point to problems with emotion regulation, stress reactivity, and behavioral control. There have been some recent attempts to examine structural differences in adolescents with BPD. These studies have found abnormalities in the orbitofrontal cortex (Chanen, Velakoulis, et al., 2008), but not in the hippocampus or amygdala (Chanen, Velakoulis, et al., 2008) or the corpus callosum (Walterfang et al., 2010). These preliminary studies serve as a good reminder that the biological abnormalities present in adult BPD may not be present in adolescent BPD.

Etiology of ASPD, Psychopathy, and Narcissism

As noted earlier in this chapter, the early development of ASPD has the largest existing evidence base from early life, likely because of the DSM-IV requirement for a conduct disorder diagnosis before age 15 in order to make a diagnosis of ASPD in adults. That is, the DSM-IV and DSM-5 approach to conceptualizing conduct disorder as the core early life feature of

ASPD would suggest that the entire body of literature on conduct disorder has implications for the etiology of ASPD. Conduct disorder diagnoses are assigned to a heterogeneous group of youth, however. Researchers have argued for distinctions based on age of onset and behavioral type, suggesting that earlier age of onset and physically aggressive behaviors may represent a more severe variant of the phenomenon (Burt, 2012; Moffitt, Caspi, Harrington, & Milne, 2002; Tackett, Krueger, Iacono, & McGue, 2005)—and one that potentially indicates greater prediction of later diagnoses such as ASPD. Distinguishing between child- and adolescent-onset conduct disorder is supported by the empirical literature (Moffitt et al., 2008), although some evidence suggests that the advantage of this distinction is better accounted for by differentiation of behavioral subtypes (Burt, Donnellan, Iacono, & McGue, 2011). Indeed, early violent behaviors indexing conduct disorder do increase risk for a later ASPD diagnosis (Gelhorn, Sakai, Price, & Crowley, 2007), although many children with conduct disorder will not go on to develop ASPD (Moffitt et al., 2008).

Extensive work has been conducted in recent years on extending the concept of psychopathy downward to childhood and adolescence (e.g., Frick, Bodin & Barry, 2000). Psychopathy includes a number of tendencies: risk taking and impulsivity, grandiosity, manipulativeness, lack of empathy and remorse, and shallow relationships (Lynam, 1997; Lynam & Gudonis, 2005). Psychopathy predicts a number of important associated features and outcomes, including more severe and stable conduct problems (Kotler & McMahon, 2005). DSM-5 has added a specifier to conduct disorder based on research on psychopathy, although the manual terms this specifier "with limited prosocial emotions" (APA, 2013, p. 470), presumably because "psychopathy" sounds too negative or stigmatizing. The limited prosocial emotions may be displayed in four ways: "lack of remorse or guilt," "callous—lack of empathy," "unconcerned about performance," and "shallow or deficient affect" (APA, 2013, pp. 470–471). As in adult populations, psychopathy in youth is associated with high rates of instrumental aggression (Blair, Peschardt, Budhani, Mitchell, & Pine, 2006). Psychopathy can be reliably measured in childhood and remains moderately stable across adolescence (Lynam et al., 2009), and psychopathy symptoms in youth predict later antisocial behavior (Salekin, Rosenbaum, & Lee, 2008).

In terms of the causes of psychopathy, childhood psychopathy appears to be at least partially heritable, and these inherited characteristics are likely to result in impaired socialization across development (Blair et al., 2006). In addition, the stability in psychopathy symptoms across adolescence is primarily influenced by genetic factors (Forsman, Lichtenstein, Andershed, & Larsson, 2008). There is also evidence for functional brain differences in adolescents with high level of psychopathic traits relative to normal controls, in that they show reduced amygdala activity to negative stimuli (especially fearful faces), which may reduce their capacity for learning from punishment (Blair, 2010; Hyde, Shaw, & Hariri, 2013). In addition, a number of other brain regions in adolescent studies have shown functional abnormalities, including prefrontal regions, insula, anterior cingulate cortex, and caudate (Hyde et al., 2013); these regions may all be implicated in the abnormalities in reward processing, learning, and decision making that are observed in more severely psychopathic youth. Studies of structural brain differences in youth point to abnormalities in many of the same brain regions identified in the functional neuroimaging studies, including, for example, amygdala, prefrontal areas, and insula (Blair, 2010; Hyde et al., 2013). Many of the structural neuroimaging studies conflict in the direction of their findings, however (Hyde et al., 2013), so more work is needed to understand how the functional and structural differences in psychopathy relate to each other.

In addition, a number of contextual contributors to psychopathy have been identified. One study found the highest levels of stability in psychopathy symptoms from adolescence to adulthood in those youth who were exposed to psychosocial stressors, such as corporal punishment, low SES, and exposure to delinquent peers (Lynam, Loeber, & Stouthamer-Loeber, 2008). Early childhood predictors of later psychopathy—including earlier psychopathy characteristics, SES, parenting risk, and youth antisocial behavior—are generalizable across race and adult criminal status as well, speaking to their robustness and stability (Vachon, Lynam, Loeber, & Stouthamer-Loeber, 2012).

Callous–unemotional traits (i.e., lack of empathy and remorse, shallow emotions and relationships) are often thought to reflect a more narrowly defined core of the psychopathy construct in childhood (Frick & Viding, 2009; see Kimonis, Frick, & McMahon, Chapter 3, this volume); the literature on these traits overlaps substantially with research on youth psychopathy. The presence of callous–unemotional traits appears to be a particularly useful way of distinguishing children diag-

nosed with conduct disorder who are most likely to go on to an adult diagnosis of ASPD (Moffitt et al., 2008); the research on these traits heavily informed the decision to frame the conduct disorder specifier in terms of "limited prosocial emotions." Even among those youth exhibiting high levels of callous–unemotional traits, recent evidence supports heterogeneity on dimensions such as anxiety (high vs. low; Kimonis, Frick, Cauffman, Goldweber, & Skeem, 2012). Thus a better understanding of the phenomenology and utility of callous–unemotional traits continues to be a primary focus for future research.

Multiple studies have identified normal personality trait correlates of youth psychopathy, which are similar to those found in adult samples: low Agreeableness, low Conscientiousness, and high Neuroticism (e.g., Lynam et al., 2005; Salekin, Leistico, Trobst, Schrum, & Lochman, 2005). Youth callous–unemotional traits can also be characterized within a broader personality/temperament framework, and generally relate to high levels of Disinhibition, high levels of Negative Affectivity (particularly reflecting alienation and antagonism), and low levels of Positive Emotionality (Decuyper, De Bolle, De Fruyt, & De Clercq, 2011; Latzman, Lilienfeld, Latzman, & Clark, 2013; Roose et al., 2012; Salekin, Debus, & Barker, 2010). At the higher-order personality trait level, then, correlates for youth psychopathy and youth BPD are largely overlapping. Differentiation between these disorders is probably best reflected in the magnitude of associations at the domain level (e.g., youth BPD should show stronger associations with trait Neuroticism than should youth psychopathy), as well as in differentiation of associations at the lower-order trait, or facet, level.

Social-cognitive processing deficits have also been identified in youth psychopathy, such as the overattribution of conflict in friendship interactions (Muñoz, Kerr, & Besic, 2008). A growing literature highlights problems with emotional recognition and social exchange behavior in youth with psychopathic traits (e.g., White, Brislin, Meffert, Sinclair, & Blair, 2013), and a recent meta-analysis suggests that emotion recognition deficits in youth psychopathy are broad and pervasive across emotions (Dawel, O'Kearney, McKone, & Palermo, 2012). In addition, one recent study found that specific components of psychopathy differentially predicted social cognitive processing in a sample of inpatient youth (Sharp, 2012). Specifically, this study found the affective component of psychopathy was related to hypermentalization (or overattribution of others' intent), whereas the interpersonal component was related to hypomentalization (or underattribution). Thus numerous aspects of social cognition and interpersonal processing appear to be relevant for the development of psychopathy in early life.

A related trait that has been studied in conjunction with conduct disorder and psychopathy in youth is narcissism. Very little research has examined the origins of narcissistic PD, but there is increasing interest in the dimensional trait of narcissism, which "refers to a sense of grandiosity, coupled with a strong need to obtain attention and admiration from others" (Thomaes, Brummelman, Reijntjes, & Bushman, 2013, p. 22). Individual differences in this trait are measurable by at least late childhood (Barry, Frick, & Killian, 2003; Thomaes et al., 2008). Narcissism in youth tends to be associated with a more manipulative and less empathic stance toward others, difficulties with regulating self-esteem, and a preoccupation with others' evaluations (Thomaes et al., 2013; Weise & Tuber, 2004). These aspects of narcissism manifest themselves in the ways that narcissistic youth interact with peers. Specifically, narcissism is associated cross-sectionally with physical, verbal, and relational aggression, both in person and on the Internet, and with antisocial and delinquent behavior; these problems with aggression are made worse when youth's self-views are threatened (Thomaes et al., 2013). Among young adolescents who are aggressive, there is greater stability of aggression when the adolescents are also narcissistic (Bukowski, Schwartzman, Santo, Bagwell, & Adams, 2009). Thus narcissism in childhood and adolescence is associated with a number of troubling outcomes, particularly in the domain of peer relationships.

Relatively little is known about the pathways leading to narcissism because few longitudinal studies have examined precursors to later narcissism. Narcissism in adolescence and early adulthood is predicted by preschool measures of interpersonal antagonism, inadequate impulse control, histrionic tendencies, high activity level, and desire to be the center of attention (Carlson & Gjerde, 2009); these results suggest that there are a number of theoretically predicted early markers of later narcissism. One prospective study of adult narcissism found that both authoritarian and indulgent maternal parenting predicted adult narcissistic traits (Cramer, 2011). An interesting theory (Thomaes, Bushman, Orobio de Castro, & Stegge, 2009) ties together these findings by suggesting that children who are higher in approach tendencies will be more reinforced by re-

wards, such as praise from others; if there are problems with socialization, such as parental overvaluing of their children's characteristics, approach temperament could shape the development of narcissistic tendencies over time. Given the links between narcissism and youth's social behavior, it will be important to begin exploring the pathways leading to narcissistic tendencies.

Etiology of Cluster C Disorders

The three Cluster C PDs—avoidant PD, dependent PD, and obsessive–compulsive PD—are described in DSM-IV and DSM-5 as the "anxious or fearful" PDs (see Table 18.1 for the primary characteristics of each one). As a group, these PDs have received the least attention in the literature on PDs in youth, and very few longitudinal studies have been conducted exploring their development over time. However, despite this lack of research on the etiology of the Cluster C PDs, both avoidant PD and obsessive–compulsive PD have been retained in the list of DSM-5 Section 3 categorical disorders. Before we discuss the possible precursors to the Cluster C PDs, it is important to note that obsessive–compulsive PD seems to be less closely related to the other two Cluster C PDs than they are to each other. Obsessive–compulsive PD is associated with relatively low levels of impairment in adolescence and adulthood (Cohen, Crawford, et al., 2005; Torgersen, 2012), whereas both avoidant and dependent PDs are associated with significant impairment in adolescence and adulthood (Bornstein, 2012b; Cohen, Crawford, et al., 2005; Torgersen, 2012). Obsessive–compulsive PD has different genetic and environmental influences from the other two PDs (Kendler et al., 2011; Reichborn-Kjennerud et al., 2007), and it has the highest disorder-specific genetic influences of all the PDs (Kendler et al., 2008). Thus, its causes are likely to be different from those of avoidant and dependent PD. The relationship between obsessive–compulsive PD and obsessive–compulsive disorder (OCD) is complex, in that although the two are sometimes comorbid, obsessive–compulsive PD does not seem to be simply a milder version of OCD (Samuels & Costa, 2012). Rather, obsessive–compulsive PD co-occurs with a wide variety of anxiety, mood, and eating disorders.

Several predisposing factors seem likely to be relevant to the development of avoidant and dependent PDs. First, the same temperament and personality traits that predispose youth and adults to develop internalizing disorders may be relevant to the development of the Cluster C PDs, given the previously described research linking the Cluster C PDs with depression and anxiety. High Negative Affectivity predicts the development of all the internalizing disorders in both youth and adults, and poor self-control, including poor attentional control, is often implicated as well (Klein, Dyson, Kujawa, & Kotov, 2012). Consistent with this research, a study found that both high anger and low levels of attentional control were observed in children manifesting trajectories indicating higher levels of social withdrawal (Eggum et al., 2009). Behavioral inhibition, the tendency to respond to novel situations with fear and withdrawal, is also associated with the development of some anxiety disorders in youth (Klein et al., 2012) and seems likely to be involved in the development of avoidant and dependent PDs. Second, many of the family factors described previously predict the emergence of the Cluster C PDs in adolescence and adulthood. Third, peer relationships are likely to be disturbed. A retrospective study found that adult avoidant PD was associated with recollections of weaker athletic performance, less involvement in hobbies, and less peer popularity earlier in life (Rettew et al., 2003). Improvements in avoidant PD symptoms from adolescence to adulthood are predicted by positive achievement and interpersonal experiences in childhood and adolescence (Skodol, Bender, et al., 2007). Trait dependency is likewise associated with unpopularity and negative perceptions by peers in childhood, and with loneliness and peer rejection in adolescence (Bornstein, 2012a). Finally, although the origins of obsessive–compulsive PD are poorly understood, the pathological trait of compulsivity (the negative extreme end of high Conscientiousness) is especially associated with obsessive–compulsive PD in adolescence and adulthood (Aelterman, Decuyper, & De Fruyt, 2010); more research on this trait in youth should help facilitate a better understanding of obsessive–compulsive PD in adulthood.

CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE RESEARCH

Research over the last two decades has made it clear that PDs exist in youth and are worthy of both research and clinical attention. PDs are prevalent by early adolescence, with at least 10% of adolescents meeting criteria for at least one PD. Although PD diagnoses are changeable in youth, PD symptoms and traits are modestly to strongly stable by adolescence and not substan-

tially less stable than in adulthood. PDs in youth pose considerable risks for development, including potential high-risk behaviors, emergence of other psychiatric disorders, and impairment in important life domains (e.g., academic achievement, relationships, work). When the diagnosis of PDs is discouraged in people under the age of 18, youth with personality pathology may receive incorrect treatment or may not receive the treatment they need (Shiner, 2007).

Although considerable progress has been made in research on PDs in youth over the last two decades, much remains to be learned about the nature and course of PDs. These conditions remain understudied, relative to other psychiatric conditions in childhood and adolescence. In the following sections, we offer suggestions for future research, focusing on two general areas: the measurement and manifestations of PDs in youth and the development of PDs over time.

Measurement and Manifestations of PDs in Childhood and Adolescence

With some notable exceptions (e.g., ASPD), the DSM systems have given little consideration to the childhood antecedents of later-emerging adult PDs, and this situation has led to a relative paucity of research on the pathways leading to PDs. In addition, contradictory views that PDs are rare in adolescence but that PD symptoms may be normative in adolescence have resulted in few attempts in the DSM systems to consider how childhood and adolescent PDs relate to other childhood disorders that involve relatively enduring patterns of behavior, cognition, and emotion (Ashton, 2007; De Fruyt & De Clercq, 2012). For example, oppositional defiant disorder involves a consistent pattern of hostile, defiant, and negativistic behavior; this sustained pattern describes a troubling pattern that could be considered an expression of pathological personality. Similarly, childhood anxiety disorders, especially social anxiety disorder (social phobia), may overlap considerably with avoidant PD symptoms in childhood and adolescence. Furthermore, in direct contrast to the normative hypothesis—often put forth to discourage research on early PDs—recent work suggests that youth personality pathology may show the strongest connections to psychopathology during developmental periods of greatest prevalence (Tackett et al., in press). In other words, diverting clinical and empirical attention from "normative" periods may be limiting attention to those periods most deserving of close scrutiny. The relationship between childhood and adolescent PDs and other disorders in youth (e.g., ADHD, autism spectrum disorder) awaits further study.

Beyond the categorical definitions of PD diagnoses, the new alternative model for diagnosing PD is an important target for future research, and one that is highly amenable to developmental research with children and adolescents. The model will require much more empirical research to examine whether it is reliable, valid, and clinically useful; this is particularly true for its use with populations of children and adolescents, given that the published empirical work on the model has focused on adult samples. From a developmental perspective, however, the model seems potentially promising. The model incorporates the literatures described in this chapter showing that personality traits, attachment, social-cognitive mechanisms, coping styles, and identity may be disturbed in youth with PDs, and that these same processes may play a causal role in the development of adult PDs. The definition of impairment specifically takes into account disturbances in attachment, other mental representations, and identity, and the requirement of pathological personality traits builds nicely on the research on such traits in youth. Future work will help to clarify the usefulness of this model for diagnosing PDs in youth. Both the pathological trait domains and the domains of impairment will require intensive investigation in youth.

Developmental Pathways Leading to Disordered Personality

We currently lack information from multiple studies about the developmental pathways leading to the emergence of personality pathology in the first two decades of life. Prospective longitudinal studies that trace the developmental pathways leading to PD are sorely needed. The one prospective, longitudinal study of all the PDs—the Children in the Community study—has made impressive contributions to extant knowledge about the development of PDs and is the source of many of the findings reviewed in this chapter. New longitudinal work on PD development can build on the findings of this study by considering what is known about normal personality development, assessing a wide range of personality differences, and measuring multiple aspects of the environment. Studies using behavior genetic or molecular genetic methods would be particularly useful for clarifying the causes of individual differences in PD. It would also be extremely

informative to begin such studies earlier in childhood to pinpoint the earliest manifestations of and influences on PD development. Most of the research reviewed in this chapter has focused on personality pathology in adolescence, leaving PDs in childhood poorly understood. Further, although adolescence seems to represent a critical juncture in the emergence of persistent personality pathology, the origins of PD cannot be understood without beginning a study well before adolescence. Studies with more frequent assessments could better identify transactions between youth and their environments over time. Well-designed studies could also address fundamental epidemiological questions about PD in youth, including changing prevalence rates over time; gender differences; differences across socioeconomic groups, ethnicities, races, and cultures; and rates of comorbidity among PDs.

In future work, it will be especially important to examine the environmental contributions to the development of personality pathology. For personality traits (Shiner, 2014), characteristic adaptations (Pomerantz & Thompson, 2008), and personal narratives (McAdams, 2008), we already know a considerable amount about how the environment contributes to personality development. The insights from this research can be incorporated into new longitudinal research examining contextual contributors to personality pathology. Extreme adversity (including significant poverty) may have negative effects on personality development, including children's emerging capacity for self-regulation (Hart, Atkins, & Matsuba, 2008). Although there is some work investigating personality development in the context of real-life contexts, other important social, cultural, and global changes in children's lives have received relatively little attention, including immigration, war, violence, illness, and abuse (Belfer, 2008). These large-scale societal challenges are likely to play a critical role in both healthy and unhealthy personality development.

Both equifinality and multifinality are likely to be evident in the developmental pathways to PDs in youth. When applied to PDs, the principle of equifinality highlights the importance of exploring whether different processes may lead to similar patterns of personality pathology. As noted earlier, although early family adversity poses significant risks for the development of personality pathology, early trauma and abuse are unlikely to be present in the histories of all youth with PDs. In contrast, some youth may struggle with such extreme traits from early in life that those traits overwhelm the effects of a generally "good enough" environment (e.g., Zanarini & Frankenburg, 2007). In short, it is important to recognize that temperament may play a more central role in some pathways, whereas trauma or adversity may be more central in other ones (Nigg, Silk, Stavro, & Miller, 2005).

Likewise, youth with similar outcomes may vary in the time course over which their personality difficulties develop. For some youth, the pathway may be more continuous and linear. For example, a child who is temperamentally prone toward hostility and impulsivity may gradually become increasingly angry and poorly regulated over time, as that child encounters more and more experiences that contribute to the development of these negative traits. In contrast, other youth may show a course that is more abrupt and nonlinear. In this kind of pathway, vulnerable youth may encounter life experiences that lead to abrupt changes in their personality functioning. In future work, it will be important to recognize the possibilities of these diverse processes leading to PDs.

The progress made in understanding PD in youth has begun to accelerate in recent years; our hope is that the upsurge in new knowledge about PD in children and adolescents will have an increasingly positive impact on clinical practice for youth.

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CHAPTER 19

Health-Related and Somatic Symptom Disorders

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A childhood chronic illness is a health problem or medical condition that endures for an extended period of time, affects a child's functional activities, and requires extensive medical care (Compas, Jaser, Dunn, & Rodriguez, 2012). Children with chronic illnesses must cope with many stressors, including the possibility of slowed or altered physical development, periodic medical procedures, unexpected health crises, and school absences. In addition, they must master the same developmental tasks and challenges as their healthy peers. Over the past decade, substantial strides have been made in understanding factors that affect the psychological well-being of children with chronic illnesses and their ability to cope with demands and stressful life events specific to their medical conditions (Roberts & Steele, 2009). In this chapter, we first provide an overview of epidemiology. We then review current research regarding psychological well-being in children with chronic illness, with an emphasis on models of psychological adaptation and on etiological and risk/protective factors. Next, we discuss various research paradigms that have been used to pursue a better understanding of psychological functioning in these children. Subsequently, we review research specific to several of the more common health-related disorders seen in children, including somatic symptom and related disorders, developmental disorders, adaptive self-care disorders, and medical disorders. We conclude by discussing emerging areas of research and new directions for investigation in this population.

EPIDEMIOLOGY

Epidemiology of Chronic Illness in Children and Adolescents

Various definitions have been employed to operationalize the construct of childhood chronic illness. Perrin, Newacheck, and Pless (1993) defined a chronic illness as a condition lasting 3 or more months that creates a functional impairment or medical needs greater than would be expected for a child of that age. More recently, Van Cleave, Gortmaker, and Perrin (2010) have defined childhood chronic illness as any physical, emotional, or mental condition that prevents a child from attending school, doing schoolwork, or participating in regular activities, and that necessitates the regular use of medication or special equipment.

Not surprisingly, estimates of the prevalence of childhood chronic illness vary considerably, depending on how the term "chronic illness" is operationalized and on which methods are used for ascertainment of cases. However, one review (van der Lee, Mokkink,

Grootenhuis, Heymans, & Offringa, 2007) has indicated that, worldwide, as many as one in four children ages 0–18 may have a chronic health condition. Prevalence rates of chronic illness in the studies reviewed by van der Lee and colleagues were significantly affected by the ages of the children and ranged from 3.5% among young children to 35% among adolescents. Other factors affecting estimates of the prevalence of childhood chronic illness include child gender, family income, and family structure, with boys, children from low-income families, and children from single-parent families being at higher risk for chronic health problems (Newacheck & Halfon, 1998). The prevalence and incidence rates for different childhood chronic conditions also vary widely. For example, the incidence of Type 1 diabetes mellitus (T1DM) in youth ages 0–18 in the United States is 15,600 cases per year (National Institute of Diabetes and Digestive and Kidney Diseases, 2011), while the incidence of hemophilia is only 5,000 cases per year (National Heart, Lung, and Blood Institute, 2013).

The prevalence of childhood chronic conditions has been increasing over time (Newacheck, Rising, & Kim, 2006). This increase is probably due to a number of factors, including the increasing rates of certain conditions (e.g., asthma, T1DM); enhanced detection and identification of certain disorders through improved screening (e.g., sickle cell disease); and improved availability and efficacy of treatments, leading to longer lifespan and/or to cure (e.g., cystic fibrosis, acute lymphoblastic leukemia). Currently, more than 90% of children with significant chronic conditions survive into adulthood (Thompson & Gustafson, 1996). Therefore, understanding those factors that affect long-term psychological health and well-being in this population is of significant importance.

Epidemiology of Comorbid Mental Health Conditions

Given the large number of stressors faced by children with chronic illness, numerous studies have sought to determine the impact of chronic health conditions on children's mental health and psychological well-being. Early studies conducted in the 1970s and 1980s suggested that significant numbers of chronically ill children were affected by mental health difficulties. However, the majority of these studies were conducted with samples of children from single medical centers. Thus they were subject to significant bias, due to the use of small convenience samples of youth who varied widely on factors such as child age, gender, and family income, which affect rates of mental health problems in the general population. Other methodological concerns affecting early studies of rates of mental health problems in chronically ill children included the use of screening questionnaires such as the Child Behavior Checklist (Achenbach, 1991; Achenbach & Rescorla, 2001); such questionnaires were subsequently found to overestimate risk for psychopathology in this population, due to the inclusion of items inquiring about the presence of somatic (physical) symptoms (Drotar, Stein, & Perrin, 1995; Friedman, Bryant, & Holmbeck, 2007).

More recently, meta-analyses, which minimize the effects of sampling bias, have been employed to investigate the epidemiology of mental health conditions in children with chronic illness. Lavigne and Faier-Routman (1992) conducted the first meta-analysis reporting on psychological adjustment in chronically ill children, which utilized data from 87 studies. They concluded that, except for chronic health conditions affecting the brain and sensory disorders, chronically ill children were at only moderately increased risk for psychological adjustment difficulties as compared to their healthy peers. The risk for internalizing problems was found to be relatively higher than the risk for externalizing problems. These findings were recently replicated in a meta-analysis of 569 studies of chronically ill youth (Pinquart & Shen, 2011), although the effects of chronic illness on psychological adjustment were weaker when youth ratings versus parent or teacher ratings were considered.

Illness-specific meta-analyses also support the contention that chronically ill children are at slightly heightened risk for psychopathology. LeBovidge, Lavigne, Donenberg, and Miller (2003) conducted a meta-analysis of 21 studies of psychological adjustment in children with chronic arthritis. Although there was a significant difference in adjustment between children with arthritis and healthy children, the overall effect size was small (0.30). However, a higher risk of adjustment difficulties was found for internalizing disorders than for externalizing disorders. A meta-analysis of 19 studies of youth with irritable bowel disorder (Neff et al., 2010) found higher rates of depressive symptoms in these youth compared to healthy controls based on parental report, but no differences were revealed in depressive symptoms based on youth self-report. Similar

findings emerged from a meta-analysis of 22 studies of youth with T1DM (Reynolds & Helgeson, 2011). Although a significant effect was found for depressive symptoms, effect sizes were small to medium and were generally lower in studies with well-matched control groups. Overall, it appears that chronically ill children should be viewed as an at-risk group for psychopathology, but that risk will cumulate in the development of significant psychopathology only as the result of a complex interplay between chronic illness parameters and additional risk and resilience factors.

Adjustment to childhood chronic illness also has been studied from the perspective of successful transition to adulthood. That is, are children with chronic illness able to master adult roles, such as living independently, holding employment, and developing successful relationships? Maslow, Haydon, McRee, Ford, and Halpern (2011) conducted a secondary analysis of data from the National Longitudinal Study of Adolescent Health and compared outcomes for over 13,000 individuals ages 18–28 years with and without a chronic illness diagnosed in adolescence or earlier. Young adults with a childhood chronic illness were as likely as those without such an illness to report satisfying romantic relationships, to be married, to have children and to be living independently. However, even after the researchers controlled for sociodemographic factors, young adults with a childhood chronic illness were less likely to have graduated from college or to be employed, and they had lower mean incomes. Such findings suggest that although the presence of clinically significant mental health symptoms is not common, childhood chronic illnesses may have more subtle effects on psychological well-being that are not easily captured by gross measures of psychopathology, and that may affect well-being and educational and occupational attainment in adulthood.

ETIOLOGY AND RISK/PROTECTIVE FACTORS

Models of Psychosocial Adjustment and Adaptation across Illnesses

Early research on factors affecting the psychological adjustment of children with chronic illness used a categorical, or illness-specific, approach and focused primarily on how disease-specific factors (e.g., duration, severity) affected outcomes (Perrin et al., 1993; van der Lee et al., 2007). However, these constructs inconsistently explained variance in child psychological outcome either cross-sectionally (Nolan & Pless, 1986; Stein & Jessop, 1984; Wallander, Varni, Babani, Banis, & Wilcox, 1989) or longitudinally (Frank et al., 1998). Such findings, coupled with trends in the coping literature toward the use of integrative models that are inclusive rather than reductionistic (Snell & DeMaso, 2010), have led to the present focus on the use of noncategorical models of adaptation. Such models propose that children with chronic illness face common stressors and challenges (Gartstein, Short, Vannatta, & Noll, 1999), and that psychological outcomes are dependent on developmental and psychosocial processes superseding illness-specific factors. Two sets of noncategorical approaches to the prediction of psychological outcomes in childhood chronic illness are reviewed below: stress and coping models, and social-ecological models.

Stress and Coping Models

Building on models of coping and adjustment in adults (Lazarus & Folkman, 1984), Wallander and Varni (1992, 1997) proposed the disability–stress–coping model. In this model, pediatric chronic illness is viewed as an ongoing, chronic strain for children and their caregivers, in that it exposes them to negative life events. Risk factors that affect adjustment include disease/disability parameters (e.g., condition visibility, disease severity, degree of cognitive impairment), with their implications for functional independence, and psychosocial stressors (e.g., illness-related problems, life events, daily hassles). Resistance factors include child intrapersonal factors (e.g., temperament, problem-solving ability, self-efficacy), ecological factors (e.g., social support, family resources) and stress-processing factors (e.g., cognitive appraisal, coping strategies). Thompson and Gustafson's (1996) transactional model of stress and coping is similar to that of Wallander and Varni, in that childhood chronic illness is conceptualized as a stressor to which the child must adapt. Risk and resilience factors that moderate and/ or mediate child outcome include illness parameters, demographic parameters (such as child age), family functioning, parental adjustment, and methods of coping. Tests of both of these models have generated support for various model components, but neither model has been comprehensively tested (Drotar, 2006).

Social-Ecological Models

The original social-ecological model was proposed by Bronfenbrenner (1979) as an attempt at more thoroughly characterizing the impact of the environment on a child's adaptation over time. It has subsequently been used to understand psychological and health outcomes in children with chronic illness (Brown, 2002; Kazak, 1992). This model depicts the process of human development as a reciprocal interchange between the individual and nested, concentric structures that mutually influence one another at the level of the microsystem (child), mesosystem (family, school, peers), exosystem (parental workplace, school system, health care system, community resources), and macrosystem (culture, laws). Extrafamilial systems are viewed as interconnected with the child and his or her family. Problem behavior such as poor adjustment to illness may be a function of difficulty within any of these systems, or may be due to difficulties that characterize the interfaces between these systems (e.g., family–health care provider relations, family–school relations, child–peer relations). In contrast to stress and coping models, the social-ecological model places greater emphasis on understanding the influence of more distal contextual factors on child adjustment, such as the influence of neighborhood, community, and health care systems. In addition, because of the focus on interactions between risk and resilience factors situated at multiple levels from the microsystem to the macrosystem, social-ecological models are multiplicative rather than additive in terms of predicting a child's level of adaptation (Schneider & Stokols, 2009). Versions of the social-ecological model have been applied to several different childhood health problems, including obesity (Davison & Birch, 2001) and severe nonadherence to medication regimens (Naar-King, Podolski, Ellis, Frey, & Templin, 2006). However, as with stress and coping models, tests of multiple model components have rarely been undertaken because of feasibility constraints. The National Institute of Child Health and Human Development, together with other U.S. government agencies, has funded the National Children's Study (*www.niehs.nih.gov/research/programs/children-study*), which will follow a cohort of 100,000 children from birth to 21 years of age; the study will include children with chronic illnesses such as asthma and diabetes. This study should thoroughly evaluate social-ecological models of psychological adaptation, as data will be collected on a wide array of multisystemic factors influencing psychological health (Georgopoulos et al., in press). We now review the literature on family, peer, and broader system influences on psychological adaptation among chronically ill children.

Impact of Various Systems on Child Psychological Adjustment

Family

Early studies of family influences on child psychological adjustment among children with chronic illness focused on global family processes such as cohesion and conflict. In a review of studies of family functioning in childhood chronic illness, Drotar (1997) reported the majority of research demonstrated that higher levels of family conflict and lower family cohesion predicted greater child psychological distress. Measures of global family functioning typically accounted for 10–15% of the variance in child adjustment. These early studies were limited by their cross-sectional nature and problems related to shared informant bias, since caregivers frequently provided data on both child adjustment and family climate. However, subsequent longitudinal studies have tended to support earlier findings. For instance, Thompson and colleagues (2003) followed 222 children with sickle cell disease over a 2-year period and gathered data on behavioral, cognitive, and family functioning at 6-month intervals. Of the sample, 9% were found to have persistently elevated behavioral or emotional difficulties across the 2-year study window. It is noteworthy that this is not much higher than for the base rate for such disorders in the general population. In addition, the presence of persistent behavior problems was significantly associated with baseline family conflict. Furthermore, increases in behavior problems over time were associated with increases in family conflict. In general, these findings appear to be nonspecific to the chronic illness—and, in fact, children who are chronically ill may not manifest any more behavioral problems than a general sample may.

Recently, the relationship between specific parenting behaviors and child adjustment has been of increased interest as investigators attempt to identify the particular family interactional sequences that are most highly associated with psychological risk in children with chronic illness. In the broader child development literature, parenting styles characterized by high levels of warmth/support, high levels of behavioral control (e.g., limit setting and supervision) and low levels of

psychological control have generally been found to promote good child adjustment (Barber, Stolz, & Olsen, 2005; Gray & Steinberg, 1999). Consistent with this literature, in a sample of young adolescents with T1DM, Butler, Skinner, Gelfand, Berg, and Wiebe (2007) found that a maternal parenting style characterized as controlling, intrusive, and rejecting was associated with higher levels of depressive symptoms in youth consistent with levels found in the general population. Eckschtain, Ellis, Kolmodin, and Naar-King (2010) also found that lower parental warmth was associated with higher levels of depressive symptoms among youth with T1DM. Similarly, Horton, Berg, Butner, and Wiebe (2009) investigated the relationship between parenting and externalizing behavior problems in adolescents with T1DM. Findings revealed that high levels of parental supervision and monitoring by both mothers and fathers were associated with lower levels of adolescent externalizing behavior problems. Even for those with a chronic illness having a significant effect on cognition, positive parenting styles have been found to play a protective role. For instance, Chapman and colleagues (2010) followed a sample of preschoolers with traumatic brain injury for 18 months to determine the impact of brain injury on the emergence of behavioral difficulties. Permissive parenting was found to be a significant risk factor for the emergence of externalizing behavior problems over time. In summary, parenting behaviors that have been associated with positive developmental outcomes for healthy children also have been found to predict psychological well-being in chronically ill youth.

Given the stressors faced by children with chronic illness, it would not be surprising to find that parenting styles are more likely to be characterized by overinvolvement or overprotectiveness than in typically developing children. Overprotectiveness could in turn impede optimal child growth and development (Power, Dahlquist, Thompson, & Warren, 2003). However, the empirical literature to date has demonstrated few links between parental overinvolvement or overprotection and poor child adjustment among chronically ill children (Mullins et al., 2004; Power et al., 2003). Risk for psychopathology has in fact most clearly been associated with parental underinvolvement (Wiebe et al., 2005). On the other hand, as noted by Ellis, Templin, and colleagues (2007), overprotection measures employed in the chronic illness literature to date are problematic because they have largely measured parental behavioral *control* (which includes parenting behaviors such as limit setting and parental monitoring), rather than parental *overprotection* (which includes intrusiveness, restriction of children's exposure to normative stressful events, and high levels of anxiety about the children). An exception is a study by Holmbeck and colleagues (2002), which employed a conceptual model that distinguished among parental overprotection, parental psychological control, and youth behavioral autonomy to develop measures of overprotection; items assessing monitoring, discipline, and related constructs (e.g., behavioral control) were not included in their overprotection measure. In this study, both mothers and fathers of children with spina bifida were found to be more overprotective than parents of healthy children, although differences were mediated by the children's cognitive abilities. In addition, parental overprotection was associated with problematic child behavioral outcomes. Clearly, further research endeavors are needed in this important area of inquiry.

The effects of family stress on child adjustment also have been a focus of considerable research interest. Stressors for families with chronically ill children can be disease-specific or may involve negative life events common to any family. Ratliffe, Harrigan, Haley, Tse, and Olson (2002) identified four types of stress particular to the families of chronically ill children: role conflicts (e.g., functioning as a parent vs. a medical caregiver, being available to care for the ill child vs. other children in the family); financial burdens associated with medical care needs; burden of daily medical care; and isolation (e.g., limitations on family activities during child health status or care needs). In an investigation of caregiver challenges in families of children with special health care needs, Kuo, Cohen, Agrawal, Berry, and Casey (2011) conducted a secondary analysis of data from the 2005–2006 National Survey of Children with Special Health Care Needs, which included over 40,000 children with a variety of chronic health conditions. Kuo and colleagues reported that caregivers of children with complex health care needs reported spending a median of 2 hours per week on health care coordination and 11–20 hours per week on direct home care of their child. More than half of families (56.8%) reported financial problems, and 54.1% reported that a family member had stopped working because of a child's health.

Studies evaluating the effects of family stress that is directly associated with childhood chronic illness have generally shown that higher levels of illness-related family stress are associated with poorer child adjust-

ment (e.g., Bender, Arnett, et al., 2000; Stein & Jessop, 2003). Since the stress literature suggests that perceptions of stress may be equally important to the prediction of health outcomes as the actual frequency of stressful events (Lazarus & Folkman, 1984), researchers also have investigated the construct of "illness burden" or "caregiver strain." Caregiver strain has been defined as the caregiver's perception of the "demands, responsibilities, difficulties, and negative psychic consequences of caring for relatives with special needs" (Brannan, Heflinger, & Bickman, 1997). Higher levels of caregiver strain also have been found to be associated with poor child adjustment (Leishman, 2010) among youth with chronic illness.

Studies also suggest that non-illness-specific family stress, such as the occurrence of negative life events, may have an impact on the adjustment of chronically ill children (von Weiss et al., 2002). In a meta-analysis of studies assessing psychosocial correlates of children's adjustment to chronic illness, Lavigne and Faier-Routman (1993) found that levels of life stress were more potent predictors of child adjustment than disease factors or socioeconomic status. In a sample of 8- to 16-year-olds with T1DM and a matched comparison control group, Holmes, Yu, and Frentz (1999) also demonstrated that the occurrence of negative life events was associated with higher levels of internalizing and externalizing behavior problems for both the chronically ill and the healthy youth.

Single-parent families represent a special population that may experience a qualitatively different set of stressors from those encountered by two-parent families. In a comprehensive review of the extant literature in this area, Brown and colleagues (2008) reported that although studies were limited, this research suggested that chronically ill children from single-parent families are at significantly higher risk for psychological adjustment difficulties than chronically ill children from two-parent families. Since the broader child development literature clearly shows the negative effects of poverty on psychological adaptation and health (Bradley & Corwyn, 2004; Duncan & Brooks-Gunn, 2000; Schreir & Chen, 2013), greater risks for psychological difficulties among chronically ill children residing in single-parent homes may be associated with lower family income (Mullins et al., 2011). However, in a single-parent home, the caregiver also must manage medical care needs for the chronically ill child with more limited social support than typically found in a two-parent home. Additional research is needed for a better understanding of how single-parent homes may affect psychological adjustment in this population, beyond that impact evident in the general population. In addition, Powell and Holmes (2008) have noted the importance of examining the psychosocial outcomes of chronically ill children living in a variety of other family constellations (e.g., blended families, cohabiting families), to determine whether such family constellations also are associated with particular patterns of risk or resilience.

Research on the influence of family factors on the psychological well-being of chronically ill children has frequently suffered from the failure to integrate a developmental perspective. From a developmental psychopathology framework, transitions between developmental periods (e.g., the transition from adolescence to young adulthood) often represent periods of risk (Cicchetti & Rogosch, 2002). Families must adapt in the face of the changing needs of their children as they mature. Despite this, little research has compared normative developmental processes and transitions in the families of healthy children to those occurring in families of children with chronic illness, to determine how these critical transitional periods may be related to child adjustment. A notable exception is the programmatic research conducted by Holmbeck and colleagues (1997), who followed a sample of 68 children with myelomeningocele and 68 matched healthy controls from school age through late adolescence. Myelomeningocele is a congenital birth defect in which the neural tube fails to close normally early in gestation, which subsequently results in a variety of health problems that may include sensory and motor impairments in the lower limbs, bowel and bladder dysfunction, hydrocephalus and related cognitive impairments, and growth problems. Hence such children face a variety of challenges common among children with other chronic illnesses. In one of these investigations, Jandasek, Holmbeck, DeLucia, and Zebracki (2009) investigated changes in family cohesion and family conflict from ages 9 to 15, to determine whether illness status would predict changes in family relationships. Findings revealed that while control families reported increases in family conflict and decreases in cohesion, as is typical during the transition to adolescence, similar changes were not found for youth with myelomeningocele who reported less increase in conflict and less decrease in cohesion than controls. Similarly, Devine, Wasserman, Gershenson, Holmbeck, and Essner (2011) found that the age at which mothers and youth reported that youth with myelomeningocele were granted decision-making au-

thority about the majority of nonmedical personal issues (e.g., what club to join, what time to come home) was delayed for youth with myelomeningocele (16–17 years) as compared to youth in the comparison control group (14–15 years). Jandasek and colleagues noted that while remaining close to parents and relinquishing decision-making authority may be optimal for promoting some outcomes in children with myelomeningocele, such as physical health, these attributes may be less optimal for promoting independent functioning or healthy peer and/or romantic relationships. Additional research that directly links such family developmental processes to psychological outcomes in children with chronic conditions is clearly warranted.

Peer and Other Extrafamily Systems

Peers may provide an important source of support for children with chronic illnesses, especially during adolescence. Early cross-sectional studies of the relationships between peer relationships and psychological adjustment suggested that positive peer relationships were predictive of better psychological adjustment in children with conditions such as T1DM (Varni, Babani, Wallander, Roc, & Frasier, 1989), congenital limb deficiencies (Varni, Setoguchi, Rappaport, & Talbot, 1992), and cancer (Varni, Katz, Colegrove, & Dolgin, 1994). However, adjustment difficulties also may result in problematic peer relations, and subsequent longitudinal studies have not always supported a protective effect of positive peer relations. For example, one longitudinal study among youth with T1DM found that although friend support was associated with psychological well-being at baseline, such support did not predict changes in psychological well-being over the course of a 1-year follow-up (Helgeson, Snyder, Escobar, Siminerio, & Becker, 2007). Similarly, in a longitudinal study of childhood cancer survivors, Thompson and colleagues (2009) found that measures of peer relationships in middle childhood did not predict externalizing behavior problems during late adolescence and early adulthood.

More recently, research on the effects of peer relationships on psychological adjustment in chronically ill children has investigated both positive (supportive) and negative (conflict) aspects of peer relationships, and has also considered the potential for differential effects of peer relationships depending on a chronically ill child's gender. In one investigation, Helgeson, Lopez, and Karmarck (2009) employed a mixed-methods approach that combined the use of self-report and ecological momentary analysis to evaluate the association between friend relationships and mood among adolescents with T1DM. Although there was no relationship between friend *support* and psychological adjustment, *conflict* with friends was associated with greater depressive symptoms. In addition, friend conflict was more strongly associated with poor psychological well-being for girls than for boys.

To date, few studies have directly investigated the effects of broader contextual factors (e.g., school resources, neighborhood advantage or health care system quality) on the psychological adjustment of chronically ill children. However, studies of healthy children would suggest that such contextual variables are important in understanding the adjustment of chronically ill children, since they are markers of exposures to particular stressors that may compound poor health and mental health outcomes (Blair & Raver, 2012), Such factors are indirectly implicated as risk or resilience factors for psychological adjustment by studies demonstrating that chronically ill children of lower socioeconomic status have poorer mental health outcomes than those from more affluent backgrounds (Frank, Blount, & Brown, 1997; Holmbeck et al., 2003; MacLean, Perrin, Gortmaker, & Pierre, 1992). However, further research examining contextual factors on the psychological adjustment and adaptation among children with chronic illness is sorely needed.

Finally, there has been a dearth of research examining contextual factors as mediators of the association between parenting variables and health outcomes. Recent research has examined the effects of specific genes on the relationship between parenting and health outcomes (Brody et al., in press). This research is important in understanding the genetic and environmental interaction that undoubtedly has a significant impact on parenting variables and health outcomes.

Racial and Ethnic Health Disparities and Access to Health Care

For the first time in history, more than one-half of U.S. infants (less than 12 months of age), and almost half (49.7%) of children less than 5 years of age, are members of racial/ethnic minorities (U.S. Census Bureau, 2012). These groups are now considered to constitute a "majority minority." As of 2011, nearly one-fourth (23.6%) of children (ages 0–17) in the United States. were Hispanic, 15.2% were black, 4.7% were Asian,

1.6% were American Indian or Alaskan Native, 0.3% were Native Hawaiian and other Pacific islander, and 4.7 were two or more races. The U.S. Department of Health and Human Services (USDHHS, 2013) *Healthy People 2020* initiative defines health disparities as "differences in health outcomes that are closely linked with social, economic and environmental disadvantage."

Health Outcomes

A review of 111 peer-reviewed child health disparity research studies has demonstrated that child health disparities are "extensive, pervasive and persistent" (Flores et al., 2010). Mortality rates were higher for all four U.S. minority ethnic groups than for white children. These include greater risk in overall mortality, death from drowning, death from ALL, and congenital heart defects. In terms of chronic disease, disparities were found for asthma, cancer, eye disorders, HIV/AIDS, kidney disease, and stroke. These child health disparities have been described as persistent because the studies reviewed suggest that most disparities have maintained or worsened over time.

The Agency for Healthcare Research and Quality (AHCRQ) tracks several markers of child health disparities, including early childhood immunizations, emergency department visits for asthma, preventive dental visits, untreated dental caries in adolescents, preventive adolescent health visits, and receipt of the meningococcal vaccine in adolescents. In a recent report (AHCRQ, 2011), black children were less likely than non-Hispanic white children to receive all recommended early childhood immunizations and to have preventive dental visits, and were more likely to be treated in the emergency department for asthma and to have untreated dental caries. However, black adolescents were more likely to have annual well adolescent visits. Health disparities for Hispanic children were noted in three areas: emergency visits for asthma, untreated dental caries, and preventive dental visits. In the only areas where data were reported for Asian youth (early childhood immunizations and meningococcal vaccine), no differences emerged.

Access to Good-Quality Care

Disparities in health outcomes are due in part to disparities in access to good-quality health care. The AHCRQ (2011) report provided findings to suggest that across all age groups and multiple quality measures, blacks received worse care than whites on 41% of the quality measures, and Hispanics received worse care than non-Hispanic whites on 30% of the quality indices. The proportions of poor care markers were lower for Asians and for American Indians and Alaska Natives (30%). However, according to a rate-of-change analysis, the quality of care had improved over the previous 5 years for all ethnic groups. Unfortunately, no change was found in terms of *access* to care. Across the measures of health care access, one-half did not show improvement, and 40% demonstrated a worsening of access for minority groups. With regard to pediatric populations, the review by Flores, Tschann, Dimea, Pasch, and de Groat (2010) documented significant health disparities in quality of pediatric primary care, asthma care, cardiovascular surgery, pneumonia hospitalizations, and care for opthalmological, orthopedic, and renal conditions.

Prevention of Unintentional Injury

Injuries are the leading cause of death for infants and children in the United States (Christian & Sege, 2010). The most recent data from the Centers for Disease Control and Prevention (CDC; 2008a) demonstrated that unintentional injuries peak during ages 1–4 and again during adolescence and emerging adulthood. For children less than 12 months of age, most fatal injuries were due to suffocation. For children ranging in age from 1 to 4 years, the majority of fatal injuries were due to drowning. For the remainder of youth, motor vehicle crashes were the leading cause of fatal injuries. The leading cause of nonfatal injuries was falls for all age groups less than 15 years. For adolescents ages 15–19, being struck by or against an object was the leading cause of nonfatal injuries, followed by falls and motor vehicle crashes. Rates of nonfatal injuries from fires, burns, and drowning were the highest in children younger than 5 years of age. Males have consistently higher rates of injuries relative to their female counterparts, as do children from lower-income families in comparison to their more affluent peers. In regard to ethnicity, American Indian or Alaskan Native children have the highest rates of injuries, whereas white and black children do not differ in injury rates.

In addition to demographic risk factors, other childhood characteristics associated with injury include externalizing behavior problems (Schwebel et al., 2011) and temperament variables such as sensation seeking (Schwebel & Gaines, 2007). The primary parent characteristic associated with pediatric injury is parental

supervision—specifically, the attention, proximity, and continuity of supervision (Petrass, Blitvich, & Finch, 2009). Parents' overestimation of children's risk-taking behavior is emerging as a protective factor (Morrongiello, Bell, Butac, & Kane, 2014).

From 2000 to 2009, the overall annual unintentional injury death rate decreased by 29%, suggesting that some prevention approaches using the "three E's" model (education, enforcement, engineering) have been effective. Effective interventions include bicycle helmets, four-sided swimming pool fencing, booster seats, smoke alarms, childproof cigarette lighters, concussion guidelines, and adolescent driving policies. However, although most of the population experienced decreases in deaths and unintentional injuries, rates increased in infants under 12 months of age because of reported suffocations. Rates also increased in adolescents ages 15–19 due to increases in poisoning related to prescription drug overdoses (CDC, 2012b). The CDC (2012a) has recently issued a new action plan for pediatric injury prevention, based on surveillance data and four decades of research. Strategies include the delivery of health messages, education and skills training at multiple levels, incorporating injury prevention into health care systems, taking advantage of recent advances in medical home care models and information systems, and continuing efforts in policy change.

Health Promotion/Disease Prevention

As nearly one-half (40%) of premature deaths can be attributed to preventable behavioral factors, the single greatest opportunity to improve health lies in changing personal behaviors (National Institutes of Health, 2012; Schroeder, 2007). The top four behaviors that contribute to early mortality and chronic illness are poor nutrition, inadequate physical activity, smoking, and abuse of alcohol (Kung, Hoyert, Xu, & Murphy, 2008). Thus approaches to the prevention of obesity, smoking, and alcohol abuse in childhood and adolescence can have a long-term impact on the health of the population and on rising health care costs.

Nutrition and Physical Activity

Obesity prevention begins with breast feeding, as numerous reviews and meta-analyses have linked breast feeding to reduced risk of childhood and adult obesity (Lawrence, 2010). In addition, a recent report from the Institute of Medicine (2012) strongly recommends increasing food literacy skills and nutrition science education at home and in school settings, as well as policy changes and social marketing campaigns to reduce sugar-sweetened beverages and increase the availability of healthy food choices in communities. Two other types of nutritional interventions have received recent attention because of their potential for disease prevention. First, interventions to increase fiber intake have had a positive impact on cholesterol levels without compromising energy intake or growth (Ruottinen et al., 2010). Second, in a nationally representative sample of children ranging in age from birth to 21 years (Kumar, Muntner, Kaskel, Hailpern, & Melamed, 2009), a shocking 70% had vitamin D insufficiency. Such insufficiency not only is associated with multiple disease markers such as cardiovascular risks, bone density, and immune function, but also has also been linked to autism spectrum disorder and psychotic symptoms among children (Cannell, 2008; Gracious, Finucane, Friedman-Campbell, Messing, & Parkhurst, 2012; Misra, Pacaud, Petryk, Collett-Solberg, & Kappy, 2008). Future research is necessary to test nutritional interventions to increase vitamin D via dietary changes or use of supplements.

Physical inactivity accelerates aging and dramatically increases health risk, such that several diseases (including coronary cardiovascular disease, Type 2 diabetes, and several cancers) are now considered hypokinetic diseases (USDHHS, 2008). Low cardiovascular fitness is estimated to cause more mortality than the combined deaths due to obesity, diabetes, and smoking (Archer & Blair, 2012). Lack of physical activity has been linked to poor mental health in children and adolescents, and interventions to increase physical activity may diminish depressive symptoms (Biddle & Asare, 2011). Thus physical activity may be the single greatest health protective behavior. Because family-based physical activity interventions have had limited success (Salmon, Booth, Phongsavan, Murphy, & Timperio, 2010), recent efforts have focused more on school-based approaches. In a recent literature review, Kriemler and colleagues (2011) identified 20 rigorous studies and all findings from these investigations demonstrated significant effects on at least one measure of physical activity. Effects were consistent for physical activity both in and out of school, and clearly warrant extensive policy changes to implement such programs in school nationwide.

Another prevention approach is to limit sedentary behavior. A review of 232 studies of sedentary behav-

ior, primarily measuring television viewing, concluded that school-age children engaging in such behavior for more than 2 hours per day had higher body fat; decreased cardiovascular fitness; and lower self-esteem, prosocial behavior, and academic achievement (Tremblay et al., 2011). Interventions including education, contingency management, and environmental control have shown small but significant effects (Biddle & Asare, 2011). One limitation is that many studies focus primarily on television viewing when today's youth have multiple options for screen use, including online gaming, multimedia sites, and social networking. Future research is necessary to test interventions targeting communication-based sedentary behaviors such as video games, instant messaging, text messaging, and other cell phone use (Leatherdale, 2010).

Not surprisingly, combined interventions targeting nutrition, physical activity, and sedentary behavior may be most effective in reducing the incidence of obesity (CDC, 2008b). A recent meta-analysis of 55 obesity prevention studies in youth (Waters et al., 2011) found significant effects on reducing body mass index (see below for obesity *treatment* studies). Successful strategies included changes in the school curriculum to focus on health behaviors, increased school opportunities for physical activity and healthy eating, support for school staff, and parent support and environmental changes in the home. However, most studies focused on children ages 6–12, and thus more research is needed for prevention in adolescents and preschool children.

Smoking Prevention

Smoking prevention programs typically target adolescence, the most common period for smoking initiation (Substance Abuse and Mental Health Services Administration, 2009). Well-designed randomized clinical trials of family-based interventions have demonstrated some success in reducing teen smoking (Thomas, Baker, & Lorenzetti, 2007), but school-based and mass media interventions have yielded mixed results (Brinn, Carson, Esterman, Chang, & Smith, 2010). Thus the most recent studies have focused on multicomponent, communitywide interventions that include age restrictions for tobacco purchase, tobacco-free public places, various mass media communications, educational and behavioral programs in schools, and parent counseling. In a Cochrane review of 25 such controlled trials (Carson et al., 2011), 10 studies were associated with a reduction in smoking initiation. Common elements of successful programs included school-based, teacher-delivered interventions; parental involvement; and a program duration of greater than 12 months. Future research is necessary to consider gender-specific intervention programs, as data suggest that girls are more likely than boys to smoke in early adolescence (Mackay, George, & Kirk, 2006; Warren, Sinha, Lee, Lea, & Jones, 2009), and some studies have shown that girls are less likely to respond to intervention (Perry et al., 2004; Schofield & Dunham, 2003). More research is also necessary to test interventions for water pipes, the most commonly used emerging tobacco product in young people (McMillen, Maduka, & Winickoff, 2012). Research is also needed into interventions for tobacco use that is linked to marijuana use when tobacco leaves are used to hold marijuana (Gardiner, 2001), as marijuana use is now more prevalent than tobacco use in high school students (Burke et al., 2012).

Another critical component of prevention is the control of exposure to secondhand smoke. The evidence is clear that pre- and postnatal exposure to smoke prospectively predicts up to a 70% increase in wheezing and up to an 80% increase in asthma in children (Lee, Middaugh, Howie, & Ezzati, 2010). Other adverse consequences of secondhand smoke exposure in children include a higher frequency of lower respiratory tract infections, middle ear infections, sudden infant death syndrome, and invasive bacterial disease (e.g., strep throat, meningitis). In addition to policy interventions eliminating smoking in public spaces, motivational and cognitive-behavioral counseling approaches with parents have demonstrated some promise (Borrelli, McQuaid, Novak, Hammond, & Becker, 2010; Emmons et al., 2001; Tyc et al., 2013).

Alcohol Use Prevention

Worldwide, nearly 4% of all deaths are associated with alcohol use. Most alcohol-related deaths are caused by alcohol resulting from injuries, cancer, cardiovascular diseases and liver cirrhosis (World Health Organization, 2011). The effects of excessive alcohol use on disability-adjusted life years increases its negative health impact. Alcohol use has declined by more than 10% among American adolescents since the 1980s (CDC, 2012c), but alcohol use significantly increases from adolescence to young adulthood, suggesting a critical need for prevention activities during this transitional period. Foxcroft and Tsertsvadze (2012) have summarized three Cochrane reviews of universal alco-

hol prevention programs for children and adolescents. Results of school-based prevention programs yielded mixed findings, suggesting that administrators must be cautious when choosing an evidence-based prevention strategy. Results of family-based prevention programs were small, but consistent and persistent over time. Although there was some evidence that multicomponent programs (particularly those delivered in multiple settings) were efficacious, there was insufficient evidence to confirm that these interventions were more effective than those programs delivered in a single setting. From these data, Foxcroft and Tsertsvadze conclude that the increase in cost associated with the delivery of multicomponent interventions may not be worthwhile. Much of alcohol-based prevention in adults occurs in primary care settings (Cayley, 2009), and there is a paucity of such studies in pediatric populations.

RESEARCH DESIGN ISSUES

Research in the field of child health psychology began with the use of clinical case studies and single-participant designs; investigators were primarily interested in describing specific psychological phenomena or conditions in particular pediatric populations with chronic health conditions or developmental disabilities. This research was fairly pervasive throughout the 1970s. Subsequently, as research in the field of child health psychology took on a more conceptual or theoretical framework, correlational studies became the basis for a greater number of research questions. Correlational studies dominated the field of child clinical health psychology up until the mid-1990s. As correlational studies became more sophisticated, and more rigorous theoretical frameworks were carefully tested, researchers also began to ask questions about factors influencing the magnitude of the relationship between variables (Baron & Kenny, 1986; Holmbeck et al., 1997, 2002). "Moderating" processes are posited when conducting studies of risk, protective, and resilience factors are conducted (Holmbeck, Zebracki, & McGoron, 2009), whereas a "mediator" variable is conceptualized as the mechanism through which one variable influences another variable.

Quasi-experimental designs, observational research designs, single-participant designs, and meta-analytic techniques predominated in the research literature throughout the 1990s, until the field entered a tertiary phase of investigation or experimental designs. These randomized controlled clinical trials actually served to test the various correlational models pervasive in the extant literature throughout the 1980s and the early to mid-1990s; in other words, they served as true experimental tests of the various theoretical tenets in the field that had been demonstrated primarily by means of correlational research (Thompson & Gustafson, 1996). The randomized controlled clinical trial is now considered the "gold standard" with regard to research methodology in the field, and in testing the various theoretical models, it has provided a compelling theoretical framework within the field. These randomized controlled clinical trials have given rise to empirically based practice that has attained burgeoning support in recent years, both within the field of child health psychology and in the broader field of clinical psychology (Nelson & Steele, 2009).

SOMATIC SYMPTOM AND RELATED DISORDERS

In our discussion of specific groups of disorders, we first turn to those disorders in which children or adolescents exhibit ongoing, persistent somatic symptoms that are distressing or may result in functional impairments on a daily basis (American Psychiatric Association [APA], 2013). While the symptoms may represent discomfort that is not symptomatic of serious or life-threatening disease, somatic symptoms without evidence of a medical explanation are not sufficient for a diagnosis of somatic symptom disorder (APA, 2013). By comparison to their adult counterparts, children typically experience a predominant single symptom. Frequent symptoms include recurrent abdominal pain, headache, fatigue and nausea (APA, 2013). Prior to adolescence, children rarely worry excessively about illness per se. Parents and caregivers frequently exert a significant influence in determining the interpretation of symptoms and also significantly influence the seeking of medical attention as well as days off from school.

Children with somatic symptom and related disorders often endure frequent disruptions in their daily lives, including missed days from school, frequent medical appointments, less time with peers in play activities and sports, and frequent disruption in family activities (APA, 2013). Health-related quality of life frequently may be impaired both mentally and physically (APA, 2013). The onset of such disorders is frequently at adolescence, and the disorders are more prevalent

among females than males (for a review, see Hadjistavropoulos, Owens, Hadjistravopoulos, & Asmundson, in press). The disorders may be comorbid with another medical condition and are frequently characterized by other psychiatric morbidity, including the internalizing disorders (i.e., anxiety disorders, depression).

Somatic Symptom Disorder and Illness Anxiety Disorder

The diagnosis of somatic symptom disorder in the *Diagnostic and Statistical Manual of Mental Disorders,* fifth edition (APA, 2013) requires a specification as to whether the disorder is persistent, and whether it is present at a mild, moderate, or severe level. Diagnostic criteria for this disorder are presented in Table 19.1. By contrast, the diagnosis of illness anxiety disorder is proposed for those children and adolescents who do not report significant somatic symptoms, yet who do describe preoccupation with a serious illness, high levels of anxiety about health, and either excessive health behavior or maladaptive avoidance (APA, 2013). This disorder is especially rare in children, although its onset may increase at late adolescence and young adulthood (APA, 2013).

The etiology underlying somatic symptom disorder is unclear to date, although genetic factors have been demonstrated to account for approximately one-third of the variance in somatization scores (Gillespie, Zhu, Health, Hickie, & Martin, 2000). Other behavioral and cognitive-behavioral models have been proposed, with the most compelling explanation being that dysfunctional beliefs about health and illness are largely the result of an individual's past experience with illness. One compelling model proposed is that interpersonal factors such as attachment may be associated with the development and maintenance of health anxiety. This interpersonal model of health anxiety (Stuart & Noyes, 1999) suggests that negative parenting styles and aversive early experiences predispose a child or adolescent to develop an insecure attachment style, resulting in a focus on bodily sensations. The child or adolescent thereby seeks reassurance about these, which allows him or her to seek emotional and interpersonal support from others; this support thus serves to alleviate the attachment insecurity. In support of the model, Noyes, Weber, and Vogler (2003) demonstrated that higher levels of health anxiety were associated with insecure relative to secure attachment styles among individuals receiving their care in an outpatient medical clinic.

TABLE 19.1. DSM-5 Diagnostic Criteria for Somatic Symptom Disorder

A. One or more somatic symptoms that are distressing or result in significant disruption of daily life.
B. Excessive thoughts, feelings, or behaviors related to the somatic symptoms or associated health concerns as manifested by at least one of the following:
   1. Disproportionate and persistent thoughts about the seriousness of one's symptoms.
   2. Persistently high level of anxiety about health or symptoms.
   3. Excessive time and energy devoted to these symptoms or health concerns.
C. Although any one somatic symptom may not be continuously present, the state of being symptomatic is persistent (typically more than 6 months).

Specify if:

With predominant pain (previously pain disorder): This specifier is for individuals whose somatic symptoms predominantly involve pain.

Specify if:

Persistent: A persistent course is characterized by severe symptoms, marked impairment, and long duration (more than 6 months).

Specify current severity:

Mild: Only one of the symptoms specified in Criterion B is fulfilled.

Moderate: Two or more of the symptoms specified in Criterion B are fulfilled.

Severe: Two or more of the symptoms specified in Criterion B are fulfilled, plus there are multiple somatic complaints (or one very severe somatic symptom).

Note. Reprinted with permission from *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (p. 311). Copyright 2013 by the American Psychiatric Association.

While these data are certainly suggestive, more experimental paradigms are needed to support the veracity of this model.

Conversion Disorder (Functional Neurological Symptom Disorder)

Conversion disorder (functional neurological symptom disorder) may include one or more symptoms of various types, including weakness or paralysis, abnormal movements, gait abnormalities, or abnormal limb posturing (APA, 2013). Other symptoms may include reduced or absent speech volume, altered articulation, or a sensation of a lump in the throat (APA, 2013). The symptoms do not have their etiology in neurological disease, and there must be clear evidence of incompatibility with any neurological disease.

Psychological Factors Affecting Other Medical Conditions

The diagnosis of psychological factors affecting other medical conditions refers to the presence of one or more clinically significant psychological or behavioral factors that have an adverse impact on an existing medical condition (APA, 2013). These psychological factors may include coping style or poor adherence to the management of the medical condition (e.g., adolescents with T1DM may not adhere to their glucose monitoring or insulin administration); the factors may either exacerbate symptoms or result in a life-threatening condition (APA, 2013).

Factitious Disorder

When an individual falsifies an illness in another individual, such as an adult counterpart, a child, or even a pet, the diagnosis is factitious disorder imposed on another (APA, 2013). It is important to note that while the victim may be given a diagnosis of abuse, it is the perpetrator and not the victim who actually receives this diagnosis (APA, 2013). Factitious disorder imposed on another is much more commonly seen with children and their parents than factitious disorder imposed on self, the other type of this disorder, is seen in children. A diagnosis of factitious disorder requires that it be demonstrated that an individual is taking specific actions to simulate, misrepresent, or cause signs or symptoms of an illness or injury. Individuals with factitious disorder are frequently at risk for experiencing psychological distress or functional impairment (APA, 2013). Such behaviors might include adding blood to urine for the purpose of falsifying a laboratory test or ingesting a substance to produce illness (APA, 2013). These behaviors are clearly associated with deception and in extreme circumstances are certainly are criminal. Moreover, when a parent or other caregiver imposes a disorder on a child, the caregiver's actions clearly represent abuse and maltreatment of the child. When the parent or caregiver is the perpetrator and the child is the victim, the disorder is often referred to as Munchausen syndrome by proxy. Frequently, the perpetrators are characterized by significant psychopathology and functional impairment. The prevalence is largely unknown because of the high levels of deception in this population, although it is estimated to occur in about 1% of the population (APA, 2013).

Somatic Symptom Disorder with Predominant Pain (Pain Disorder)

When children present with primary symptoms of pain without motor, sensory, or seizure symptoms, a DSM-5 diagnosis of somatic symptom disorder with predominant pain is given (APA, 2013). In DSM-IV (APA, 1994), a separate diagnosis of pain disorder was given, and this disorder could be one of two types: pain disorder associated with psychological factors, or pain disorder associated with both psychological factors and a general medical condition. (Pain disorder associated with a general medical condition was not considered a mental disorder. This condition was typically associated with an active disease process, such as sickle cell disease.)

Pain that occurs in otherwise healthy children and is not considered to be symptomatic of an underlying disease is referred to as "recurrent pain" and frequently comes to the attention of clinical or pediatric psychologists. Headaches and recurrent abdominal pain are the types of recurrent pain that come most often to the attention of mental health professionals.

Headaches

For children and adolescents, headaches typically begin at the age of 7–8 years, and the prevalence is associated with chronological age: A higher prevalence of headaches has typically been associated with older youth (Gauthier, Ivers, & Carrier, 1996). Boys report headaches at a higher frequency during childhood, while

girls report headaches at a higher frequency at adolescence. In the absence of a physical origin, headaches are typically classified as one of two types: tension and migraine headaches. Tension headaches are believed to have their etiology in sustained tension in pericranial muscles, whereas migraine headaches are believed to be caused by constriction of intra- and extracranial arteries (Gauthier et al., 1996). Type of headache has important implications for management of the condition. Finally, although there is scant research pertaining to the long-term outcome of children and adolescents who suffer from headaches, in general many children and adolescents who suffer from headaches continue to experience headaches as young adults.

Biofeedback training has been demonstrated to be an evidence-based treatment for the management of headaches. The procedure involves the monitoring and quantification of physical response and subsequently conveying this information to the child or adolescent, so that the child is able to perceive even small changes in his or her physiological functioning (Dahlquist & Nagel, 2009). Electromyographic (EMG) biofeedback has been employed as a means to teach a child to relax the frontalis muscle (Hermann & Blanchard, 2002), while biofeedback procedures for migraines target vascular activity in the body by teaching a child to warm an index finger (Hermann & Blanchard, 2002; Holden, Deichmann, & Levy, 1999). As Dahlquist and Nagel (2009) have concluded, EMG biofeedback has had an impressive track record for managing both migraine and tension headaches in both the short and long terms (up to a year following cessation of treatment).

Another particularly well-supported treatment for the management of headaches is progressive muscle relaxation, whereby children are taught to tense and subsequently relax specific groups of muscles. Larsson, Carlsson, Fichtel, and Melin (2005) conducted a number of randomized controlled clinical trials of relaxation therapy for adolescents suffering from headaches. Findings revealed that relaxation therapy, compared to a number of attention control conditions (e.g., self-monitoring), was especially efficacious in reducing both headache days and headache intensity. The study by Larsson and colleagues is especially encouraging given issues with regard to access to health care, particularly among youth of low socioeconomic status. Specifically, the study indicates that this pain management procedure can be delivered by school nurses during school hours. It should be noted, however, that the delivery of the treatment program was most efficacious when it was delivered by professionally trained therapists.

Finally, the use of a computer-based intervention has been demonstrated to be particularly promising for the management of headaches. In an investigation by Connelly, Rapoff, Thompson, and Connelly (2006) employing a CD-ROM program (*Headstrong*), participants reported significant improvements in headache pain relative to a wait-list control group. Like the study by Larsson and colleagues (2005), the Connelly and colleagues research has especially important implications for issues of access in health care, since it suggests that a psychological treatment for pain may be delivered without any need for outpatient clinic appointments.

Recurrent Abdominal Pain

Recurrent abdominal pain (RAP) is characterized by paroxysmal pain that occurs in three or more episodes over a 6-month period and significantly results in functional impairment across multiple domains of a child's life (e.g., school attendance, family and social functioning) (for a review, see Banez & Cunningham, 2009). RAP is quite common in childhood and results in significant health care utilization, including frequent visits to the doctor with symptoms including nausea, vomiting, and abdominal pain. Children with RAP frequently suffer from other types of pain, including headaches and limb pain. Unlike other abdominal pain having its etiology in related gastrointestinal disorders, such as irritable bowel syndrome and inflammatory bowel disease, children with RAP are not identified with an organic basis for their pain. Hence RAP is classified in some systems as a somatoform disorder (Banez & Cunningham, 2009). The disorder differs from encopresis due to the disabling pain associated with RAP. Symptoms of the disorder include lactose intolerance and constipation, and pain is of such severity that it results in numerous functional impairments, such as missed days from school and peer relationship difficulties.

Interestingly, recent investigation has revealed RAP to be most primarily associated with family functioning (for a review, see Walker, Smith, Garber, & Van Slyke, 1997). Of interest is the finding that symptom frequency and severity have both been demonstrated to be associated with family functioning and stressors affecting the family system (Walker, Garber, Smith, Van

Slyke, & Lewis Claar, 2001). RAP also has been associated with both poor and ineffective coping skills on the part of both caregivers and the children themselves. Modeling has been offered as one reason underlying nonphysiologically based RAP, whereby younger children observe caregivers with pain or other somatic symptoms—and, more importantly, have the opportunity to observe positive consequences associated with the pain behavior (Walker, 1999).

Management of RAP has included psychological treatment as well as physical management (Banez & Cunningham, 2009). This includes the use of family systems psychotherapy, particularly at diagnosis, at recurrence, and at critical points during treatment-related issues. Those therapies that have demonstrated the most promise include multisystemic treatments including physical treatments (e.g., the use of fiber to increase the frequency of bowel movements, coupled with relaxation treatments) (Walker, 1999). In addition, the use of self-monitoring or a "stomachache" diary has demonstrated a significant reduction in the number of pain attacks for children with RAP (Feldman, McGrath, Hodgeson, Ritter, & Shipman, 1985). It is important to note that the treatment approaches for RAP demonstrating the most efficacy are those that are employed in combination, rather than individual treatments employed alone (Banez & Cunningham, 2009). Given that there is now a tertiary wave of research to test evidence-based treatments for the psychological adaptation to various chronic illnesses, this finding strongly suggests that multimodal therapies should be considered for enhancing the quality of life of children suffering from RAP (as well as many other physical disorders that frequently affect psychological adaptation, or where enhanced disease management is associated with better psychological adjustment).

DEVELOPMENTAL DISORDERS

In recent years, there has been considerable research interest in those children who are at biological risk from birth or early childhood. Because a complete review of all children and adolescents who are at biological risk is not possible within the scope of this chapter, we focus our discussion on children with prematurity and central nervous system (CNS) disorders, including epilepsy, spina bifida, traumatic brain injury, and spinal cord injury.

Prematurity

Children who are born at less than 37 weeks' gestational age are considered to be premature, and prematurity is the leading cause of perinatal mortality and morbidity (Aylward, 2009). Mortality rates in preterm infants have decreased by nearly one-half in the past two decades, and major advances in medical technology have been a significant contributor in decreasing mortality. However, the improved survival rates of infants with low birth weight (<2,500 grams), very low birth weight (1,500 grams), and extremely low birth weight (<1,000 grams) have concomitantly increased the need for specialized services (Aylward, 2009; Saigal & Doyle, 2008). Birth weight and gestational age have typically been the proxies for prematurity. More recently, with the improved technology of fetal ultrasound, gestational age estimation has been a stronger index for infant mortality and morbidity (Institute of Medicine, 2006). Nonetheless, many experts still maintain that both birth weight and gestational age should be considered in classifying infants as premature (Aylward, 2009). In addition to birth weight and gestational age, other variables that have been demonstrated to be predictive of prematurity include the severity of the neonatal course; sociodemographic factors; and other comorbidities, including (but not limited to) chronic lung disease, asphyxia, and low heart rate (bradycardia). In recent years, illness severity scores have been developed as a means of quantifying severity of illness, although predictions from risk scores to developmental outcome have generally been demonstrated to be weak (Aylward, 2009).

With the increased survival rate of premature infants, investigators have turned to examining the long-term outcomes of these children in the areas of intellectual functioning, visual–motor skills, language, academic achievement, and behavior. When compared to controls with normal birth weight, children who are born at low birth weight have typically scored on average from one-third to one-half of a standard deviation lower on measures of cognitive functioning (Aylward, 2002a, 2002b, 2005). Investigators have cautioned against the sole use of summary scores in evaluating cognitive functioning, however, and have recommended the assessment of specific functions. Intellectual deficits have been found to be accompanied by impairments in visual–motor and other fine motor functioning (Dewey, Crawford, Creighton, & Sauve, 1998).

Other impairments have been demonstrated in verbal working memory, and specific learning impairments significantly affect their academic achievement, with approximately 20% of these children receiving special education services. Other problems frequently include symptoms associated with attention-deficit/hyperactivity disorder (ADHD), including impairments in behavioral regulation and executive functioning skills.

CNS Disorders

It has been estimated that 1.9% of children have CNS disorders that include primarily neurodevelopmental disorders. CNS impairments impede children's adaptive functioning and participation in age-appropriate activities (e.g., recreational, academic, or household activities) (Deidrick, Grissom, & Farmer, 2009). Children with CNS disorders are also at particular risk for cognitive impairments, academic and school-related difficulties, and behavioral and emotional difficulties. While a complete review of the psychological sequelae of all CNS impairments is not possible within the scope of this chapter, we have chosen to describe four conditions—epilepsy, spina bifida, traumatic brain injury, and spinal cord injury—and provide recent research with regard to evidence-based assessment and management of these conditions.

Epilepsy

"Seizures" are atypical electrical discharges in the brain that may cause loss of consciousness, loss of muscle tone, or increased muscle tone or automatisms. When a seizure is not identified with a particular event such as a closed head injury, a diagnosis of epilepsy is made (Hauser & Beghi, 2008). It has been estimated that 1% of U.S. children under the age of 20 years are diagnosed with epilepsy (Deidrick et al., 2009). Seizures are characterized in accordance with their type of onset (generalized vs. partial), as well as the effects of the seizures (e.g., "absence" seizures with staring, "tonic" seizures with stiffening of the muscles, and "atonic" seizures with loss of muscle tone) (Friedman & Sharieff, 2006). Antiepileptic drugs are employed in 80–90% of children with various types of seizures, although these drugs are not without adverse effects—the most notable of which are drowsiness and lethargy, which can result in cognitive impairments.

With regard to cognitive functioning, the general intellectual functioning of children with seizure disorders has been demonstrated to be in the average range; however, cognitive impairment has been found to be related to seizure type, age at onset of the seizure disorder, the presence of other neurological abnormalities, and finally seizure intractability (Nolan et al., 2004; Williams, 2003). When seizures are not well controlled in children, there is typically a greater risk for impairments in attention and memory as well as processing speed. Children with epilepsy receive special education services at higher rates than do their peers and are at particular risk for academic underachievement (Berg et al., 2005). Control of the seizures has been demonstrated to be the most efficacious approach to minimizing cognitive impairments, although controlling seizures is not always attainable. Moreover, as noted above, one adverse effect of antiepileptic medications is sedation, although recent developments in psychopharmacology have enhanced the side effect profile of these medications.

In the behavioral and emotional domain, children with epilepsy have been demonstrated to be at greater risk for psychopathology, including symptoms of depression (Wagner & Smith, 2006). Whether such symptoms are associated with the social stigma of the disease is not entirely clear. Variables that have been demonstrated to moderate the association between psychopathology and seizure disorders include the use of antiepileptic drugs, individual and family adaptation to seizure disorders, family stress, and other neurological impairments that may be associated with the seizures. Children with seizure disorders have been found to have poorer social skills than their healthy counterparts (Tse, Hamiwka, Sherman, & Wirrell, 2007).

Spina Bifida

Spina bifida is a neural tube defect occurring when the neural tube does not fuse properly early in pregnancy (Deidrick et al., 2009; Mitchell et al., 2004). The eventual result is malformation of the spinal cord and cerebral cortex. The most common form of spina bifida is myelomeningocele, in which (as noted earlier in this chapter) the meninges and spinal nerves are not contained in the spinal cord and protrude from the open vertebrae. The results are weakness or paralysis of the lower extremities, as well as problems with bowel and bladder control. Children with spina bifida and their families often must endure multiple surgeries and ongoing medical follow-up to manage neurological impairments, including implantation and revisions of a

shunt (a device employed to divert cerebrospinal fluid from the ventricles to the abdominal cavity); skin care to prevent pressure sores due to braces or prolonged positioning in a wheelchair; and orthopedic health issues.

In the cognitive domain, a consensus of the general research literature indicates that children with spina bifida evidence generally low-average intellectual functioning, with specific weaknesses in visual–spatial and visual–motor functioning (Dennis, Landry, Barnes, & Fletcher, 2006). In addition, these children evidence difficulties in learning, long-term memory, and retrieval problems. There is also some research to suggest that these children also evidence impairments in attention and other executive functioning deficits (Rose & Holmbeck, 2007). It has been suggested that the impairments exhibited by children with spina bifida have their origin in basic processing deficits in posterior attention systems and in the areas of timing and motor control (Dennis, Landry, et al., 2006). Yeates, Loss, Colvin, and Enrile (2003) have provided compelling evidence to suggest that a subset of these children may exhibit a nonverbal learning disability. Thus it should be no surprise that children with spina bifida frequently evidence specific learning disabilities in mathematics (Barnes et al., 2006). Due to their array of cognitive impairments, coupled with the overrepresentation of children from lower socioeconomic backgrounds among children with spina bifida, they often perform more poorly academically than their healthy peers and receive poorer grades in school (Holmbeck et al., 2003).

In the areas of emotional and behavioral functioning, the data are generally mixed, suggesting both internalizing and externalizing behavioral symptoms. The most common disorders are ADHD and anxiety disorders (Ammerman et al., 1998).

Traumatic Brain Injury

Traumatic brain injury is a brain insult that is the result of an external mechanical force. By definition, insults that are acquired from nontraumatic causes, including anoxia or tumors (Wade, Walz, & Bosques, 2009), are not included in this group of injuries. It has been estimated that approximately 500,000 children under 15 years of age suffer from traumatic brain injury per year. While most children with traumatic brain injury do survive, such injuries are the leading cause of death among children, with falls being the leading cause of these injuries among toddlers. Traumatic brain injuries associated with automobile accidents and assaults are the most common types among adolescents, and the occurrence is nearly double for males than for females (Keenan & Bratton, 2006). Traumatic brain injuries are typically classified as having "primary" and "secondary" effects. The primary effects are the results of the trauma itself, such as skull fractures, contusions, and hemorrhages; the secondary effects occur subsequent to the trauma and include brain swelling, elevated intracranial pressure due to cerebral edema, hypoxia, mass lesions, and seizures. It should be noted that traumatic brain injuries are frequently associated with cognitive morbidity, including impairments in intellectual functioning, language and nonverbal skills, attention, memory, and executive functioning (Ewing-Cobbs et al., 2004). Frequently children with traumatic brain injuries demonstrate impairments similar to those with ADHD or learning disabilities; these include problems with concentration, memory, and variable academic performance. Behavioral and psychiatric problems also are prevalent among children who have sustained traumatic brain injuries; these include emotional disorders, disinhibited disorders, impulsivity, anxiety, and conduct disorder (Wade et al., 2009). Of course, it is frequently difficult to estimate the effects of traumatic brain injury on children's behavior, as children with behavioral or learning problems are often more likely to sustain traumatic brain injuries than are their typically developing peers (Goldstrohm & Arffa, 2005). Finally, it should come as no surprise that traumatic brain injuries are associated with a high frequency of psychological symptoms and distress among family members (Wade, Taylor, Drotar, Stancin, & Yeates, 1998).

Spinal Cord Injury

It has been estimated that approximately 2 children per 100,000 sustain spinal cord injuries in the United States (Vitale, Goss, Matsumoto, & Royce, 2006); males are three times more likely to sustain spinal cord injuries than their female counterparts, particularly at adolescence. Motor vehicle accidents account for the majority of spinal cord injuries, and other causes include gunshot wounds and sports injuries. African American children have been found to sustain spinal cord injuries at a higher rate than other ethnic and racial groups (Vitale et al., 2006). Due to advances in medical technology, an increasing number of children are surviving such devastating injuries. Spinal cord injuries typically affect neurological input and output, and are associated with loss of sensation and motoric

functioning (National Institute of Neurological Disorders and Stroke, 2003). Various medical complications frequently ensue, including pressure ulcers, deep vein thrombosis, and pulmonary embolisms; each of these can result in morbidity and mortality following the injury, particularly if the spinal cord injury is not appropriately managed. Other complications include loss of ambulation if the injury is high enough, as well as loss of diaphragm control (which requires mechanical ventilation).

Few studies have actually examined the short- and long-term psychological sequelae of pediatric spinal cord injuries, and the scanty research available suggests a multitude of psychological symptoms (e.g., depression, anxiety) and posttraumatic stress disorder (PTSD) (Boyer, Knolls, Kafkalas, Tollen, & Swartz, 2000). Younger age at onset of injury, higher educational attainment, greater financial resources, higher-functioning families, fewer medical complications, and greater participation in everyday activities have been demonstrated to be most predictive of more positive medical and psychosocial outcomes. Parental and child psychological adjustment and adaptation to the injury are closely linked, and caregivers frequently experience depressive symptoms and PTSD themselves (Boyer et al., 2000; Dreer, Elliot, Shewchuk, Berry, & Rivara, 2007). For this reason, facilitating parental and family functioning and adaptation to the injury is important in enhancing child adaptation to the injury.

Assessment and Management

Through their careful review of the neurodevelopmental and pediatric rehabilitation literatures, Deidrick and colleagues (2009) have concluded that assessment and treatment of developmental disorders and CNS disorders should be based on principles from the extant literatures in these two areas of research—including (1) focusing on child and familial strengths for the purpose of enhancing functional outcomes; (2) focusing interventions within a child's environment and daily activities; (3) employing a team approach for the purpose of addressing a child's diverse needs; (4) recognizing the interaction of children's development with the disease or injury; and, finally, (5) addressing the association between cognition and psychological functioning by means of remedial, compensatory, and supportive strategies (Farmer, Kanne, Grissom, & Kemp, 2010).

In the spirit of the evidence-based literature, a model for family-based consultation with children and their families with neurodevelopmental disorders has been recommended by Deidrick and colleagues (2009). This model is based on the work of Kazak, Simms, and Rourke (2002), who have worked extensively with families of children with chronic illness. The model emphasizes family competence and reframes behaviors that may be problematic for the medical team by assisting the family and the child to cope with stressors. The family is assisted in employing coping skills for the purpose of reducing distress, enhancing positive relationships between the family and the consultation team, and finally managing the specific concerns that may have resulted in the initial consultation. A core component of the model is the identification of family strengths, which the family and the medical team may subsequently use in assuring positive adaptation to the child's disorder.

Typically children with CNS disorders receive comprehensive services from physical therapists, occupational therapists, and speech and language therapists. The use of cognitive rehabilitation and assisting children and adolescents to employ compensatory strategies has received some support in the extant literature (Butler et al., 2008). Of course, a detailed assessment must be conducted for the purpose of identifying both strengths and weaknesses across a number of cognitive and psychosocial domains (for a review, see Deidrick et al., 2009). In addition, various family support interventions have been described in the clinical literature, including coordinating care, psychoeducation, family therapy, and informal emotional support. Finally, an area of concern for children and their families with CNS disorders is their transition to young adulthood, to which there has been scant attention in the research literature. This is clearly an area ripe for future investigation in enhancing the quality of life for these individuals and their families.

ADAPTIVE SELF-CARE DISORDERS

We now turn our review to adaptive self-care disorders. These include feeding and vomiting problems, obesity, eating disorders, elimination disorders, and sleep disorders.

Feeding and Vomiting Problems

Feeding problems typically include the failure to master feeding skills consistent with a child's level of de-

velopment, which can lead to suboptimal growth, food refusal, disruptive mealtime behaviors, and finally food refusal (Lyons-Ruth, Zeanah, Benoit, Madigan, & Mills-Koonce, Chapter 15, this volume; Silverman & Tarbell, 2009). Generally, feeding problems are identified during the first 3 years of life when the child fails to progress from one feeding stage to the next. While younger children typically have greater rates of feeding problems than do their older counterparts, the occurrence of feeding problems typically ranges from one-fourth to nearly one-half of the general pediatric population. The etiology of feeding problems may typically be multifaceted and may include developmental disabilities, sensory processing problems associated with neurological anomalies, and social/environmental factors (Silverman & Tarbell, 2009). Assessment of feeding disorders often consists of a review of medical records, questionnaires completed by caregivers, a clinical interview, and a direct observation of child–caregiver interactions during mealtime.

Behavioral treatments of feeding disorders in children have been empirically supported and well established in the evidence-based literature. Those behavioral treatments that have received empirical support include the implementation of a feeding schedule, appetite manipulation, and parent training. The creation of a predictable feeding environment is critical (e.g., a specific dining area), as are the use of specific and appropriate seating for the child (e.g., a highchair) and the removal of distractions (e.g., television) from the environment. Research has suggested that mealtimes that are too short (Mathisen, Skuse, Wolke, & Reilly, 1989) or too long (Linscheid, Budd, & Rasnake, 1995) are frequently associated with a greater frequency and severity of feeding problems. Thus creating a predictable feeding schedule and motivating children to reach specific feeding goals will also teach them to be responsive to consequences of hunger following a low-volume or "failed" meal. More importantly, these approaches teach children to be responsive to internal cues of hunger and satiation. Other strategies to increase feeding behaviors include the use of positive and negative reinforcement, as well as discrimination training (Linscheid, 2006). Caregiver training is frequently most successful in the home environment with the use of either *in vivo* or remote coaching (Silverman & Tarbell, 2009).

Functional vomiting disorders are characterized by chronic gastrointestinal symptoms for which no medical etiology has been identified (Rasquin et al., 2006). The etiology of these disorders is largely unknown, although several physiological theories have been posited, including perturbation of the hypothalamic–pituitary–adrenocortical axis, abnormal sympathetic function and postural hypotension, and mitochondrial disorders (inherited conditions that affect cellular energy production). No randomized clinical trials for the pharmacological management of functional vomiting disorders can be located, although some clinical reports in the literature have suggested that tricyclic antidepressants, beta blockers, oral contraceptives, and antiseizure medications have been used with some success to prevent attacks (Pareek, Fleisher, & Abell, 2007). Psychosocial factors including family and school difficulties have been demonstrated to be comorbid with functional vomiting; specifically, children have been found to miss over 1 month of school due to functional vomiting (Li & Misiewicz, 2003). Finally, functional vomiting also has been associated with a higher frequency of internalizing psychiatric disorders (Forbes, Withers, Silburn, & McKelvey, 1999). With regard to empirically validated behavioral treatments of functional vomiting, the literature is scant. In the absence of such research, it has been recommended that the types of nonsomatic therapies (e.g., hypnotherapy, biofeedback, guided imagery, cognitive-behavioral therapy) employed for other gastrointestinal complaints (e.g., irritable bowel syndrome, RAP), coupled with empirically supported treatments for the management of comorbid depression and anxiety, should be the treatments of choice for these disorders (Silverman & Tarbell, 2009).

Obesity

Childhood "overweight" is defined as having a body mass index (BMI) at or above the 85th percentile, while childhood "obesity" is defined as having a BMI at or above the 95th percentile for children of the same age and sex (Barlow, 2007). In this section, however, we frequently refer to overweight and obesity together as "obesity," unless a distinction between the two is necessary. Despite an increased focus on the problem of childhood obesity in recent years, rates of pediatric obesity have not declined significantly in the past decade (Ogden, Carroll, Kit, & Flegal, 2012). In 2009–2010, one-third of children and adolescents were overweight or obese, with minority adolescents at highest risk. During these years, over one-fifth (21.2%) of Hispanic children and adolescents and nearly one-fourth (24.3%) of non-Hispanic black children and adolescents were

obese, compared with 14.0% of non-Hispanic white children and adolescents. Obese children are more likely to have high blood pressure and high cholesterol, which are primary risk factors for cardiovascular disease (Nadeau, Maahs, Daniels, & Eckel, 2011). Moreover, these children are at increased risk for breathing problems, including apnea and asthma (Fiorino & Brooks, 2009), and they are more likely to suffer from musculoskeletal problems (Chan & Chen, 2009). Obesity is associated with impaired glucose tolerance, and rates of adolescent prediabetes/diabetes have increased from 9% in 1998 to 23% in 2008. The economic burden of so many children and adolescents' being overweight or obese is high. The CDC (2008b) has reported that in one 2-year period, taxpayers in the United States spent $127 million on hospital costs associated with caring for overweight/obese children and adolescents. In addition, elevated BMI in childhood is associated with an estimated $14.1 billion in additional prescription drug, emergency room, and outpatient visit costs annually (Trasande & Chatterjee, 2009).

Psychological Factors and Obesity

Obesity is the result of a positive energy balance caused by an interaction among physiology, eating behavior, and physical activity. There are many risk factors that influence eating behavior and physical activity; within a social-ecological model, these range from individual factors such as child mental health status (e.g., depression) to contextual factors such as family food environments and cultural norms about eating (Davison & Birch, 2001). Individual child risk factors include weight-specific factors, such as eating behavior, as well as non-weight-specific factors such as self-efficacy (Kohl & Hobbs, 1998). Clinical samples of youth with obesity demonstrate high rates of eating disorders, particularly binge eating (Britz et al., 2000; Isnard et al., 2003; Tanofsky-Kraff et al., 2004). More recently, researchers have applied an addictional model to the development of obesity (Gearhardt, Corbin, & Brownell, 2009) and describe high levels of food addiction in obese youth (Merlo, Klingman, Malasanos, & Silverstein, 2009; Pretlow, 2011). General psychopathology and behavior problems have long been associated with obesity in cross-sectional studies (Banis et al., 1988; Israel & Shapiro, 1985; Morgan et al., 2002; Pearce, Boergers, & Prinstein, 2002; Stradmeijer, Bosch, Koops, & Seidell, 2000). More recently, longitudinal studies have confirmed that childhood behavioral problems are predictive of obesity later in childhood (Anderson, He, Schoppe-Sullivan, & Must, 2010) and in young adulthood (Mamun et al., 2009).

In regard to family factors, the best predictor of obesity among youth has consistently been shown to be parental obesity (Brogan et al., 2012; Davison & Birch, 2002; Martin, 2008). Although this may obviously reflect heritable tendencies toward weight gain, potential environmental family influences on youth obesity include parents' dietary intake, food preferences, feeding practices, activity level, and nutritional knowledge. It has been suggested that obese parents create an "obesigenic" environment, in which calorie-dense foods are easily accessible, large portion sizes are normative, and low levels of physical activity/high levels of sedentary activity are likely (Davison, Francis, & Birch, 2005). Structural equation models of sibling data from the National Longitudinal Study of Adolescent Health demonstrated that family lifestyle variables, particularly meal frequency and inactivity, were as predictive of obesity as having an obese parent (Martin, 2008). Research on the association between family interactions (e.g., family conflict) and having an adolescent with obesity has yielded conflicting results, most likely due to differences in the methodologies employed (questionnaire, observational, case–control) and differences in the definitions of family functioning across the various studies. However, studies of parenting practices related to food may be more informative. One observational study of overweight adolescents showed that they ate bigger bites and accelerated their rate of eating toward the end of a meal when their mothers were present (Laessle, Uhl, & Lindel, 2001). Another observational study of mealtime interactions demonstrated that parents of obese youth were more likely to engage in permissive food-related behaviors (e.g., allowing second helpings) than parents of youth who were of normal weight (Moens, Braet, & Soetens, 2007). Qualitative research on parents of obese, low-income, minority youth also suggests that families have considerable variability in daily meal patterns, resulting in unstructured eating (Seibold, Knafl, & Grey, 2003). In a controlled comparison of obese and nonobese African American youth, nonobese youth had caregivers who exhibited lower levels of distress and who engaged in more monitoring and supervision of exercise (Brogan et al., 2012).

There is more limited research on peer, school, and community/cultural influences on pediatric obesity. However, available studies suggest that children's dietary intake and physical activity are associated with

those of their peers (Leatherdale & Wong, 2008; Salvy, Romero, Paluch, & Epstein, 2007). Overweight and obese minority youth report lower levels of peer support than their nonobese peers do (Brogan et al., 2012). School-related influences on obesity include availability of vending machines and opportunities for physical activity. School norms and rules regarding food also are important. For example, Kubik, Lytle, and Story (2005) found that school food practices such as acceptability of snacking throughout the day were predictive of student BMI. Cultural and community factors include cultural norms for food preferences and ideal body image; the availability of healthy foods; and limited opportunities for exercise, for reasons that include neighborhood safety concerns (Caprio et al., 2008). Obese youth are more likely to reside in high-poverty neighborhoods, with high numbers of fast-food restaurants and limited access to healthy foods in grocery stores (Contento, Basch, & Zybert, 2003; Kipke et al., 2007). However, even these factors may be modifiable, as parents of African American adolescents who were not overweight were more likely to report shopping in full-service grocery stores (vs. convenience stores), compared to parents of overweight youth from similar neighborhoods (Brogan et al., 2012).

Management of Obesity

Following an extensive review of the literature, the American Academy of Pediatrics published guidelines for a stepped approach to treatment of pediatric overweight and obesity (Barlow, 2007). The first step is to modify lifestyle behaviors in various ways: consuming more fruits and vegetables, minimizing sugar-sweetened beverage consumptions, decreasing screen time to 2 hours or less per day, engaging in physical activity for at least 1 hour per day, making meals at home, eating at the table at least five times per week, eating a healthy breakfast every day, involving the whole family in healthy lifestyle behaviors, and allowing the child to self-regulate and avoid overly restrictive feeding behaviors. If after 3–6 months there is no improvement in BMI, the next step is a structured weight management program: a daily eating plan, structured daily meals/planned snacks, reduction of screen time to 1 hour per day, monitoring food and exercise behaviors through the use of logs, and planned reinforcement for achieving targeted behaviors. Recommendations also include the utilization of a dietician and staff trained to provide parenting skills; motivational interviewing, a method of communication designed to increase intrinsic motivation for change, also has been recommended (Miller & Rollnick, 2013). The next level of intervention is to increase the frequency of physician visits to at least weekly, followed by the consideration of use of medication and/or surgery for adolescents with severe obesity.

The most recent Cochrane review of pediatric obesity treatment studies included 64 randomized clinical trials (Oude Luttikhuis et al., 2009). Interventions were categorized as behavioral interventions, dietary-only interventions, physical-activity-only interventions, and drug interventions with or without a lifestyle component. None of the surgical intervention studies met criteria for inclusion. Meta-analyses indicated a reduction in overweight at 6- and 12-month follow-ups in lifestyle interventions (behavioral, dietary, or activity), as well as lifestyle interventions combined with pharmacotherapy (orlistat or sibutramine) for adolescents. Adverse effects were noted in drug trials. There remains a paucity of evidence on interventions to treat minority youth who are most at risk. It was also noted that there are limited good-quality data to support endorsing one intervention over another, but that family-based interventions combining dietary, physical activity, and behavioral approaches appear to be effective. Similarly, a review of cost-effectiveness of obesity interventions concludes that though the limited evidence available suggests that obesity treatment and prevention interventions may be successful in combining health improvements and cost savings, the evidence to date is insufficient to permit a comparison of programs (John, Wenig, & Wolfenstetter, 2010).

Eating Disorders

Eating disorders typically begin at adolescence, although they have frequently been identified in children as young as elementary school age (Commission on Adolescent Eating Disorders, 2005). There is a full chapter related to eating disorders in this volume (von Ranson & Wallace, Chapter 17), and hence the topic is not included in this chapter.

Elimination Disorders

Enuresis

Enuresis is defined as repeatedly voiding urine into clothing or bedding by children with a chronological or developmental age of at least 5 years; the behavior

must occur at a rate of twice per week for a period of at least 3 consecutive months (APA, 2013). Enuresis must result in clinically important distress or impairment in educational, social, or other important areas of functioning, and it cannot be due to a substance (diuretic, antipsychotic medication) or a general medical condition (e.g., T1DM, spina bifida) (APA, 2013). DSM-5 delineates three subtypes of enuresis: nocturnal only, diurnal only (urinary incontinence), and nocturnal and diurnal (nonmonosymptomatic enuresis). Overall estimates of enuresis are approximately 5–10% among 5-year-olds, 3–5% among 10-year-olds, and approximately 1% among those age 15 years or older (Butler, Golding, Northstone, & ALSPAC Study Team, 2005). Nocturnal enuresis occurs more than twice as often among boys as among girls, while diurnal enuresis is more common among females (APA, 2013; Butler et al., 2005). Prevalence rates decline progressively with age; as noted above, only approximately 1% of youth have enuresis by midadolescence.

In the majority of children, nocturnal enuresis results from a maturational delay in the ability to recognize a full bladder during sleep (Yeung et al., 2002). It also has been suggested that children with enuresis may produce an excessively large amount of urine due to insufficient production of the antidiuretic hormone vasopressin (Devitt et al., 1999). There is a strong genetic component to the disorder, since nearly 80% of children with enuresis have a first-degree relative with the disorder (for a review, see Von Gontard et al., 2001). There are few cases of enuresis that may be attributable to an organic etiology. Some children with nocturnal enuresis also experience daytime urination (approximately 5–10%). Urinary urgency typically has its etiology in muscle spasms of the bladder wall, as well as small bladder capacity (for a review, see Campbell, Cox, & Borowitz, 2009).

Although some clinical lore suggests that either nocturnal or diurnal enuresis has its etiology in psychological factors, there are no empirical data to support this. In fact, heritability has been demonstrated in family and twin studies, and risk for enuresis is 10.1 times higher in the presence of paternal urinary incontinence (APA, 2013). Nonetheless, emotional and behavioral problems may result from the disorder, due to the stigma of having wetting accidents. With regard to comorbidity of psychological problems among children with nocturnal and diurnal enuresis, the literature has been mixed. Some studies have suggested no increase in psychological problems (Friman, Jones, Smith, Daly, & Larzelere, 1997), while other studies have demonstrated higher rates of language, learning, internalizing, externalizing, and attention problems among children with enuresis (APA, 2013). There also is some evidence that children with daytime enuresis exhibit higher frequencies of parent-reported externalizing symptoms than children with only nocturnal enuresis (Joinson, Heron, Butler, von Gontard, & ALSPAC Study Team, 2006).

Enuresis typically has a high rate of spontaneous remission by late childhood, although early resolution of the enuresis is likely to mitigate the psychosocial impact of the problem on the child and the family. Organic causes of urinary incontinence should always be ruled out before any type of behavioral intervention is begun. The most effective intervention for the management of enuresis is a urine alarm (Mellon & McGrath, 2000). This is an alarm that is activated by moisture sensors and is placed either on the mattress or on night garments; it has proven more efficacious for enuresis than pharmacotherapy or other forms of therapy. Although the urine alarm is considered an empirically supported treatment, there have been few controlled clinical trials or large-scale treatment studies for the management of either nocturnal or diurnal enuresis.

The use of the medication desmopressin acetate, which is a synthetic analogue of the hormone vasopressin, has been demonstrated to be a useful and viable treatment for nocturnal enuresis (for a review, see Campbell et al., 2009). Children typically respond quickly to the medication, although the efficacy of the medication dissipates rapidly upon discontinuation (Glazener & Evans, 2002). There also is some evidence that the combination of desmopressin with the urine alarm may enhance the success rate of the urine alarm, particularly for those families at risk for dropping out of treatment prematurely (Mellon & McGrath, 2000). Finally, imipramine, a tricyclic antidepressant, has been employed in the management of enuresis; however, due to its adverse side effects (especially cardiotoxicity), it has been reserved only for those children who have failed to respond to standard treatment (Gepertz & Neveus, 2004).

Encopresis

Encopresis involves a child's repeatedly passing feces into inappropriate places (e.g., clothing, floor); the child must have reached a chronological and developmental age of at least 4 years (APA, 2013). The behavior must

occur at the rate of one event or more per month for at least 3 months and cannot be caused by a substance or a medical condition. Constipation and overflow incontinence also must be indicated as being present or absent. It has been estimated that over 80% of children with encopresis have a history of constipation, with the majority of these children developing constipation before the age of 3 years (for a review, see Campbell et al., 2009). The disorder rarely has a medical etiology, although medical intervention is necessary to alleviate chronic constipation. Although few epidemiological studies are available, estimates of the prevalence of encopresis range from 1 to 7.5% of the elementary school population (Loening-Bauke & Swidsinski, 1996). Males are four to six times more likely to develop encopresis than their female peers (Levine, 1975).

The pathophysiology of constipation frequently results from stool-withholding behavior due to painful defecation, toilet-related fears, aversion to unfamiliar bathrooms, or dietary changes (Benninga, Voskuijl, & Taminiau, 2004). Psychopathology is not believed to be a primary cause of encopresis, although frequently there are comorbid behavioral problems and developmental delays that may be sufficiently severe to impede treatment adherence (Joinson et al., 2006). There also has been some evidence that children with encopresis are more apt to exhibit attention problems, disruptive behaviors, anxiety, poorer academic success, and poorer social competencies (Cox, Morris, Borowitz, & Sutphen, 2002; Joinson et al., 2006). Clinical lore has suggested that encopresis may be an indicator of sexual abuse, but studies in this area have not included appropriate control groups, thereby making it difficult to determine the prevalence of sexual abuse in children with encopresis versus the general population (Mellon, Whiteside, & Friedrich, 2006).

With regard to the treatment of encopresis, combining medical treatment with behavioral approaches has long been the standard of care in managing encopresis (Brazzelli, Griffiths, Cody, & Tappin, 2011). As with enuresis, prior to initiating treatment for encopresis, children should be referred to their pediatricians to rule out any organic cause of constipation (such as Hirschsprung's disease or neurological disorders). Treatment typically begins with the use of high-dose orally administered laxatives or enemas. This is frequently followed by daily maintenance of laxatives to prevent recurrence of constipation and to strengthen the urge to defecate (Benninga et al., 2004). In addition, dietary recommendations include increasing dietary fiber with fruits, vegetables, whole grains, and fiber supplements, while also increasing fluid intake.

Finally, it is recommended that behavioral procedures be employed in combination with medical interventions for children with encopresis. These interventions typically have focused on appropriate and immediate response to rectal distension or the urge to defecate with trips to the toilet, resolution of toilet avoidance or fear, appropriate toilet sitting and defecation, having the child spend sufficient time on the toilet to promote complete evacuation, and finally the implementation of a toilet-sitting schedule 10–30 minutes following breakfast and dinner (Ritterband et al., 2003). Behavioral interventions in combination with laxatives have been demonstrated to be more efficacious than either treatment employed alone (Borowitz, Cox, Sutphen, & Kovatchev, 2002; Brazzelli et al., 2011). There has been some history of the use of biofeedback in the management of encopresis, although compelling empirical evidence suggests that biofeedback therapy does not provide any additional benefit beyond the combination of medical and behavioral therapy (Brazzelli et al., 2011).

Sleep Disorders

For children and adolescents, sleep typically changes over the course of development. Thus insufficient sleep will manifest itself differently among toddlers, preschoolers, and adolescents. For example, with insufficient sleep, toddlers may become overactive, while adolescents may become lethargic and moody (Meltzer & Mindell, 2009). A comprehensive sleep history should include information about bedtime (e.g., the amount of time it takes a child to fall asleep); the sleep environment (e.g., room conditions); timing, frequency, and durations of night wakings; sleep-disordered breathing (e.g., snoring); the presence of sleepwalking or night terrors; and, finally, information about the time the child awakens in the morning, whether it is difficult to wake the child, timing and duration of naps, and daytime sleepiness (Meltzer & Mindell, 2009). The clinical interview should always be supplemented with the use of sleep diaries, questionnaires, an actigraph (a watch-sized activity monitor worn on the wrist or ankle, for differentiating between sleep and wake periods), and polysomnography (for a review, see Meltzer & Mindell, 2009).

Pediatric sleep disorders may be classified as behavioral insomnia of childhood, insomnia, circadian rhythm disorder, partial-arousal parasomnias, obstruc-

tive sleep apnea, narcolepsy, restless legs syndrome, and sleep-related rhythmic movement disorder.

Behavioral Insomnia of Childhood

The most pervasive behavioral sleep disorder experienced by children is behavioral insomnia of childhood. Typically, families complain of bedtime problems and frequent night waking (American Academy of Sleep Medicine, 2005). Behavioral interventions have proven most efficacious for behavioral insomnia of childhood, and treatment approaches typically include standard extinction, graduated extinction, positive routines, and parent education (Mindell et al., 2006; Morgenthaler et al., 2006). Graduated extinction involving parental checks on the child has been demonstrated to be most efficacious and has gained the most parental acceptance, thereby making parents most adherent to this approach (Mindell, 2005).

Insomnia

Insomnia is an especially complex problem that involves initiating or maintaining sleep. Insomnia has its origins in maladaptive sleep behaviors and negative cognitions associated with sleep (Meltzer & Mindell, 2009). Frequently the disorder is a symptom of a psychiatric disorder (e.g., anxiety, depression) or a consequence of a medical disorder (e.g., pain, medication to treat a disorder). Cognitive-behavioral treatments have been demonstrated to be quite efficacious for the management of insomnia among adults (Edinger & Means, 2005); they also have shown some promise in children and adolescents, although controlled clinical trials are needed to demonstrate their efficacy among children (Meltzer & Mindell, 2009).

Circadian Rhythm Disorder

Circadian rhythm disorder is characterized by difficulty falling asleep before the early hours of the morning, in combination with difficulty waking for school and daytime sleepiness (American Association of Sleep Medicine, 2005). The disorder is typically encountered among adolescents, and management for the disorder frequently involves a gradual shift in the sleep schedule (Morgenthaler et al., 2007). The use of melatonin also has been recommended as an adjunct to behavioral approaches, although the safety and efficacy of melatonin in children and adolescents have not been established.

Partial-Arousal Parasomnias

Partial-arousal parasomnias represent a spectrum of arousal disorders and include confusion arousals, sleep terrors, and sleepwalking. These typically occur from the transition to slow-wave sleep to lighter sleep, during rapid-eye-movement sleep, or during brief arousals where children appear to be awake but are really asleep (Meltzer & Mindell, 2009). Parasomnias occur regularly among children, with the incidence being approximately 3%, and up to 40% of children sleepwalking on at least one occasion (Mindell & Owens, 2003). Triggers for parasomnias include insufficient sleep, sleep deprivation, and changes in sleep routines (e.g., changes in school schedules, vacations). The parasomnias also appear to have a strong genetic component, with first-degree relatives commonly having a history of this type of sleep disorder. Management of parasomnias includes increasing sleeping time; maintaining safety for the child; and instructing the family not to wake the child, as this can serve to prolong the event (for a review, see Meltzer & Mindell, 2009).

Obstructive Sleep Apnea

Obstructive sleep apnea has been estimated to occur in 1–3% of all children (Lumeng & Chervin, 2008). The most common etiology in young children involves enlarged tonsils and adenoids resulting in airway obstruction during sleep. Obstructive sleep apnea also can be due to a crowded airway associated with craniofacial anomalies, to intellectual disability, or to having a large tongue. Treatment for obstructive sleep apnea typically includes removal of enlarged tonsils and adenoids when these are present, or the use of positive airway pressure whereby the airway is forced to remain open during sleep. Adherence to positive airway pressure is problematic for at least one-third of children, however due to the inability to tolerate the discomfort (Uong, Epperson, Bathon, & Jeffe, 2007).

Narcolepsy

Narcolepsy is a disorder associated with excessive daytime sleepiness. Narcolepsy is typically diagnosed by means of polysomnography for the purpose of ruling out other sleep disorders (for a review, see Meltzer & Mindell, 2009). Management of narcolepsy includes the use of stimulant medication, the use of regular sleep–wake schedules, and daytime naps.

Restless Legs Syndrome

Restless legs syndrome is a disorder in which the child reports an uncomfortable sensation in the legs and the discomfort is relieved with movement of the legs. The sensation also becomes worse in the evening. The most common etiology of restless legs syndrome in children is low iron. Treatment typically includes iron supplements (Standards of Practice Committee of the American Association of Sleep Medicine, 2004).

Sleep-Related Rhythmic Movement Disorder

Sleep-related rhythmic movement disorder refers to repetitive movement such as head banging and body rocking that is present at the onset of sleep (American Association of Sleep Medicine, 2005). The disorder is common in young children, with approximately 3–15% of children believed to have significant head banging at sleep. Management of this disorder includes safety (e.g., installing guard rails on the crib or bed) and behavioral management (e.g., avoiding reinforcement of the behavior).

Medical and Psychiatric Disorders Associated with Sleep Disturbances

Sleep disturbances also occur among children and adolescents with various medical conditions, as well as many of those with psychiatric disorders (Palermo & Owens, 2008). Such medical disorders include chronic pain (e.g., migraine headaches, sickle cell disease), asthma, and traumatic brain injury; hospitalization may also be a factor (Meltzer, Davis, & Mindell, 2008). Sleep disturbances have likewise been associated with various psychiatric disorders in children, including ADHD (see Golan, Shahar, Ravid, & Pillar, 2004; Nigg & Barkley, Chapter 2, this volume), autism spectrum disorder (Wiggs & Stores, 2004), depression (Ivanenko, Crabtree, & Gozal, 2005; Liu et al., 2007), and anxiety disorders (Alfano, Ginsburg, & Kingery, 2007).

MEDICAL DISORDERS

We now review recent research related to various medical disorders commonly encountered in pediatric populations, including asthma, cystic fibrosis (CF), T1DM, sickle cell disease (SCD), pediatric cancers, HIV/AIDS, juvenile rheumatoid arthritis (JRA), and cardiovascular disease. In our review, we also highlight major issues associated with poor disease adaptation and psychological sequelae, as well as treatment approaches used to address obstacles to disease management.

Asthma

Asthma is the most common disease of childhood and the second most common cause of hospitalization in children, with an estimated 500,000 hospitalizations annually in the United States (National Center for Health Statistics, 2006). Asthma is a chronic inflammatory disease of the airways in the lungs (Castro, 1999). This inflammation causes the airways to become overreactive, producing increased mucus, mucosal swelling, and muscle contraction. Symptoms of asthma include coughing, wheezing, shortness of breath, chest tightness, and sputum production, although the specific pattern of symptoms is unique to the individual. Inflammation can be triggered by many different stimuli, and it is not uncommon for symptoms to be precipitated or be worsened by behavioral and environmental triggers (including the presence of exercise, emotion, viral infection, mold, animal dander, smoke, changes in weather, pollen, dust, and airborne chemicals).

Asthma can be classified as intermittent or persistent. Persistent asthma can be further characterized as mild, moderate, or severe (National Asthma Education and Prevention Program [NAEPP], 2007), based on frequency, severity, and persistence of symptoms. If moderate to severe asthma is not properly managed, severe complications may occur over time from remodeling of the airways, which leads to chronic lung disease. In addition, severe asthma attacks can be fatal. Poorly controlled asthma also leads to increased use of oral steroids for management; such medications are associated with numerous adverse side effects, including growth suppression, increased susceptibility to infection, and poor bone mineralization.

Significant health disparities are evident in the different rates of morbidity and mortality from pediatric asthma among children and adolescents of different ethnicities. For example, asthma is 26% more prevalent among black children than their white counterparts (CDC, 1996, 2000). Risk factors for asthma that disproportionately affect minority youth include exposure to environmental allergens, inadequate health care (poorer access to care, continuity of care, quality of care), and family stress (Crain et al., 1999; Grant, Alp,

& Weiss, 1999). In addition, ethnic minorities not only have higher rates of asthma, but also experience more emergency room visits, frequencies of hospitalizations, and fatalities from asthma than whites do (Evans, 1992; Gergen, Mullally, & Evans, 1988; Lozano, Connell, & Koepsell, 1995; Targonski, Persky, Orris, & Addington, 1994; Weiss, Gergen, & Crain, 1992). For example black adolescents are much more likely than white adolescents to suffer fatal asthma episodes (CDC, 1996; Fuemmeler, Moriarty, & Brown, 2009; McDaniel, Rolland, Freetham, & Miller, 2006). In one study, even after the researchers controlled for socioeconomic variables, children of color had worse asthma status than did their nonminority counterparts (Lieu et al., 2002).

The goals of asthma management are to prevent chronic symptoms, maintain near-normal pulmonary function, maintain normal activity levels, prevent recurrent exacerbations of asthma, and minimize the need for emergency department visits or hospitalizations (NAEPP, 2007). Asthma treatment regimens may require use of various types of medications, which are determined by severity of symptoms (Annett, 2004). Children with persistent asthma often require both medications that provide long-term control of their disease and pharmacotherapies that provide quick relief ("rescue") from symptoms when an attack occurs. Although medications relieve symptoms and control inflammation, children and families must also make environmental changes to avoid known allergens and respiratory irritants, in order to maintain overall health and lessen the possibility of attacks. Environmental control strategies include dusting frequently, using mattress covers, avoiding exposure to secondhand smoke, and keeping pets outside the home. Children with asthma may also need to use medical devices such as a peak flow meter to monitor airway clearance between medical visits.

Patient–Provider Interactions

Optimal communication between children/caregivers and health care providers is crucial to the adequate management of asthma because objective measures of lung functioning and airway obstruction do not always correspond well to occurrence of daily symptoms. In addition, because national guidelines for asthma management recommend that physicians tailor medication regimens to the severity of children's symptoms, communication with families and health care providers is critical (Diette & Rand, 2007). In addition, high relationship quality between adolescents with asthma and their physicians has been demonstrated to be associated with objective measures of medication adherence, as well as with the frequency of urgent office visits (Gavin, Wamboldt, Sorokin, Levy, & Wamboldt, 1999). Therefore, characterizing various aspects of patient–provider interactions among children with asthma and their health care providers has been an important research focus in recent years.

Clark and colleagues (2008) studied communication patterns between 452 parents of children with asthma and 48 different health care providers managing the children's asthma. Parents rated the frequency of a variety of physician communication behaviors at their most recent office visit, including aspects of communication style and communication content. Children's health outcomes were assessed over a 12-month period. Parents who reported that their children's physicians used an interactive conversational style, reviewed short-term goals of the prescribed asthma treatment, and provided specific criteria for decision making at home regarding the recommended treatment had children with fewer urgent office visits for asthma care. Moreover, parents who reported that their children's physicians tailored medical regimens to their children's daily routines and needs had fewer emergency department visits for asthma care. Physician communication that included the review of long-term treatment goals was also associated with lower rates of urgent office visits, emergency department visits, and inpatient hospitalizations among children.

Although a collaborative interactional style in which providers seek information and tailor medical regimens to the needs of children and their families appears to be related to improved health outcomes for children with asthma, several studies suggest that such an interactional style may not be used with sufficient frequency. Wissow and colleagues (1998) examined characteristics of patient–provider communication during emergency department care in a sample of 104 children with asthma. Only 43% of parents were moderately or very satisfied with the extent to which their doctors had asked their opinion about treatment, and only 40% were moderately or very satisfied with the extent to which they had been encouraged to talk about their worries or concerns about asthma care or treatment recommendations. Similar findings emerged from a study of children with asthma who were being seen for routine outpatient management (Sleath et al., 2011). Patient–provider interactions were coded from audio-

tapes of treatment sessions. The occurrence of communication behaviors recommended for the promotion of good asthma management in national standards of care was of particular interest. The investigators found that while providers discussed the frequency of use of prescribed asthma controller medications and the medications' availability in most visits, the purpose of the controller medications and their efficacy were only addressed during one-third to one-quarter of office visits. In addition, family adherence to the use of controller medications was assessed at fewer than 40% of the visits. Consistent with the lack of assessment of adherence with medications, the investigators found that providers almost never elicited information regarding the occurrence of side effects or family concerns about the use of controller medications. Additional studies in this area may help to clarify factors that influence whether or not providers gather information that is important to guiding illness management for children with asthma.

A written asthma action plan that documents a child's daily treatment, and describes how to handle worsening asthma symptoms, constitutes another important form of patient–provider communication. Using a Medicaid sample, Finkelstein, Lozano, Farber, Miroshnik, and Lieu (2002) demonstrated that children who had received written asthma action plans from their health care providers were more adherent with controller medications than those who had not participated in such planning. In an intervention trial, Agrawal, Singh, Mathew, and Malhi (2005) randomly assigned youth to receive a written asthma action plan versus oral directions for asthma care. Youth who received a written plan had significantly fewer missed days of school and fewer daily asthma symptoms. In a literature review, Gibson and Powell (2004) observed that the use of a written action plan that included two to four personalized action points based on a child's current asthma status was consistently predictive of improved asthma outcomes over those obtained with a more generic plan. In summary, optimization of both written and oral aspects of patient–provider communication can improve adherence to asthma care and health outcomes for children with asthma.

Cystic Fibrosis

CF is a common genetic disease within the white population in the United States, with the disease occurring in 1 in 2,500–3,500 white newborns (Cystic Fibrosis Foundation Patient Registry, 2009). It is an autosomal recessive disorder, which means that both parents must pass on the gene for CF in order for the child to develop the condition. In persons with CF, aberrations in the gene that codes for a membrane conductance regulator protein results in an abnormal ion transport, which causes difficulties in secretory cells through the body (Boucher et al., 2008). Cells produce thickened secretions that plug the lumen of organs throughout the body. Common signs and symptoms of CF include poor mucus clearance and respiratory infections, leading to sinus problems and progressive damage to the lungs; pancreatic insufficiency, leading to poor growth and in some cases diabetes; and gastrointestinal problems, such as poor nutrient absorption. A significant subset of children with CF also experience pain as a consequence of their chronic condition, including chest pain and headaches (Ernst, Johnson, & Stark, 2010). Lung disease is the primary cause of death for 85% of persons with CF (FitzSimmons, 1993). As compared to the past, individuals with CF now typically survive well into adulthood, with a mean predicted survival age of 37 years (Cystic Fibrosis Foundation Patient Registry, 2009). Nevertheless, given shortened lifespans in persons with CF, some adolescents with CF must cope with end-of-life issues.

Children with CF must follow a demanding medical regimen with multiple components. Typically, these include airway clearance procedures, such as use of medications and chest percussion therapy; treatment with oral antibiotics for lung infections; consumption of pancreatic enzymes at each meal and snack; and a high-calorie diet (125–150% of required dietary requirements) to address absorption problems. In addition, inpatient hospitalizations of 1–2 weeks for a course of intensive airway clearance and intravenous antibiotics are recommended when lung functioning declines below 15% of baseline (Hains et al., 2009). Thus children with CF often experience multiple hospitalizations as part of their disease management.

One important marker of psychological well-being in children with chronic health conditions is the capacity to make a successful transition to the adult health care system. However, as noted by McLaughlin and colleagues (2008), while the transition from pediatric to adult care settings is usually age-dependent, many older adolescents with CF may not have acquired those skills necessary for a successful transition, such as the ability to explain their health concerns to a doctor or independently schedule appointments. Tuchman, Slap, and Britto (2008) conducted a qualitative study of 22

adolescents making the transition to adult care. Interviews were conducted both before and after transitions. The researchers found that most adolescents held a neutral or negative view about transition prior to the transfer of care, but identified many benefits of adult care subsequent to transfer. They noted that the early development of a formal transition plan within the pediatric care setting, ongoing discussions regarding the benefits of transfer, and tailoring the timeline of transfer to meet the needs of each individual adolescent may increase the likelihood of successful transition to adult care.

Type 1 Diabetes Mellitus

T1DM affects approximately 120,000 children each year in the United States (Libman, Songer, & LaPorte, 1993), with the age of onset typically occurring during the late school age to early adolescent years (ages 7–11). T1DM is an autoimmune disease in which the islet cells of the pancreas that are responsible for producing insulin are destroyed. Insulin is a hormone that allows the body to metabolize blood glucose. The onset of diabetes is typically marked by increased thirst and urination. Many children are not diagnosed with T1DM until they develop diabetic ketoacidosis, a life-threatening condition that occurs in the absence of insulin and typically results in hospitalization.

Caring for T1DM requires the child and family to follow a complicated medical regimen. The four main components of the regimen are insulin administration, blood glucose testing, dietary management, and exercise. Regimens for the treatment of T1DM require the daily administration of insulin, either by multiple insulin injections or by an insulin infusion pump. Hypoglycemia, or low blood glucose, can result in shakiness, dizziness, moodiness, disorientation, loss of consciousness, and (in extreme cases) seizures. Hyperglycemia, or high blood glucose, may not produce any consistent set of immediate symptoms. Therefore, the primary impact of high blood glucose is through its long-term and chronic effects. Microvascular complications of high blood glucose include nephropathy, retinopathy, and neuropathy; macrovascular complications include heart attack and stroke. The goal of T1DM management is therefore to maintain blood glucose within as normal a range as possible. The success of management is measured by laboratory measures of metabolic control. The most commonly used metric is hemoglobin A1c, a measure of the child's average blood glucose levels during the previous 2–3 months.

An important landmark study in the treatment of T1DM was the Diabetes Control and Complications Trial (DCCT; DCCT Research Group, 1993, 1994). The DCCT was the first study to demonstrate that good control of blood glucose significantly decreased microvascular complications. In the trial, even a 10% improvement in metabolic control reduced relative risks of complications by approximately 40%. Long-term follow-up of the adolescent cohort also has supported reductions in long-term complications through reductions in levels of blood glucose (DCCT/Epidemiology of Diabetes Interventions and Complications Research Group, 2001). The DCCT also demonstrated the importance of diabetes management behaviors for optimizing health outcomes.

Adherence

A significant body of research has investigated factors that affect regimen adherence among children with T1DM. For these children, the adolescent developmental period is marked by worsening of both regimen adherence and metabolic control (Helgeson, Siminerio, Escobar, & Becker, 2009; Rausch et al., 2012; Urbach et al., 2005). The hormonal changes that occur at puberty can directly affect an adolescent's metabolic control by reducing the effectiveness of insulin (Amiel, Sherwin, Simson, Lauritano, & Tamborlane, 1986; Moran et al., 1999). However, adolescents are more likely to be nonadherent with almost every aspect of T1DM management (Burdick et al., 2004; Johnson, Perwien, & Silverstein, 2000; Thomas, Peterson, & Goldstein, 1997; Weissberg-Benchell et al., 1995), including the use of newer management technologies such as continuous blood glucose monitors (Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, 2008). One study found that one-fourth of an adolescent sample reported that they had missed insulin injections in the past 10 days (Weissberg-Benchell et al., 1995); importantly, parents significantly underestimated the amount of their children's mismanagement of diabetes care. A recent multicenter study of 241 adolescents with T1DM provided data indicating that almost one-third of the sample reported recent *intentional* over- and/or underdosing of insulin, while another 28% reported management problems that led to unintentionally incorrect insulin dosages (Schober et al., 2011).

Although adolescents are often assumed by parents and caregivers to have the capacity to be responsible

for their own T1DM care, the literature suggests that significant parental monitoring and oversight are still needed. However, an inverse relationship between parental involvement in diabetes care and child age has frequently been reported (Anderson, Ho, Brackett, Finkelstein, & Laffel, 1997; Ingerski, Anderson, Dolan, & Hood, 2010; Wiebe et al., 2005). For example, Palmer, Roze, Valentine, and Spinas (2004) found that pubertal status and chronological age were stronger predictors of maternal reports of their degree of involvement in diabetes care than were mothers' ratings of the youth's psychosocial maturity. These data suggest that the transfer of care to adolescents is more dependent on physical signs of maturity than on cognitive readiness to self-manage. Palmer and colleagues also demonstrated that parental stress related to having to supervise the youth was an important predictor of the decision to transfer care.

As noted, adolescence may be a particularly stressful developmental period for children with T1DM, due to the numerous transitions into new roles and the need for increased independence—including more independence with diabetes care. Stress may interfere directly with the completion of diabetes care tasks or may increase psychological symptoms (e.g., depression) that negatively affect adherence to diabetes care tasks (Helgeson, Escobar, Siminerio, & Becker, 2010). In fact, many cross-sectional and longitudinal studies demonstrate that stress affects both adherence and metabolic control in children with T1DM (Farrell, Hains, Davies, Smith, & Parton, 2004; Helgeson et al., 2010; Peyrot, McMurry, & Kruger, 1999). It also has been suggested that an individual's perceptions of and style of coping with stress may have more influence upon the stress–adherence relationship than the amount or severity of stress that is actually experienced. In support of this notion, the use of coping styles that include wishful thinking and avoidance (e.g., not thinking about stressful events, giving up) has been found to be associated with lower rates of adherence and/or poor metabolic control among children with T1DM (Delamater, Kurtz, Bubb, White, & Santiago, 1987; Graue, Hanestad, Wentzel-Larsen, Oddmund, & Edvin, 2004). In a recent investigation of 252 adolescents with T1DM, Tran, Johnson, Almeida-Chen, and Schwartz (2011) investigated the effects of "benefit finding," or the ability to identify positive outcomes in the face of stress and adversity, on affective stress and adherence. Results revealed that benefit finding was associated with better adherence. Benefit finding also was found to buffer the disruptive effects of negative affective reactions to stress on adherence.

A number of other child characteristics have been linked to poor diabetes adherence. Poorer behavioral and emotional adjustment has been shown repeatedly to predict poorer self-management (Cohen, Lumley, Naar-King, Partridge, & Cakan, 2004; Leonard, Jang, Savik, Plumbo, & Christensen, 2005). For example, a study by Kovacs, Goldston, Obrosky, and Lyngar (1992) found that 60% of youth with T1DM and severe adherence problems could be diagnosed with a formal psychiatric disorder. A longitudinal study by Northam and colleagues (2009) found that one-half of their sample characterized by persistent poor metabolic control over the course of 10 years met formal diagnostic criteria for a psychiatric disorder; this was true of only 25% of those with adequate control during the same period. Depression also has been associated with frequent inpatient admissions for diabetic ketoacidosis (Garrison, Katon, & Richardson, 2005; Liss et al., 1998; Stewart, Rao, Emslie, Klein, & White, 2005), which in the postdiagnostic period occurs primarily due to missed insulin doses (Musey et al., 1995; Smith, Firth, Bennett, Howard, & Chisholm, 1998).

Multiple studies suggest that children with T1DM who come from families with maladaptive interaction patterns, such as high levels of conflict, low levels of cohesion, and/ or poor communication skills, have poorer adherence and health outcomes (Hanson, DeGuire, Schinkel, Henggeler, & Burghen, 1992; Hauser et al., 1990; Jacobson et al., 1994; Wysocki, 1993). Diabetes-specific family and parenting variables, such as lower caregiver support for diabetes care (Liss et al., 1998) and higher levels of diabetes-specific conflict (Hilliard, Guilfoyle, Dolan, & Hood, 2011; Hood, Butler, Anderson, & Laffel, 2007, Ingerski et al., 2010), also have been found to be associated with poorer adherence and metabolic control. Higher levels of parental supervision and monitoring of diabetes care constitute an important protective factor for youth adherence (Ellis, Podolski, et al., 2007; Horton et al., 2009). In a recent investigation, Ellis and colleagues (2012) investigated a variety of methods that parents of adolescents with T1DM used to monitor completion of diabetes care, including being present during or directly observing diabetes care, asking the adolescent about diabetes care, gathering information from others regarding the adolescent's diabetes care, and hearing the adolescent's spontaneous disclosure of information regarding diabetes care. Of these methods, only two—parental pres-

ence/direct observation and youth disclosure—were predictive of adolescent illness management and metabolic control. These data suggest that although asking youth about their care completion is clearly a way in which parents gather information about diabetes care, frequent checking with youth regarding diabetes care is not associated with either improved diabetes care completion or to better metabolic control. Parents who frequently ask about diabetes care completion may run the risk of being perceived by their children as controlling or nagging. Conversely, frequent asking about diabetes care completion may be a marker of lack of opportunities for directly observing this completion, such as in single-parent homes where job responsibilities may reduce parental presence at crucial points for care completion.

The existing literature on peer relationships and adherence to diabetes care suggests that children with T1DM often have difficulty maintaining good adherence behavior when they are with peers (Delamater, Smith, Lankester, & Santiago, 1988; La Greca & Hanna, 1983; Schlundt et al., 1994). One study (Thomas et al., 1997) proposed hypothetical situations to adolescents with T1DM in which they had to choose between peer impression management (e.g., eating food that was inconsistent with a meal plan in order to fit in with friends) and appropriate adherence. Results revealed that adolescents were more likely than younger children to choose regimen noncompliance in order to avoid perceived peer conflict or teasing. Therefore, contexts where adolescents interact with peers with minimal adult supervision, or with the supervision of adults who have limited knowledge of their regimen requirements, should be considered to convey increased risk for poor adherence. Other studies have similarly implicated children's expectations about peer reactions as an important factor affecting adherence with diabetes care. Hains, Berlin, Davis, Parton, and Alemzadeh (2006) investigated the relationship between cognitions regarding peers and adherence with diabetes care in a sample of 101 youth with T1DM. Results demonstrated that adolescents who expected friends to have negative reactions to their self-care completion were more likely to report difficulties with regimen adherence. Path modeling revealed that negative attributions regarding peers were also predictive of increased diabetes-related stress, which in turn predicted poorer metabolic control.

Many risk factors for poor adherence to the diabetes regimen also can be identified within the broader social ecology of children with T1DM. The interface between the family and the medical care system plays a crucial role in adherence behavior, as better adherence is associated with more positive relationships between adolescents/parents and medical care providers (Hanson et al., 1988). Examination of community context also shows that poor adherence with diabetes care is more common among children who come from disadvantaged groups, such as families of lower socioeconomic status, families using public insurance, single-parent-headed households, and members of minority groups (Harris, Greco, Wysocki, Elder-Danda, & White, 1999; Palta et al., 1997). Black children with T1DM in particular have been found to be at significantly greater risk for problems with treatment adherence and metabolic control (Auslander, Thompson, Dreitzer, White, & Santiago, 1997; Frey, Templin, Ellis, Gutai, & Podolski, 2007).

In summary, descriptive studies of adherence show that risk factors within the child, family, and community systems contribute to the development of adherence problems in children with T1DM. Therefore, interventions to improve adherence may need to address a variety of factors across multiple contexts in order to be successful.

Sickle Cell Disease

SCD is an inherited disorder of hemoglobin, the oxygen-carrying red blood cell protein (Lemanek & Ranalli, 2009). The disease is typically encountered among individuals of African descent, but also occurs among individuals of Mediterranean descent. SCD occurs in approximately 1 in 599 black American births (National Heart, Lung, and Blood Institute, 1996). What produces the disease is a genetic alteration or a mutation in the beta globin gene (Kral, Brown, & Hynd, 2001). Numerous morbidities are associated with the disease, including urinary tract infections among women, splenic infarction, and involvement with the vital organs (e.g., heart, lungs, kidneys). The pathophysiology of the disorder involves contortion of the blood cells into a sickle shape; these rigid and deformed blood cells are unable to pass through narrow blood vessels, thereby producing reduced blood flow to the tissues.

Clinical manifestations of SCD depend on the sickle cell genotype, the presence of comorbid diseases (e.g., asthma), and adherence to prescribed drug regimens, in addition to psychosocial factors (Lemanek & Ranalli, 2009). In many children and adolescents with SCD, pain, infectious complications, pulmonary/cardiac complications, and strokes/other CNS complications occur, as well as impairments in cognitive and academic functioning. Other complications may include skel-

etal complications (e.g., weakened bones), prolonged painful erections in males, and amenorrhea and infertility among females. Below, we review the literature on pain and pain management as well as cognitive and academic functioning, as these issues are particularly salient among children with SCD.

Chronic/Recurrent Pain and Its Management

One clinical hallmark feature of SCD is recurring episodes of pain or "vaso-occlusive crises." These crises typically vary in intensity, location, and quality. Children and adolescents with SCD report pain on the average of 7–39% of diary days, with an average duration of 2.5 days (Dampier, Ely, Brodecki, & O'Neil, 2002). Pain frequently occurs in the extremities, the hips, or the abdomen, and is often described as steady and uncomfortable. Pain may occur either spontaneously or as a function of environmental factors (e.g., exposure to cold or heat), physiological factors (e.g., dehydration, infection), or psychosocial stressors (e.g., peer conflicts). Although pain may frequently be managed at home, two-thirds of hospital admissions among children and adolescents with SCD are accounted for by vaso-occlusive crises. Medical management of SCD includes intravenous analgesia, fluids, rest, and mild exercise.

Both pharmacotherapy and behavioral interventions have been demonstrated to be effective in the management of SCD. It has been observed that practitioners' limited knowledge of SCD, inadequate pain assessment, and fears about the use of analgesia due to tolerance and potential physical dependence/addiction pose major obstacles to effective pain management among children with SCD (National Heart, Lung, and Blood Institute, 1996). Of interest is that oral analgesia has been rated as only somewhat effective by caregivers (Beyer & Simmons, 2004). Efforts aimed at preventing pain episodes or at stopping the pain from worsening (e.g., administering oral pain analgesia, applying heat or touch, and administration of fluids) also have been demonstrated to be efficacious. Unfortunately, there have been virtually no controlled clinical trials examining the efficacy of behavioral and social support interventions for the management of pain among youth with SCD. Cognitive-behavioral techniques that include calming self-statements and progressive muscle relaxation have been demonstrated as probably efficacious for the management of pain among children with SCD, but additional studies are necessary to provide further empirical evidence (Lemanek & Ranalli, 2009).

Cognitive and Academic Functioning

A considerable body of research indicates that youth with SCD are at risk for developmental delays, cognitive impairments, and problems with academic functioning (Kral et al., 2001). Deficits in numerous areas have been demonstrated across studies; these include general intelligence, visual–motor skills, sequential memory, language abilities, executive functions, and attention. Given such cognitive impairments, it should be no surprise that school functioning is also affected. In fact, Schatz, Brown, Pascual, Hsu, and DeBaum (2001) found that over one-third of their sample evidenced deficits in academic skills. With the improvements in medical management for SCD and the longer life expectancy of these children, research has focused on intervention efforts designed to enhance cognitive functioning and academic achievement. For example, in a recent controlled clinical trial by Daly and colleagues (2012), the use of methylphenidate (MPH), a stimulant medication widely used for the management of ADHD, showed some promise in ameliorating the attentional deficits and concomitant memory impairments among children with SCD. Such programmatic efforts to manage these cognitive impairments remain fertile areas for future research.

Pediatric Cancers

Cancer is the leading cause of death for children, although such monumental strides have been made in medical technology that 5-year survival rates are now over 80% (Vannatta, Salley, & Gerhardt, 2009). Progress in treating this group of diseases has resulted in very aggressive medical protocols that may include chemotherapy, radiation, and surgery, or a combination of all three therapies. Although many young adults are now survivors of childhood cancer, it has resulted in significant morbidity for many children and young adults. Recent investigation has devoted considerable attention to quality-of-life issues for these children and their families over both the short and long terms. There exist many different types of childhood cancer, including acute lymphoblastic leukemia (ALL), which is the most prevalent of these cancers but has one of the most favorable prognoses. Similarly, Hodgkin's disease also has an excellent survival rate, beyond 90% for most children and adolescents. In contrast, brain and bone tumors are characterized by lower survival rates and longer treatment periods (Vannatta et al., 2009).

Until approximately 15 years ago, much of the literature focused on medical procedures and the pain associ-

ated with such procedures, including bone marrow aspirations, lumbar punctures and finger pricks (Dahlquist & Swithin-Nagel, 2009). However, given the improved prognosis of the disease and seminal developments made in the area of pain management, recent research has focused on the physical and functional morbidities that emerge following the cessation of treatment (for a review, see Brown, Daly, & Beidas, 2010). Another line of research has emerged that has focused on those health challenges associated with survivorship.

Several physical morbidities associated with chemotherapy and radiation have been demonstrated, including growth impairment, hormonal/endocrine disorders, and cardiac toxicity that may not actually be evident until cessation of treatment or even during adulthood (Ness & Gurney, 2007). Thus management of these morbidities or "late effects" is by necessity multidisciplinary, and cancer survivors are often treated by many specialists as well as pediatric oncologists. Most importantly, ongoing surveillance is necessary for both the potential identification of long-term late effects and their subsequent management.

A major contribution to the pediatric oncology literature has been made by clinical psychologists and neuropsychologists in their identification of the consequences of CNS malignancies, as well as CNS-directed treatments that have been employed prophylactically as a means of preventing the proliferation of cancer cells further into the CNS (Mulhern & Butler, 2004). Much of the research in this area has demonstrated declines in important neurocognitive skills, including (but not limited to) working memory, processing speed, attention, and executive functioning; these declines often result in general lack of developmental progress and/or overall impairment in cognitive and academic functioning. For example, the literature pertaining to prophylactic CNS radiation for children with ALL has suggested significant intellectual and academic impairments; research on the subsequent use of chemotherapy as a CNS prophylaxis has generally suggested impairments in specific neurocognitive functions, including attention and processing speed (Brown et al., 2010). Subsequent research has attempted to identify those variables that predict toxicity associated with radiation and chemotherapy, including dose of therapy, age at treatment, gender, and demographic characteristics. In general, the literature has revealed that age at treatment, dose of chemotherapy or radiation, and gender have been the most robust predictors of neurocognitive sequelae associated with CNS treatment (for a review, see Brown et al., 2010).

Very recently, research has emerged linking cognitive and psychosocial impairments for children who have survived cancer. In general, the research has suggested some impact of cognitive factors on the psychosocial domain, although studies of the mechanisms accounting for the association between neurocognitive late effects and psychosocial outcomes have been especially limited (for a review, see Vannatta et al., 2009). One research group (Campbell et al., 2007) has suggested that neurocognitive late effects may actually exert their impact on behavioral functioning by altering coping strategies that are frequently dependent on higher-order cognitive processing. Should this hypothesized association gain further empirical support, it is likely to prove valuable in developing programs to assist these children and their families in coping with the ongoing stressors of the cancer experience. Finally, over the past three decades, Kazak and her associates (for a review, see Kazak, Schneider, & Kassam-Adams, 2009) have provided valuable data to document the impact of cancer treatments on family functioning. It will be important for future research to examine the long-term impact of cognitive and psychosocial late effects on family functioning, and to develop intervention programs designed to enhance family functioning among cancer survivors.

Childhood cancer survivors are potentially at higher risk for future malignancies than are their healthy peers, in addition to suffering from physical late effects coupled with potential cognitive and emotional late effects (Vannatta et al., 2009). This has resulted in a burgeoning of research to identify and intervene in maladaptive health behaviors that may be present or emerging among cancer survivors, particularly as they reach adolescence (Tercyak & Tyc, 2006). The result has been the development of efforts to address and mitigate smoking and other risk-taking behaviors during adolescence (Tyc et al., 2005). The promotion of healthier behaviors, including physical activity and healthy nutrition, is also an important goal in enhancing the quality of life for these cancer survivors.

Finally, paralleling the identification of physical, cognitive, and psychosocial late effects in the pediatric oncology literature, a literature has emerged pertaining to the management and treatment of these late effects. For example, Butler and colleagues (2008) conducted a multicenter randomized clinical trial of a cognitive remediation program for childhood survivors of pediatric malignancy, with some success. Two other recent multicenter clinical trials were conducted examining the efficacy of stimulant medication to manage problems in attention among pediatric cancer survivors (Conklin

et al., 2009, 2010). Important data have been provided to suggest improvements in sustained attention among these survivors. It is hoped that as cancer survivorship increases, intervention programs will focus with even greater intensity on enhancing the quality of life for these survivors and their families.

Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome

HIV is the virus that can lead to AIDS. HIV destroys CD4+ T cells, which are critical immune cells that fight disease. HIV is an infectious disease and is transmitted via blood, semen, vaginal secretions, and breast milk. The most common route of infection in children is perinatal transmission, the transmission of HIV from mother to child during pregnancy, labor and delivery, or breast feeding. Behaviorally infected adolescents and young adults acquire HIV through unprotected sexual acts and (less commonly) through needle sharing during drug use. HIV management includes the regular attendance of primary HIV care appointments and good adherence to antiretroviral therapy (ART)—medications used in combination to reduce the replication HIV, ideally until the virus is undetectable in blood tests.

Because of the effectiveness of ART, most perinatally HIV-infected youth in the United States are aging into adolescence and young adulthood (Hazra, Siberry, & Mofenson, 2010); and because of the effectiveness of ART during pregnancy to prevent transmission, the rate of new perinatal infections has dramatically declined. However, HIV rates are increasing among adolescents and young adults who are infected through risky behaviors. An estimated 8,294 young persons were diagnosed with HIV infection in 2009 in the 40 states that provide long-term reporting (CDC, 2011). African Americans are disproportionately affected and account for 65% of new diagnoses of HIV in this age group. Among young African American men who have sex with men, new HIV infections increased by 48% from 2006 through 2009.

The last few years have seen dramatic changes in the guidelines for starting treatment, in the simplification of regimens, and in the overall effectiveness of ART. Historically, HIV management required complicated regiments of multiple medications, administered at certain times of the day, often with instructions for whether to take medications with or without food. Currently, medication regimens have been substantially simplified with fixed-dose combination ART that can be taken once daily, though youth who are resistant to many medications may still be on complicated regimens. Whereas studies of older medications suggest that 95% adherence was required to achieve viral suppression, newer and more potent medications appear to be more forgiving (Raffa et al., 2008). However, adherence continues to pose a great challenge, particularly for adolescents and young adults. As the newest guidelines recommend beginning ART soon after diagnosis regardless of health status (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2012), young adults will be the largest group of ART initiators during a developmental period when nonadherence is common.

Several psychosocial issues are unique to HIV. First are the public health implications. HIV is most commonly transmitted through sexual contact—a particular concern for adolescents and young adults because of the peak of unprotected sex during this developmental period. Interventions to improve medication adherence are now considered a public health intervention, as well as interventions to improve individual health and wellness, as HIV transmission between persons is less likely when viral load is suppressed through better medication adherence (Cohen et al., 2011). Although health-related stigma is not unique to HIV/AIDS, the stigma in this case is compounded by the overlay of HIV's infectious disease status with other psychosocial issues, such as poverty, sexual practices, and substance use. HIV/AIDS stigma is associated with elevated depression in youth (Tanney, Naar-King, & MacDonnel, 2012) and has been shown to impede retention in care and ART adherence in adults (Mahajan et al., 2008).

Juvenile Rheumatoid Arthritis

JRA, also referred to as juvenile idiopathic arthritis, is the most common rheumatological disease of children (Gowdie & Tse, 2012). It accounts for approximately 70% of arthritic disease in children (Brown, Daly, & Beidas, 2010). In the United States, it is estimated that approximately 300,000 children ranging in age from infancy to 17 years are affected with JRA or other rheumatological conditions (Helmick et al., 2008). Although the etiology of JRA is unknown, it is thought to be caused by a combination of factors—such as environmental exposure to triggers (viruses, stress) under conditions of genetic susceptibility—that result in a pathological autoimmune response.

There are three main subtypes of JRA: oligarticular disease, polyarticular disease, and systemic disease

(Rapoff, 2006). Oligarticular disease occurs in 40–50% of children with JRA and is defined as involvement of four or fewer joints in the first 6 months of the disease. Large joints such as the knees, wrists, or ankles are most commonly involved. In this subtype, eye inflammation (uveitis) is also common. Polyarticular disease occurs in about 40% of children with JRA and is defined as involvement of five or more joints, including both small and large joints. This subtype is serious and progressive, with the potential to cause significant functional disability by adulthood (Gowdie & Tse, 2012). Finally, systemic disease affects approximately 10% of children with JRA. In systemic disease, a characteristic rash and/or cyclic fevers are present in addition to arthritis. Serositis, or inflammation of the lining of the heart, lungs, and abdominal organs, can also be present.

Common symptoms experienced by children with JRA include pain, persistent inflammation/contracture of joints, stiffness/decreased mobility, and slowed growth (Brown et al., 2010). Stiffness is worse after periods of immobility, such as in the morning upon wakening. Approximately one-fourth to one-third of children with JRA report pain intensities in the moderate to severe range (Schanberg, Lefebvre, Keefe, Kredich, & Gil, 1997). In addition, fatigue and poor appetite can occur secondary to pain and inflammation.

Management of JRA requires taking medications to reduce pain and inflammation and to maintain functioning in affected joints (Rapoff, McGrath, & Lindsley, 2003). The first-line treatment for most children with JRA is treatment with nonsteroidal anti-inflammatory drugs. For children with more severe disease or with poor treatment response, corticosteroids or disease-modifying antirheumatic drugs, such as methotrexate, may also be employed in treatment regimens. In addition, children with JRA are typically expected to participate in occupational and physical therapy, both to manage pain and to maintain joint mobility and overall strength. Mastery of nonpharmacological pain management strategies may help children with JRA to manage recurrent and/or chronic pain (Brown et al., 2010). Recent research also suggests that promoting sleep hygiene may be an important component of pain management for children with JRA. Children with JRA have been reported to have significantly more sleep disturbances than healthy children, and such sleep problems are related to pain ratings (Bloom et al., 2002; Passarelli et al., 2006). Although JRA-related pain could result in difficulties with sleeping, studies in fact have provided more support for the hypothesis that pain is worsened by inadequate sleep. For instance, Bromberg, Gil, and Schanberg (2012) used a daily diary method to track pain, sleep quality, and mood over 2 months in a sample ($N = 51$) of 8- to 16-year-old children with JRA. Poorer sleep quality was found to predict higher pain ratings the following day; however, daily pain ratings were unrelated to nightly sleep quality. Mood also was found to moderate the relationship between pain and sleep: As positive mood increased, the relationship between poorer sleep quality and higher pain weakened.

Cardiovascular Disease

Due to monumental strides in advanced surgical techniques, children with cardiovascular disease can now often lead relatively normal lives. Cardiovascular disease in children includes congenital heart disease, acquired heart disease, arrhythmias, and systemic hypertension. Congenital heart disease includes a number of disorders that involve structural defects to the heart itself or the coronary blood vessels, many of which occur during fetal development. The prevalence of congenital heart defects is between 5 and 8 in 1,000 live births, and many cases are actually diagnosed prenatally (Bernstein, 2004). For mild congenital heart defects, little or no intervention may be needed, whereas for moderate or severe congenital heart defects, surgery or heart transplantation may be necessary.

Due to the improved prognosis of children suffering from cardiovascular disease, researchers have been recently interested in the psychological and cognitive effects among such children, particularly those with congenital heart disease (Delamater & Jent, 2009). In recent years, several studies have examined the cognitive development and behavioral functioning of children with congenital heart defects; the findings have generally suggested that the types of defects, disease severity, preoperative factors, types of surgeries, postoperative factors, and family dynamics moderate the effects of these defects on children's cognitive and behavioral functioning. In general, research has demonstrated that infants with congenital heart defects who require cardiovascular surgery are at increased risk for problematic parent–infant interactions and adverse neurodevelopmental outcomes (for a review, see Delamater & Jent, 2009). These impairments include less responsiveness to parental cues, as well as more withdrawn and intense negative emotional reactions (Lobo, 1992). In addition, preexisting genetic anomalies (including Turner syndrome and Down syndrome) have been associated with greater impairments in neurodevelopmental outcomes.

Factors that occur prior to surgery, including acidosis, hypoxia, cerebral oxygen saturation, and seizure activity, also have been associated with adverse neurodevelopmental outcomes among children with congenital heart disease. Finally, some studies have examined the cognitive and behavioral sequelae of specific life support mechanisms (i.e., deep hypothermic circulatory arrest and cardiopulmonary bypass) during and following cardiac surgery among children with congenital heart disease. In a follow-up of a large randomized clinical trial, a higher prevalence of motor skill, expressive language, and neurological impairments was found among children who received deep hypothermic circulatory arrest versus those who received cardiopulmonary bypass (Bellinger et al., 1995; Bellinger, Rappaport, Wypij, Wernovsky, & Newburger, 1997). Cardiac arrest time during surgery has also been associated with neurodevelopmental impairment (Wray, 2006).

With regard to heart transplantation, there has been some research to suggest that cognitive and psychosocial problems may be present after transplantation. Although the degree to which cognitive status is affected by transplantation itself or by factors associated with the medical condition that necessitated the transplant is uncertain, some studies have found that children who received heart transplants demonstrated cognitive development within the normal range, but had an increased prevalence of developmental and motor delays (Freier et al., 2004; Wray & Radley-Smith, 2004a, 2004b). In one investigation employing magnetic resonance imaging among children who had undergone cardiac surgery, findings revealed the presence of new brain injuries following surgery (Miller et al., 2007). More importantly, developmental disabilities were predicted by postoperative brain injuries (Limperopoulos et al., 2002). Finally, children who have received heart transplants are (not surprisingly) likely to have greater problems at school, including difficulties with participating in sports and other recreational activities, with social functioning at school, and with peer relationships.

It is important to note that much of the aforementioned research is limited by methodological concerns, including small sample sizes, predominantly white middle-class samples, and heterogeneity with regard to cardiac defects (Delamater & Jent, 2009). Moreover, few of the studies have employed comparison control groups or have accounted for preoperative, operative, and postoperative factors. Clearly, more studies are needed in this very important area, particularly longitudinal investigations that evaluate these children over the course of time.

EMERGING AREAS OF RESEARCH

Psychopharmacology

As reviewed in this chapter, children with chronic medical conditions have significantly higher rates of emotional, behavioral, and cognitive problems. These may be results of either a chronic illness itself, an underlying disorder that manifests itself under the stress of the condition, or adjustment concerns. Not only is there limited research on the pharmacodynamics and pharmacokinetics of many psychotropic medications in children and adolescents; even less is known about the effects of medications on biological systems already affected by pediatric chronic conditions, or about the interactions of many psychotropic medications with those used to treat these conditions.

Although the research to date is limited, a few examples pave the way for future efforts.

1. *Cancer and SCD.* Two randomized clinical trials examined the efficacy of MPH, a stimulant medication widely used to manage attentional problems among children with ADHD, to ameliorate the neurocognitive late effects of cancer treatment in children (Mulhern et al., 2004; Thompson et al., 2001). Both investigations provided data to suggest improvements in sustained attention, and the one study comparing doses of MPH did not find greater improvements with a moderate dose compared to a low dose of MPH. As noted earlier in the chapter, Daly and colleagues (2012) pilot-tested the use of MPH to improve cognitive performance and attention in children with SCD who evidenced cerebrovascular complications. A double-blind controlled trial compared low-dose MPH, moderate-dose MPH, and placebo over a 3-week period. Unlike the cancer studies, results revealed improvements in attention for the moderate dose of MPH only, with no serious adverse side effects.

2. *HIV/AIDS.* It is estimated that 30–40% of persons with HIV suffer from depression, but psychopharmacology studies to date have focused on adults (Ferrando, 2009). The National Institutes of Health Adolescent Medicine Trials Network for HIV/AIDS Interventions (*www.nichd.nih.gov/research/supported/Pages/atn.aspx*) is completing the first feasibility study of combined cognitive-behavioral treatment and medical management of depression in youth with HIV. The results will have implications not only for the mental health of these youth, but also for the health of the public, as sexual risk behaviors associated with transmission are more

likely in the context of depression (Kahn et al., 2009). Clearly, more research is necessary to determine safe and effective psychopharmacotherapies for youth with chronic medical conditions, and studies of adherence to such medications in the context of chronic illness management will be critical to ensure treatment efficacy.

Psychoneuroimmunology

The field of psychoneuroimmunology (PNI) focuses on the bidirectional interactions between biological and psychosocial processes—particularly the pathways between psychosocial factors on the one hand, and the immune system and disease on the other. For example, the association between stress and health outcomes in pediatric illness has been clearly demonstrated (e.g., Helgeson et al., 2010; Howland et al., 2000; Turyk et al., 2008), though experimental research is lacking. Recent research has elucidated the biological mechanisms by which stress affects the immune system and disease susceptibility and progression in adults (Cohen, Irby, Boles, Jordan, & Skelton, 2012). Under conditions of prolonged stress, immune cells are desensitized to cortisol's regulatory effects, resulting in uncontrolled inflammation; this is believed to promote the development and progression of many pediatric diseases, including asthma, diabetes, obesity, and HIV (Cohen, Fouladi, & Katz, 2005). Thus studies are needed to elucidate the mechanisms by which stress affects pediatric acute and chronic medical conditions. Another critical area for research is PNI during pregnancy. Stress reactivity is increased during pregnancy, and the effects of inflammation on the fetus as well as on long-term child outcomes are largely unknown and constitute a fertile area for future investigation (Christian, 2012).

The only review of pediatric PNI intervention research (Nassau, Tien, & Fritz, 2008) identified few randomized clinical trials that tested psychological interventions to improve immune function. These included relaxation training, hypnosis, and cognitive-behavioral stress management. Although most investigations demonstrated effects on immune function, all were small-sample pilot trials, and most excluded youth with chronic medical conditions. This body of research is still in its infancy, and additional research is necessary to determine the effects of psychological interventions on immune function and health outcomes in youth with chronic medical conditions. Furthermore, pediatric PNI intervention research has yet to take advantage of advances in cognitive-behavioral treatments. New approaches that promote nonjudgmental acceptance of life events and awareness of internal responses to stress (i.e., mindfulness) have been shown to be effective for adults with chronic medical conditions (Chiesa & Serretti, 2010; Merkes, 2010).

Genomics

The traditional uses of population-based genetic testing were to identify rare inherited conditions at birth or to provide such information to adults ready to bear children. This process included physician oversight and interactions with a genetics counselor. Subsequently, scientific advances allowed for predictive genetic testing, allowing asymptomatic adults to assess their risk for developing certain diseases. In the decade since the mapping of the human genome (the full set of human chromosomes), it is possible to identify a wider range of disease risks. A number of private companies have begun marketing direct-to-consumer predictive genomic testing that provides information about a person's likelihood of developing a range of diseases (Lenzer & Brownlee, 2008), but without physician oversight or counseling opportunities.

These advances have significant implications for the well-being of parents and children. Although such information may encourage individuals to adopt preventive health behaviors, much of the information may not be easily interpretable and may cause unnecessary psychological distress. Parents have the additional burden of determining when and how to inform their children of this information. Although many of the arguments for and against predictive genomic testing in minors are testable hypotheses, there remain minimal data to support guidelines or policies (Mand, Gillam, Delatycki, & Duncan, 2012). Thus the field is wide open for studies of parent and child attitudes, psychological consequences, and the adoption of health behaviors in response to predictive genomic testing.

Another critical issue is the preparation of the health care system to manage genomic information, to make evidence-based clinical decisions, and to support families (McBride & Guttmacher, 2009). Again, research in this area is scant. One investigation (O'Neill et al., 2009), conducted with adolescent medicine providers, found that providers were unlikely to offer testing as a primary prevention approach. Rather, providers were more likely to offer testing to those with preexisting conditions (e.g., testing for the likelihood of nicotine addiction among patients with asthma, or testing for the potential of lung cancer in patients who were already smokers). These data suggest that providers will need

significant interventions to be ready to utilize genomic testing as a primary disease prevention strategy in childhood and adolescence as is expected in the near future (Tercyak, 2009).

Another implication of genomics is the opportunity to separate the effects of genetics and environment by mapping interactions between environmental exposures and genome-wide disease associations (Murcray, Lewinger, & Gauderman, 2009). In the next decade, the National

Children's Study will begin to examine the effects of environmental influences on the health and development of more than 100,000 children. The study is designed to differentiate genomic information from social, environmental, cultural, and economic influences. Collaboration among multiple disciplines will be necessary to translate these innovative scientific developments into novel interventions for the purpose of enhancing the health of children and preventing future disease. Indeed, the National Institutes of Health have issued a call to action for Translation 1 ("bench to bedside") research in behavioral science—that is, the translation of basic behavioral science discoveries into new ways to prevent and treat disease (Czajkowski, 2011).

Team Science

"Team science" is one of the three key initiatives of the National Institutes of Health Roadmap's Research Teams of the Future theme. As noted above, the convergence of perspectives from multiple disciplines is necessary to address challenging and complex problems in biomedical and behavioral research (e.g., obesity, diabetes, cardiovascular disease, cerebrovascular disease, HIV/AIDS). Team science is categorized by three levels of collaboration (Adler & Stewart, 2010): (1) "Multidisciplinarity" is attained when investigators from a range of disciplines work independently on a problem and then eventually combine their findings; (2) "interdisciplinarity" is accomplished when researchers from different disciplines work together and contribute their perspectives to work on a common problem; and (3) transdisciplinarity is achieved when the interdisciplinary team develops a new overarching model or framework that transcends individual disciplines. The "science of team science" (SciTS) studies the processes and outcomes of these approaches to research (Stokols, Hall, Taylor, & Moser, 2008). SciTS focuses on barriers and facilitators of collaborative research at multiple levels, from the individual to the organization, and hopes to test interventions to promote increased collaboration and ultimately transdisciplinary solutions to global health concerns (Falk-Krzesinski et al., 2010). The National Cancer Institute is leading the way with SciTS studies in three networks: (1) the Transdisciplinary Tobacco Use Research Centers initiative, (2) the Transdisciplinary Research on Energetics and Cancer initiative, and (3) the Centers for Population Health and Health Disparities initiative. Within these initiatives, researchers are developing new methods, measures, and analytical tools to study team science. As the networks target both adult and child populations, the next decade will see emerging research in how team science can improve child health and well-being.

e-Health Issues in Pediatric Health Psychology

Technology that provides the active ingredient in treatment, or "e-health," has increasingly become a focus of research in pediatric health psychology and a subject of recent reviews and meta-analyses. Stinson (2009) reviewed the evidence up to that time on Internet-based pediatric adherence interventions. Nine studies met eligibility criteria for the meta-analysis, and most suggested that interventions were effective in improving disease management and/or health outcomes. Subsequently, Cushing, Jensen, and Steele (2011) expanded the review to include non-Internet-based e-health interventions. A sufficient number of studies ($N = 33$) met eligibility criteria to allow for a meta-analytic review. Weight control was the most common focus ($n = 14$), followed by asthma ($n = 9$). Results demonstrated a small but significant omnibus effect. Although no differences emerged between interventions using different combinations of technology and face-to-face contact, e-health interventions that included a behavioral component such as self-monitoring or goal setting had larger effect sizes than interventions focusing on education alone.

These two reviews focused on health behavior change and did not include interventions for pediatric pain—an emerging area where technologies such as virtual reality distraction (Li , Montano, Chen, & Gold, 2011) and Internet-based cognitive-behavioral treatment have received some compelling support (Palermo, Wilson, Peters, Lewandowski, & Somhegyi, 2009). Furthermore, it is necessary to ensure diversity in study samples, as digital disparities remain. For example, low-income families and parents who did not complete high school are less likely to use the Internet, and minority families are more likely to use "smart phones" (Zickuhr & Smith, 2012). Thus e-health intervention research to

reduce health disparities also may need to consider mobile technology, as opposed to wired Internet-delivered interventions.

Positive Psychology

Positive psychology was introduced at the beginning of the new millennium as a science of positive human functioning and thriving communities, in contrast to the traditional focus on remediating damage (Seligman & Csikszentmihalyi, 2000). Kirschman, Johnson, Bender, and Roberts (2009) organize positive psychology research for children and adolescents around four major themes: hope, optimism, benefit finding, and quality of life. While studies of children with health conditions have long addressed quality-of-life issues (Payot & Barrington, 2011), other constructs have received less attention. Earlier studies in pediatric psychology linked hope to treatment adherence in asthma and organ transplantation (Berg, Rapoff, Snyder, & Belmont, 2007; Maikranz, Steele, Dreyer, Startman, & Bovaird, 2007), and to lower levels of behavioral problems in adolescent burn patients. However, more studies are needed to take advantage of advances in methods and measures in the field of positive psychology, and to target a broader range of pediatric health conditions. There is emerging evidence to suggest that hope interventions may be effective among high-risk urban youth (Kirschman, Roberts, Shadlow, & Pelley, 2010) and in college students (Berg, Snyder, & Hamilton, 2008), and may lead to a new paradigm for intervention development to improve pediatric health and well-being.

In positive psychology, optimism is an explanatory style, attributing positive events as due to internal causes ("I did it"), permanent ("It will last"), and persistent ("It will extend to other events"). Optimism can also be dispositional—a pattern of positive expectations for the future. In a meta-analysis of 83 studies of both healthy and chronically ill adult samples, optimism was significantly related to both subjective and objective health outcomes, though the relationship was stronger for subjective measures. Although there is a history of studies of attribution style within pediatric psychology, there is little research on optimism and health outcomes in children. However, a recent longitudinal study (Patton et al., 2011) demonstrated that adolescents' optimism predicted lower rates of depression, substance use, and antisocial behavior. Furthermore, the Penn Resiliency Program—a group intervention program using cognitive-behavioral therapy to promote a more optimistic explanatory style—resulted in significant improvements in adolescent optimism and reductions in depression symptoms across multiple trials (Brunwasser, Gillham, & Kim, 2009).

"Benefit finding," "sense making," and "posttraumatic growth" are terms used interchangeably to refer to the positive cognitions that people use to interpret a traumatic event and the positive outcomes that result (Kirschman et al., 2009). Studies of posttraumatic growth in pediatric illness have focused on describing responses to cancer; these studies have shown that most children show evidence of benefit finding, but have unexpectedly found that posttraumatic growth is also associated with symptoms of posttraumatic stress (Phipps, Long, Hudson, & Rai, 2005). These studies have been cross-sectional, so causality cannot be determined, as it is possible that children experiencing greater trauma during cancer treatment are those who also show the greatest growth. In a review of 25 studies of growth in response to different types of trauma in children (Meyerson, Grant, Carter, & Kilmer, 2011), most of the investigations reported significant relationships between posttraumatic growth and posttraumatic stress symptoms. Some studies have suggested a curvilinear relationship, such that moderate levels of posttraumatic stress symptoms are associated with posttraumatic growth (Levine, Laufer, Hamama-Raz, Stein, & Solomon, 2008). Clearly, further research is necessary to clarify the relationships, to understand post-traumatic grown in the context of other chronic conditions, and to develop interventions to increase benefit finding in the face of traumatic health events.

Summary of New Directions for Research

Over the past several years, there have been major research accomplishments in the field of child health and health-related disorders, as well as the delivery of health care. In part, this research has continued at a high pitch with the improved prognosis of many diseases frequently found among children and adolescents. Moreover, health services research and advances in the area of adherence have had the impact of making health care available for a greater number of children in this nation. There has been a trend in recent research toward examining genetic and physiological factors, as these variables have an impact on psychosocial variables. Conversely, there has been a trend toward examining psychosocial variables as they affect biological factors. Until recently, however, research in child health psychology has been primarily at the correlational level.

With the growing importance of evidence-based medicine, a greater emphasis has been placed on the use of controlled clinical trials for the purpose of validating correlational studies, as well as demonstrating the empirical efficacy of various psychological therapies.

Although research in the area of child health psychology has soared over the past 15 years, there are still enormous opportunities for future research efforts in the field. These include novel delivery approaches with regard to various therapies, including the use of e-health and computer delivery of various therapies. Technology holds the potential for more precise decision management regarding treatment, as well as for facilitating better adherence to the various treatments now available for childhood diseases. Research in the delivery of psychosocial aspects of health care has taken the direction of "team science." Given that most research on the psychological adaptation to chronic illness in children and adolescents involves dependent variables that are both physiological and psychological, collaborative efforts are essential. Typically, most research studies are conducted as team efforts in which physicians, nurses, and research psychologists work simultaneously, with members of each discipline contributing their field's expertise to a particular area of investigation. With the monumental advances in health care and the fact that children are surviving catastrophic diseases for which the prognosis in previous years was quite guarded, there is no doubt that there will be significant opportunities in working with children and adolescent health and developmental issues over the years to come. This underscores the importance of training clinical health professionals in pathophysiology and the use of dependent measures that are physiological in nature. This is an exciting time for behavioral scientists who are choosing to study disease in children and adolescents. We hope that this review has underscored the numerous research opportunities for behavioral scientists working in pediatric settings. More importantly, we anticipate that this research will enhance the quality of life for these children and adolescents and their families.

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