A Developmental Perspective on Attention-Deficit/Hyperactivity Disorder (ADHD)

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Attention-deficit/hyperactivity disorder (ADHD), among the most common psychiatric disorders of childhood, has been the subject of research for over a century (Barkley, 1997, 2006). The intense interest in ADHD has produced a huge corpus of empirical data on putative etiological factors, the complex genetic and neurobiological mechanisms that appear to underlie ADHD, profiles of behavioral and cognitive functioning that characterize the disorder, the developmental course of ADHD from early childhood to adulthood, and treatments that are effective for some children with a diagnosis of ADHD. At the same time, specific causal mechanisms remain elusive, and the general consensus is that there are multiple causal pathways to ADHD, with environmental factors primarily serving to exacerbate or ameliorate symptom expression in children who are at some degree of biological risk for the disorder (Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005; Sonuga-Barke, Auerbach, Campbell, Daley, & Thompson, 2005).

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In this chapter, we will first discuss diagnostic criteria for ADHD and its clinical presentation across the age range from early childhood to early adulthood. We will also examine the current diagnostic nomenclature as described in DSM-IV-TR (2000) and the proposed changes that are being considered for DSM-V (Coghill & Seth, 2011; http://www.dsm5.org). We will briefly review recent epidemiological studies of ADHD. Etiological considerations, with an emphasis on recent genetic and neurobiological findings, will be discussed, followed by an examination of other factors that may be important in understanding the etiological heterogeneity of ADHD. When the research on ADHD is considered from a developmental psychopathology perspective (Cummings, Davies, & Campbell, 2000; Sonuga-Barke & Halperin, 2010), the etiological heterogeneity, high level of comorbidity, and biological and psychosocial/family correlates of ADHD underscore the need to posit multiple developmental pathways to the disorder (Sonuga-Barke et al., 2005; Sonuga-Barke & Halperin, 2010). Furthermore, these initial pathways are likely to be mediated and moderated by a variety of within child and family contextual factors that are associated with either the diminution of symptoms over time or their exacerbation. These issues will be addressed, as will their implications for the treatment of ADHD (Sonuga-Barke & Halperin, 2010), especially in early childhood (Halperin, Bédard, & Curchack-Lichtin, 2012; Halperin & Healey, 2011). Throughout, directions for future research will be noted.

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Diagnostic Issues

Over the last 60 years, various terms have been used to describe the disorder that we now call ADHD, including hyperkinetic impulse disorder, minimal brain dysfunction, hyperactivity, attention deficit disorder, and most recently, ADHD (Barkley, 2006). These differences in terminology reflect different conceptions of the primary symptoms and putative underlying pathophysiology of the disorder, despite general agreement that the core features are inattention, impulsivity, and hyperactivity. The DSM-IV (American Psychiatric Association, 2000) includes three distinct subtypes of ADHD: the combined type requiring at least six symptoms of inattention (out of a possible nine) and six symptoms of hyperactivity-impulsivity (out of a possible nine); the inattentive type requiring at least six symptoms of inattention, but fewer than six symptoms of hyperactivity-impulsivity; and the hyperactive-impulsive type requiring at least six hyperactivity-impulsivity symptoms, but fewer than six symptoms of inattention (see Table 22.1). In addition, symptoms must be present for at least 6 months, be inappropriate for the child's age and developmental level, be evident by age 7, be of concern across settings (e.g., home and school), interfere with social and/or academic functioning, and not be due to another disorder such as autism. Research on ADHD over the last 20 years or so has primarily utilized these diagnostic criteria or focused on the symptoms listed in the DSM-IV, although some longitudinal studies that have followed children from the 1980s to adulthood (e.g., Barkley, Fischer, Smallish, & Fletcher, 2006; Mannuzza, Klein, Bessler, Malloy, & Hynes, 1997) began when earlier criteria were in use.

Debates about the diagnostic criteria, both for ADHD and for childhood disorders more generally (e.g., Coghill & Sonuga-Barke, 2012; Pickles & Angold, 2003), have emphasized the pros and cons of using a categorical in contrast to a dimensional approach, a topic that is beyond the scope of this chapter. In regard to ADHD, this debate has been intertwined with arguments about the validity and diagnostic utility of the subtypes.

Table 22.1 Symptoms of ADHD in the DSM-IV and proposed for the *DSM-V*

Inattention	Hyperactivity	Impulsivity
Fails to attend to details, careless	Often fidgets or squirms	Blurts out answers
Difficulty sustaining attention	Is often restless	Difficulty awaiting turn
Does not listen	Often runs about or climbs	Interrupts or intrudes on others
Does not follow instructions	Excessively loud or noisy	*Tends to act without thinking*
Difficulty organizing tasks	Often "on the go"	*Is often impatient*
Avoids tasks requiring mental effort	Talks excessively	*Is uncomfortable doing things slowly*
Often loses things		*Finds it difficult to resist temptations*
Easily distracted		
Often forgetful		

Note: Symptoms added to the DSM-V are in italics

For example, Milich, Balentine, and Lynam (2001) have contended that the inattentive type of ADHD should be considered a separate categorical disorder. In contrast, Lahey and Willcutt (2010) have argued for inclusion of a dimensional characterization of inattention and hyperactivity-impulsivity rather than nominal or categorical subtypes. This is because a longitudinal study showed that the subtypes are inherently unstable (Lahey, Pelham, Loney, Lee, & Willcutt, 2005). On reflection, it is hardly surprising that when children are followed from early to middle childhood, they shift from one subtype to another. These shifts across subtypes illustrate a number of problems with the diagnostic criteria including the arbitrariness of symptom thresholds that may lead to artifactual classifications (e.g., a child with six inattention and six hyperactivity-impulsivity symptoms will get a different subtype diagnosis than a child with six inattention and five hyperactivity-impulsivity symptoms), developmental changes in symptom expression as a function of both maturation and changing social and cognitive demands (e.g., Hart, Lahey, Loeber, Applegate, & Frick, 1995), and the likelihood that different symptoms will be emphasized

by different reporters as a function of situational demands and expectations (e.g., parents may be especially aware of impulsivity, but teachers may be more aware than parents of inattention).

It is noteworthy, however, that different patterns of deficits and comorbidities are associated with the combined in contrast to the inattentive type in some studies, with children with combined symptoms more likely to evidence comorbid oppositional and conduct problems (e.g., Beauchaine, Hinshaw, & Pang, 2010) and children with the inattentive type more likely to show comorbid anxiety and learning problems (e.g., Milich et al., 2001; Willcutt & Pennington, 2000). Furthermore, severity and subtype designation are somewhat confounded (Lahey & Willcutt, 2010). Although all children with an ADHD diagnosis looked worse than controls over an 8-year follow-up, children with the combined-type diagnosis at intake looked worse on a range of measures of academic and social functioning at follow-up than children with an initial diagnosis of either inattentive or hyperactive-impulsive type; indeed, whereas 82 % of children with a combined designation met criteria for ADHD (regardless of type) 8–9 years later, only about half (53.8 %) of those with either of the other subtype designations did. These results underscore the complexity of trying to describe the heterogeneity of ADHD across the inattention and hyperactivity-impulsivity dimensions, while adhering to a categorical diagnostic system and taking severity and variability in symptom expression over time into account.

Another problem with the DSM-IV is the generally vague and nonspecific description of symptoms. Although the DSM-IV states that symptoms must be "inappropriate for age and developmental level," there are no guidelines delineating what to expect of children of different ages from preschool age to adolescence when the clinical presentation and associated symptoms vary widely. More recent research on adult ADHD has added another level of complexity to the diagnostic picture, both in terms of symptom thresholds and clinical presentation (Barkley, Murphy, & Fischer, 2007; Faraone et al., 2006). Finally, as already noted, ADHD is almost always comorbid with another disorder, including oppositional defiant and conduct disorders, anxiety disorders, and learning difficulties (Angold, Costello, & Erklani, 1999; Willcutt & Pennington, 2000). These co-occurring problems complicate clinical management of the disorder, as well as research on clinical presentation, cognitive and social profiles, developmental course, and family correlates.

The revisions to the diagnostic criteria for ADHD, proposed in the DSM-V (see Coghill & Seth, 2011; http://www.dsm5.org) and currently being tested in field trials, may or may not solve some of these problems. Four new impulsivity symptoms are proposed (see Table 22.1), meant to better capture the poor self-regulation that is a hallmark of the disorder. In addition, the descriptions of some symptoms have been enhanced to clarify the clinical presentation in late adolescence and early adulthood. The age of onset criterion has been changed to require only that several symptoms were evident by age 12; in contrast, in the DSM-IV more impairing symptoms had to be evident by age 7. This change is likely to result in an increase in the prevalence of the inattentive presentation and allow for the diagnosis of more late-onset cases, but it is unlikely to enhance our understanding of the emergence, developmental course, or etiology of ADHD. In addition, the criteria for a diagnosis in late adolescence or early adulthood require only four symptoms of either inattention or hyperactivity-impulsivity, further widening the net of individuals likely to receive the diagnosis.

The biggest change proposed in the DSM-V involves the subtype designations. In an attempt to recognize the instability of ADHD subtypes, the fact that clinical presentation is likely to change with age, and the heterogeneity of symptoms across the dimensions of inattention and hyperactivity-impulsivity, subtypes will now be specified as "current presentation," based on the symptom picture in the last 6 months. This allows for developmental changes and tries to avoid reifying subtypes. Further, the inattentive presentation is divided into two: *predominately inattentive* allows for three to five symptoms of hyperactivity-impulsivity, whereas the *restrictive inattentive*

presentation allows for no more than two symptoms of hyperactivity-impulsivity. This may result in even more confusion about the inattentive type than currently exists, but the ongoing field trials, meant to test the appropriateness of these new criteria, may lead to further modifications. Although the proposed revisions include elaborations of the clinical presentation of ADHD in older adolescents and adults, they still do a poor job of describing symptoms in younger children or discussing potential early developmental markers, despite attempts to diagnose this disorder in younger and younger children (Egger & Angold, 2006; Zito et al., 2000). An emphasis on impairment and social context is especially important when assessing ADHD and related problems in young children (Campbell, 2002; Egger & Angold, 2006; Healey, Miller, Castelli, Marks, & Halperin, 2008). Perhaps further refinement will lead to a clearer distinction between emerging ADHD symptoms in preschool-age children and age-related and transient behaviors reflecting high energy, exuberance, and/or uneven development.

Developmental Course and Clinical Presentation

Despite variations in both the conceptualization of and diagnostic criteria for ADHD over the last several decades, the clinical picture remains essentially unchanged. Children with ADHD are most often referred for assessment between the of ages 5 and 8 when their high energy level, fidgetiness and difficulty sitting still, disorganization, lack of persistence on cognitive tasks, poor concentration, difficulty regulating behavior in social situations, and lack of social judgment lead to a myriad of social and academic problems. Difficulties are evident at home where children with ADHD often have problems following rules and routines; may create disturbances at mealtime, bedtime, or family outings; are in frequent conflict with siblings; and rarely complete homework without parental supervision. In the classroom, children with ADHD often stand out because of their lack of attention to ongoing lessons, failure to follow classroom rules and routines, activity level, inappropriate and disruptive behavior, and difficulty working either independently or collaboratively with classmates on group projects. In the peer group, children with ADHD are often avoided or actively rejected because of their insensitive or overbearing behavior; they may provoke fights, disrupt the activities of others, barge into a game and try to change the rules, or have difficulty taking turns and recognizing the needs of others.

Although ADHD is often not identified until children enter school, a developmental psychopathology perspective mandates a focus on the early emergence of ADHD. Most theoretical conceptualizations of early signs or precursors of ADHD (e.g., Campbell, 2002; Nigg, Goldsmith, & Sachek, 2004; Sonuga-Barke et al., 2005) focus partly on infant temperament, especially high levels of reactivity (approach, negative emotionality, activity level) and low levels of regulation (impulsivity, attentional control) (Nigg et al., 2004; Rothbart & Bates, 1998) as potential risk factors for later ADHD. Based on the consensus that temperamental characteristics are highly heritable, moderately stable within developmental periods, and form the building blocks for later personality (Nigg et al., 2004; Rothbart & Bates, 1998), it is likely that active, irritable, easily aroused, difficult to soothe infants will be more likely than their more quiet and manageable counterparts to develop ADHD (see Sonuga-Barke et al., 2005). In one prospective study of children at risk for ADHD because of elevated symptoms in their fathers, Auerbach et al. (2008) found that both mothers and fathers of high-risk infants reported higher levels of activity and negative affect and lower levels of attentional and inhibitory control than did parents of control infants. By 24 months, group differences in effortful control were also apparent. Early dysregulation of affect, attention, activity level, and impulse control may cascade into more serious problems, especially in the context of cognitive delays and/or harsh and inconsistent parenting (Campbell, 2002; Graziano, Calkins, & Keane, 2011; Sonuga-Barke et al., 2005). Given the heritability of these behaviors, it is also likely that

some children showing these problems early will be raised in families where at least one parent is also impulsive and dysregulated (Mokrova, O'Brien, Calkins, & Keane, 2010).

By toddlerhood and the preschool period, children with signs of emerging ADHD are likely to be extremely overactive, difficult to calm down, rambunctious, noncompliant, and prone to temper tantrums in the face of parental prohibitions (Campbell, 2002). Cognitive and language delays may also be evident, along with difficulties on measures of executive functioning and school readiness (Campbell & von Stauffenberg, 2009; DuPaul & Kern, 2011). Furthermore, these children are likely to have problems in the peer group, given their difficulties taking turns, sharing toys, following rules, and playing quietly. Moreover, their poor ability to regulate behavior in response to others may result in high levels of reactive aggression that in turn leads to peer rejection. For example, Campbell, Pierce, March, Ewing, and Szumowski (1994) studied preschool boys with elevated ratings of hyperactivity and impulsivity on observational measures of activity, regulation, and compliance in the laboratory and their preschool classrooms. Compared to control boys, boys at risk for ADHD were more active during free play and structured tasks, less focused on specific toys during play, less able to resist touching a tempting but forbidden toy, and less compliant with their mother during a toy cleanup. In their preschool classrooms, at-risk boys were observed to be more disruptive with peers and less compliant with teachers. More recent studies of preschoolers at risk for ADHD and associated behavior problems have likewise reported that poorer regulation of emotion and attention predicted chronic problems across ages 2–5 (Hill, Degnan, Calkins, & Keane, 2006), including specific links between observed effortful control and cross-informant ratings of inattention and impulsivity at age 3 (Olson, Sameroff, Kerr, Lopez, & Wellman, 2005). Other studies have indicated that preschoolers with ADHD show more difficulties on measures of executive functioning (Berwid et al., 2005; Sonuga-Barke, Dalen, Daley, & Remington, 2002). These difficulties even result in some children being asked to leave their child care or preschool setting. In one study, 16 % of preschoolers with a diagnosis of ADHD had been expelled from preschool or child care (Egger & Angold, 2006). Moreover, longitudinal studies indicate that ADHD identified in early childhood often persists through middle childhood and into adolescence (Lee, Lahey, Owens, & Hinshaw, 2008; Pierce, Ewing, & Campbell, 1999).

School entry brings its own set of challenges as children need to follow stricter rules for self-regulation of behavior, follow classroom routines, attend to lessons and assignments, and cooperate in a larger peer group setting (Campbell & von Stauffenberg, 2008). Teachers routinely note that children with ADHD do more poorly on academic tasks and have more peer problems (e.g., Lahey & Willcutt, 2010; Lee & Hinshaw, 2006). Laboratory assessments reveal more difficulties on a range of executive function tests including those assessing verbal and nonverbal working memory, response inhibition, vigilance, and planning (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005) in comparison to children without any diagnosis, but the degree to which these deficits are specific to ADHD remains in question (Frazier, Demaree, & Youngstrom, 2004; Halperin & Schulz, 2006). Furthermore, follow-up studies from school age to adolescence indicate that problems persist in most children with a diagnosis and especially in those with comorbid disorders (e.g., Barkley, Fischer, Edelbrock, & Smallish, 1990; Biederman et al., 1996). Children with ADHD are at heightened risk for adolescent psychopathology (Mannuzza et al., 1991; Miller et al., 2008), including higher rates of antisocial behavior (Barkley et al., 1990; Mannuzza et al., 1991), substance use disorders (Mannuzza et al., 1991; Molina & Pelham, 2003), personality disorders (Miller et al., 2008), and persistent ADHD symptoms (Mannuzza et al., 1991; Mick et al., 2011). They also have poorer academic and employment histories, more automobile accidents and driving impairments, and more difficulties with friendships and intimate relationships (Barkley, 2006; Barkley, Guevremont, Anastopoulos, DuPaul, & Shelton, 1993). These follow-up studies have focused almost exclusively on boys, but studies following

girls with ADHD through adolescence also indicate that problems in academic and social functioning persist, as do ADHD symptoms (Hinshaw, Owens, Sami, & Fargeon, 2006; Mick et al., 2011).

Studies of children with ADHD followed into adulthood also indicate high levels of persistent problems. For example, Barkley, Fischer, Smallish, and Fletcher (2004) followed a sample of children with and without ADHD into early adulthood (mean age 20–21); the ADHD group reported a range of negative outcomes including more arrests, thefts, assaults, and drug use. However, when the ADHD group was divided into those with and without co-occurring CD, only the comorbid group differed from controls; young adults with a history of both ADHD and CD not only were more likely to engage in substance use, but they used a greater variety of substances including alcohol, cocaine, and hallucinogens, and they used these more often than either control subjects or young adults with a history of ADHD alone. A growing body of research has shown that ADHD, but especially ADHD and CD, acts as a risk factor for drug use and smoking (Harty, Ivanov, Newcorn, & Halperin, 2011; Molina, Bukstein, & Lynch, 2002). In addition, data from Barkley et al. (2006) and others (Mannuzza et al., 1997; Weiss & Hechtman, 1993) indicate poorer academic and educational achievement, lower job satisfaction and employment stability, and less stable friendships and marital relationships in adults with a childhood history of ADHD. Although comorbid antisocial behavior accounts for some of these poor outcomes, academic and occupational difficulties are also associated with ADHD alone (Barkley et al., 2006).

Follow-up studies to adulthood indicate that although problems are not outgrown, the nature of symptoms may change, with gross motor activity less salient, but internal feelings of restlessness evident (Weiss & Hechtman, 1993). A recent increase in the number of college students with ADHD has also been reported (Weyant & DuPaul, 2006); they are more likely than comparison students to seek help with academic and social problems in college counseling centers; they also, not surprisingly, have lower grade point averages, are more likely to be on academic probation, and are more likely to drop out than students without ADHD. This is consistent with the long-term follow-up studies of Barkley et al. (2006) and Mannuzza et al. (1997) cited above, who likewise reported that their ADHD subjects had lower academic achievement and occupational success than controls, even with cognitive ability controlled.

Epidemiology

In studies assessing representative samples of preschool children, rates of ADHD range from 2 % to 5.7 % depending on whether impairment criteria must be met and clinical consensus is required (Egger & Angold, 2006). In general, rates are lower than in school-age children, presumably because expectations for self-control, activity, and inattention are lower. However, follow-up studies indicate (e.g., Lahey et al., 2005; Lee et al., 2008) that when rigorous diagnostic criteria are utilized to diagnose 4- and 5-year-olds with ADHD, problems are likely to persist to school entry and beyond. At the same time, Egger and Angold (2006) report that certain defining symptoms, especially those on the hyperactivity-impulsivity dimension, are very frequent in young children including difficulty sitting still, talking excessively, and often interrupting others. This highlights the importance of not overpathologizing typical behavior (Campbell, 2002), despite the importance of accurately identifying children and families in need of intervention (Egger & Angold, 2006; Halperin et al., 2012).

In school-age children and adolescents, the prevalence of ADHD varies widely based on whether impairment criteria are employed and whether data are obtained from both parents and teachers. The DSM-IV (American Psychiatric Association, 2000) estimates the prevalence of ADHD to range from 3 % to 7 % of school-age children. Using data from the 1,420 9- to 13-year-olds participating in the Great Smoky Mountain Study, Costello, Mustillo, Erklani, Keeler, and Angold (2003) estimated cumulative prevalence at 4.1 % by age 16, but with a marked sex difference

(1.1 % in girls and 7.0 % in boys). According to the Centers for Disease Control website (http://www.CDC.gov), parents report that approximately 9.5 % of children between the ages of 4 and 17 have ever been diagnosed with ADHD, with 13.2 % of boys and 5.6 % of girls receiving a diagnosis. The CDC also reports that the prevalence of ADHD increased systematically between 1997 and 2007, primarily reflected in higher rates of ADHD diagnoses among adolescents. This is presumably at least partly a reflection of the recent emphasis on identifying and treating ADHD in high school and college students (Weyant & DuPaul, 2006) as well as in adults more generally (Barkley et al., 2007).

Etiological Models

Etiological models focus on genetic and environmental influences, their correlations and interactions, and their effects on brain structure and function, which presumably mediate symptom expression. Yet research has not adequately integrated findings across these multiple levels of analysis or been informed by a developmental perspective (e.g., Coghill, Nigg, Rothenberger, Sonuga-Barke, & Tannock, 2005; Sonuga-Barke & Halperin, 2010). More research is needed to establish clear links between putative underlying genetic and neural processes and the behavioral manifestations of ADHD.

Genetic and Environmental Influences and Gene–Environment Interplay

Genetic factors shape ADHD developmental pathways, although ADHD is not a genetic disorder in any simple sense (Thapar, O'Donovan, & Owen, 2005). Genetic explanations of ADHD have been driven by data from family and twin studies showing that the condition is familial and highly heritable, with heritability estimates averaging around 76 % (Faraone et al., 2005). Attempts to identify the source of these genetic effects using a candidate gene approach to detect common genetic variants associated with ADHD have had limited success (Neale et al., 2010). A meta-analysis indicated small but significant effects for a number of putative functional variants in genes regulating brain neurochemistry especially in the dopamine system (e.g., D4 and the dopamine transporter (DAT1); Faraone et al., 2005). Common variants in genes in other neuromodulator systems (i.e., serotonin and norepinephrine; Oades et al., 2008) have also been implicated along with genes regulating more general brain function and growth (e.g., Brophy, Hawi, Kirley, Fitzgerald, & Gill, 2002). Despite these isolated findings, candidate gene associations account for little variation in ADHD expression (Faraone et al., 2005; Neale et al., 2010). Linkage studies have not found replicable disease susceptibility loci for ADHD. Hypothesis-free genome-wide association studies which tag a very large number of markers of common genetic variants in very large samples, while confirming the overall genetic contribution to ADHD, have failed to identify genome-wide significant effects for individual markers (Neale et al., 2010).

Several factors might account for the gap between the high heritability estimates and very small effects of common genetic variants. First, if genetic effects on ADHD are solely due to common genetic variants, a large number of markers of diminishingly small effect will be implicated (Faraone et al., 2005), and much larger samples will be required to detect genetic variants of smaller and smaller effects (Neale et al., 2010). Second, if one assumes genetic heterogeneity—with ADHD in different individuals determined by different genetic variants—then the goal is to create more uniform subgroups by identifying biologically meaningful networks of genetic variants (Poelmans, Pauls, Buitelaar, & Franke, 2011) or partitioning genetic heterogeneity on the basis of intermediate, potentially genetically more simple, pathophysiological or behavioral phenotypes. Third, genetic effects in ADHD may not result from common variants but rather from rare variants with larger effects (Gibson, 2012). Recent findings of an increased rate of de novo and inherited chromosomal deletions and/or duplications (so-called copy number variants—CNVs)

in ADHD (Lionel et al., 2011) have spurred interest, despite inconsistencies in the gene system affected and the lack of specificity to ADHD. Fourth, and most relevant from a developmental perspective, virtually all genetic studies are cross sectional, and many combine participants with wide age ranges, potentially obfuscating developmental variation in genetic effects and related behaviors. By combining children and adolescents in the same sample, developmentally sensitive relations between genes, brain, and behavior are likely to remain undetected.

Another reason why genetic main effects are difficult to isolate may be that gene–environment associations rather than genetic main effects drive high heritability estimates; these effects are not captured in genetic studies that do not take environmental factors into account. Such a view is at the heart of a developmental psychopathology framework and consistent with the argument that the study of genes cannot be isolated from the study of environments (Rutter, 2000, 2006). ADHD has been associated with increased levels of pre-, peri-, and postnatal environmental risk, although the effects are small and their causal status difficult to discern due to the observational nature of most studies (Taylor & Rogers, 2005). The dominant focus has been on *prenatal factors*. Both maternal smoking (Thapar et al., 2003) and alcohol consumption (Vaurio, Riley, & Mattson, 2008) during pregnancy have been suggested as environmental risk factors. Maternal use of drugs of abuse (Linares et al., 2006) and drugs prescribed for therapeutic reasons may also be implicated, although it is difficult to disentangle these effects from variations in maternal psychological disorder during pregnancy. Furthermore, maternal stress, perhaps via dysregulation of the HPA axis, may play a role (O'Connor, Heron, Golding, & Glover, 2003). Prematurity (Bhutta, Cleves, Casey, Craddock, & Anand, 2002) and pregnancy complications (Ben Amor et al., 2005) are also associated with ADHD, although these risks are not specific to ADHD and the direction of causality is often unclear (Taylor & Rogers, 2005).

In addition to these pre- and perinatal risk factors, parenting and family stress may be implicated in ADHD and also represent examples of gene–environment correlation or interaction. ADHD symptoms elicit negative, intrusive, and harsh responses from parents (Campbell, Pierce, Moore, Marakovitz, & Newby, 1996; Seipp & Johnston, 2005) which are thought to set up negative cycles of parent–child interaction that perpetuate and exacerbate patterns of impairment in ADHD. Links between harsh parenting and the aggravation of symptoms may reflect the reciprocal relations between impulsive parents and impulsive children. The extent to which this can induce ADHD itself or alter its long-term trajectory, rather than potentiate the emergence of comorbid social and emotional problems remains to be determined. Parent training interventions, in as much as they reduce core ADHD symptoms, provide support for the therapeutic value of positive parenting, clear and proactive limit-setting, and family structure (see below), regardless of how these problems initially began.

In addition to the social–emotional aspects of the family environment, the degree of intellectual and physical stimulation that a child receives may affect brain development and in turn behavior in children with ADHD (Halperin & Healey, 2011). Animal research has clearly documented the positive impact of environmental enrichment, cognitive stimulation, and physical exercise on neural and behavioral development. To the extent that children with ADHD show delays in brain development (Shaw et al., 2007), the degree to which the child's environment provides adequate stimulation may alter risk and affect the trajectory of the disorder. Interventions such as working memory training (Klingberg et al., 2005) or more broadly based cognitive enhancement programs (Halperin et al., 2013; Tamm, Nakonezny, & Hughes, 2012) highlight the potential of the postnatal environment to change the brain and the behavior of children with ADHD, although findings are largely preliminary and further research is clearly needed.

Nevertheless, the high level of covariation among genetic and environmental risks, nested within patterns of lifestyle and economic adversity, makes it difficult to separate genetic from environmental effects (Taylor & Rogers, 2005).

For instance, recent studies using adoption and artificial conception designs have suggested that many of the reported effects of maternal smoking may be due to genetic effects shared by mothers who smoke during pregnancy and their ADHD offspring (Nomura, Marks, & Halperin, 2010; Thapar et al., 2009).

Most importantly, we need to consider gene by environment interactions (G×E). For example, genes may moderate the effects of environmental exposures—as in the classic study whereby carrying a risk or susceptibility genotype of the serotonin transporter determined the long-term effects on mood of adverse social environments (Caspi et al., 2003). ADHD G×E studies to date have focused on dopamine genes, with evidence that genotypes moderate the effects of prenatal exposure to nicotine and alcohol (e.g., Becker, El-Faddagh, Schmidt, Esser, & Laucht, 2008; Brookes et al., 2006). Postnatal social influences may also be moderated by genetic factors. Serotonin and/or dopamine genes may moderate the effects of social adversity increasing risk for externalizing problems in general, as well as ADHD in particular (Lahey et al., 2011; Sonuga-Barke et al., 2009). Notably, children with the DRD4 7-repeat allele, as compared to those without that allele, were found to be more sensitive to the quality of parenting received (Sheese, Voelker, Rothbart, & Posner, 2007) and to respond better to parenting interventions (Bakermans-Kranenburg, Van Ijzendoorn, Mesman, Alink, & Juffer, 2008), again, suggesting genetic differences in the degree to which environmental factors influence developmental trajectories in children with ADHD. Most recently variations in DAT1 were found to moderate the responses of children with ADHD to behavioral parent training (van den Hoofdakker et al., 2012).

A second possibility is that environmental exposures moderate genetic effects through epigenetic modifications of the genome. In brief the epigenetic hypothesis is that environmental exposure can modify the expression of ADHD risk genes altering the likelihood of the condition. While such effects are well established in animal models, human epigenetics is in its infancy (see Meaney, 2010 for a discussion). Exploring the role of epigenetic mechanisms in ADHD represents a major research priority.

This framework highlights the potential significance of the developmental timing of putative risk and protective processes by raising the possibility that these processes operate both early and later in development. Although genetic factors are typically thought of as operating in a fixed way across the life span, that is unlikely to be the case. In contrast our model of ADHD pathogenesis makes a distinction between early and late operating genetic effects—this begs the question of whether genetic factors are implicated in determining continuity, discontinuity, and progression of the disorder. Greven, Asherson, Rijsdijk, and Plomin (2011) demonstrated, using longitudinal twin data, that patterns of stability and change in ADHD symptoms were the result of relatively stable genetic influences but also newly appearing influences emerging at different points across the life span. With regard to environmental influences, key questions relate to the primacy of early experience and sensitive periods (Do adverse environments have to be experienced during specific time windows? Can early adversity be overcome by later environmental enrichment?). There are currently very few studies that have the relevant combination of genetic/high-risk designs and longitudinal data to address these issues.

Neurobiological Mediators

According to our framework, genetic and environmental risk set the context for the development of ADHD via structural and functional alterations in key brain networks. Testing such a mediational model requires answers to three questions (1) In what way are ADHD developmental pathways related to altered developmental trajectories of brain structure and function? (2) Are such alterations associated with genetic and environmental factors shown to be linked to ADHD? (3) Do these ADHD-related neurodevelopmental alterations differentially operate early or late in development? Because so few studies of brain function have been longitudinal, our capacity to address these questions is limited.

ADHD and Brain Structure

Structural alterations in multiple brain systems have been implicated in ADHD (Sonuga-Barke & Fairchild, 2012). As compared to typically developing peers, studies have reported significantly smaller brains in children and adolescents with ADHD in contrast to non-ADHD controls (Castellanos et al., 2002) with the cerebellum, corpus callosum, and striatal (i.e., caudate nucleus, putamen and globus pallidus; Ellison-Wright, Ellison-Wright, & Bullmore, 2008) and frontal regions (e.g., dorsolateral prefrontal cortex) (DLPFC; Valera, Faraone, Murray, & Seidman, 2007) especially affected. Others have reported that children with ADHD evidence reduced cortical thickness, especially in the DLPFC (Batty et al., 2010). There is also evidence of altered patterns of cortical folding—effects often related to early environmental factors (Wolosin, Richardson, Hennessey, Denckla, & Mostofsky, 2009). Diffusion tensor imaging suggests alterations in white matter integrity in a range of fiber pathways thought to subserve cognitive functions implicated in ADHD (van Ewijk, Heslenfeld, Zwiers, Buitelaar, & Oosterlaan, 2012). Key regions in reward and emotion processing networks such as the ventral striatum and the amygdala may also be implicated (Carmona et al., 2009; Plessen et al., 2006).

The few studies that have examined developmental changes in brain structure related to ADHD have demonstrated some continuity in group differences over time, although several differences between those with and without ADHD in childhood were no longer evident by adolescence (Castellanos et al., 2002). More recent analyses of cortical thickness have supported the notion of a delayed developmental pattern in ADHD rather than a fixed deficit such that children with ADHD follow a trajectory of cortical development that is similar to but delayed by 2–3 years relative to their typically developing peers (Shaw et al., 2007). Emerging evidence from this longitudinal study of cortical thickness suggests that remission of symptoms may be associated with relative normalization of brain structure (Shaw et al., 2007). Consistent with this, neuroimaging (Schulz, Newcorn, Fan, Tang, & Halperin, 2005) and neuropsychological (Halperin, Trampush, Miller, Marks, & Newcorn, 2008) prospective studies of children with ADHD suggest parallels between clinical improvement and structural and functional normalization of the brain, although these latter studies also show evidence for enduring neural anomalies irrespective of clinical improvement.

ADHD and Brain Chemistry

The hypothesis that ADHD is a dopamine (DA) dysregulation disorder is partially supported by genetic, imaging, and pharmacological studies (Oades et al., 2005; Pliszka, 2005). PET studies have produced mixed results with some suggesting that ADHD is a hypo-dopaminergic and others a hyper-dopaminergic syndrome. This is supported by the fact that DA agonists (e.g., methylphenidate) reduce ADHD symptoms, probably through the increase of extracellular DA (Pliszka, 2005). DA neurons innervate brain networks (see below) implicated in ADHD. Methylphenidate improves functioning across some neuropsychological domains deficient in ADHD (e.g., Bush et al., 2008). The DA hypothesis is further supported by genetic studies implicating DA genes (see above) and by studies using animal models with pharmacological lesions and gene knockouts of catecholamine systems (Madras, Miller, & Fischman, 2005). Clearly other neurochemicals, such as norepinephrine (Arnsten, Steere, & Hunt, 1996) and serotonin (Oades et al., 2008), are also implicated in ADHD. Because the interactions among neurotransmitters are complex, it is difficult to isolate the effects of one (e.g., DA) from the others (e.g., serotonin or acetylcholine).

ADHD and Brain Function

Simple models of ADHD as a disorder of executive function have been replaced by models of pathophysiological heterogeneity (Durston, van Belle, & de Zeeuw, 2011; Halperin et al., 2008; Nigg, 2006; Sonuga-Barke, Bitsakou, & Thompson, 2010). At the neuropsychological level, ADHD is associated with deficits in a range of executive functions (Willcutt et al., 2005), especially in inhibitory control (Barkley, 1997),

working memory (Rapport et al., 2008), planning, and attentional flexibility (Willcutt et al., 2005). Functional neuroimaging data suggest that inhibitory-based deficits are linked to hypoactivation in the prefrontal cortex (Rubia, Smith, Brammer, Toone, & Taylor, 2005) and the dorsal striatum (Vaidya, Bunge, Dudukovic, & Zalecki, 2005), while working memory deficits implicate a network linking posterior regions of the prefrontal and anterior regions of the parietal cortex (Dickstein, Bannon, Castellanos, & Milham, 2006). Altered patterns of functional connectivity between key executive brain regions have also been identified.

Altered motivational and reward-related processes are also implicated in ADHD. Functional MRI studies suggest hypoactivation in the ventral striatum/nucleus accumbens and the orbitofrontal cortex in response to anticipated rewards (Scheres, Milham, Knutson, & Castellanos, 2006). Findings are less clear at the behavioral level with some studies suggesting that ADHD children are less sensitive to reinforcement, while others suggest oversensitivity. A consistent finding is that ADHD individuals respond differently to delayed reward (e.g., Marco et al., 2009). Alternatively, data suggest that ADHD is associated with delay aversion (a negative affective state induced by delay cues) and that escape from delay is a primary motivator for ADHD (Sonuga-Barke et al., 2010). Consistent with this view, brain regions involved in processing negative emotional stimuli (amygdala and anterior insula) are hyperactivated to cues of impending delay.

The default mode network (Broyd et al., 2009) is also attracting increased attention. This "resting state network" is active during rest and deactivates during task performance (Sonuga-Barke & Castellanos, 2007). During task performance activity in this network is associated with intermittent errors thought to reflect attentional lapses. In individuals with ADHD, this network shows reduced connectivity during rest (Fair et al., 2011) and not the typical decline in activity during rest-to-task transitions (e.g., Peterson et al., 2009), both effects that can be normalized with stimulant medication (e.g., Liddle et al., 2011).

Research on reward and delay highlights the context dependent nature of ADHD deficits. An alternative perspective on this issue is provided by the state regulation model, which posits that children with ADHD have particular difficulties regulating their psychophysiological state during periods of under- or overactivation (Wiersema, Van der Meere, Antrop, & Roeyers, 2006). ADHD children may be less capable of effectively allocating effort to regulate suboptimal states (Sergeant, 2005). Although the biological basis of this model is not well studied, supporting evidence comes from the repeated finding that performance in children with ADHD deteriorates under fast and slow event rate conditions, which should reduce activation/arousal (Metin, Roeyers, Wiersema, van der Meere, & Sonuga-Barke, 2012).

Integration from a Developmental Psychopathology Perspective

Children with ADHD are heterogeneous with respect to symptom picture, patterns of comorbidity, types of impairment, and family dysfunction. Developmentally, such heterogeneity is reflected in diverse trajectories of ADHD marked by differential patterns of continuity, discontinuity, and progression in clinical presentation (Lahey et al., 2005; Willoughby, Pek, Greenberg, & The Family Life Project Investigators, 2012). This clinical diversity is almost certainly mirrored in underlying pathogenesis—with ADHD risk associated with an array of interacting genetic and environmental factors—and mediated by multiple brain networks, with different individuals affected in different ways and to varying degrees. The field, however, is hampered by a dependence on simplistic disease models of etiology, built on the notion that ADHD is the result of a fixed and stable pattern of core dysfunction. A developmental psychopathology perspective offers an alternative formulation which provides a dynamic and flexible account of the pathogenesis of complex and heterogeneous conditions, such as ADHD (e.g., Halperin et al., 2013; Sonuga-Barke & Halperin, 2010). This approach moves beyond a merely *descriptive*

developmental approach (characterizing patterns of change across the life span) to an *explanatory developmental approach*, that considers the processes underpinning diverse developmental patterns and focuses on the dynamic interplay among different causal factors and pathogenic processes.

We posit that the clinical syndrome is a manifestation of neurodevelopmental liability, mediated by alterations in brain structure and function in response to multiple interacting early- (genetic and prenatal) and later-operating genetic and environmental risk and resilience factors, and later environmental protective processes (Rutter, 2000, 2006). Furthermore, building on a recent review that provides compelling evidence against discrete (or unique) causal factors or pathophysiological conditions marking diagnostic boundaries across the ADHD continuum of severity (Coghill & Sonuga-Barke, 2012), our model assumes a spectrum of liability for ADHD that is related to clinical severity in a dose-like manner.

Consistent with this view, we argue that multiple, rather than single, deficit models of ADHD reflect the heterogeneity in both the clinical picture and the underlying genetic and neurobiological patterns discussed above. ADHD is almost certainly not a single neurobiological entity but rather an umbrella term covering a range of different phenotypes, each with a specific pathophysiological profile. The notion of multiple deficits that may be distinct in some children and overlap in others is most clearly illustrated by data on cognitive and motivational functioning in children with ADHD. Indeed evidence indicates that each deficit (e.g., executive, reward/delay, state regulation) affects only a minority of cases (Sonuga-Barke et al., 2010). Distinct groups of ADHD children affected exclusively by either executive function problems or delay aversion and timing problems have been identified (Sonuga-Barke et al., 2010). On the basis of this and other data, multiple pathway models have been proposed (Coghill et al., 2005; Durston et al., 2011; Nigg, 2006; Sonuga-Barke et al., 2005), building on the functionally segregated nature of reward and cognitive anterior brain systems (Winstanley, Eagle, & Robbins, 2006).

Furthermore, as noted by Coghill et al. (2005), cognitive and executive dysfunctions appear to be more closely associated with the inattention dimension and poor academic achievement. Motivational deficits and delay aversion, on the other hand, appear to be associated with hyperactivity and impulsivity. Presumably some children have deficits in all of these areas. Considering these deficits in the broader context of family, school, and peer functioning, one can posit that the academic and regulatory difficulties that emerge from delayed development of executive functions in school-age children may cascade into more serious learning and interpersonal problems, possibly associated with school failure, poor decision-making, and peer rejection. Similarly, the high activity level and impulsivity associated with difficulties in reward processing may be reflected not only in symptoms of ADHD but also in higher levels of noncompliance at home, reactive aggression with peers, and disruptive behavior in the classroom. A stressful family context may also exacerbate problems via harsh parenting, inadequate support for self-regulation, and poor role models. It is well-documented that more severe family adversity, including marital conflict, parental psychopathology, and stressful life events, is associated with persistent ADHD over and above co-occurring ODD and CD (Biederman, Faraone, & Monuteaux, 2002; Counts, Nigg, Stawicki, Rappeley, & Von Eye, 2005). In contrast, supportive parenting paired with clear limit-setting may be reflected in a decline in symptoms and better social and academic functioning. Treatment outcome data (see below) suggest the importance of parent management and the parent–child relationship for children with ADHD.

Although follow-up studies indicate that problems persist in many children with ADHD, especially those with the combined presentation and comorbid conduct problems, little is known about developmental continuities and age-related changes in the psycho-pathophysiological underpinnings of ADHD or about brain structure and function in ADHD at different developmental periods. However, it is clear that individuals with ADHD are affected by cognitive problems across

the life span (Seidman, 2006) with motivational and energetic factors also playing a role in preschool, childhood, adolescence, and adulthood (e.g., Marco et al., 2009; Wiersema et al., 2006). A few recent studies suggest that developmental change may be evident in underlying cognitive and neural processes, related to continuity and discontinuity in the clinical manifestations of ADHD. Halperin and colleagues (2008) found that individuals who showed a persistent pattern of disorder from childhood through adolescence could be distinguished from those who remitted on the basis of the integrity of their executive or effortful control processes, a finding which the authors argue is consistent with the idea that recovery from ADHD is associated with emergence of well-functioning executive control. However, the so-called ADHD remitters continued to show impairments on less consciously controlled cognitive processes, despite improvements in executive control. These findings are consistent with preliminary fMRI data indicating that the magnitude of prefrontal activation in response to inhibition in adolescents with childhood ADHD corresponds to the persistence of symptoms; those who were less symptomatic appeared more like never-ADHD controls (Schulz et al., 2005).

In studies of the transition from preschool to school, earlier delays in executive functions seem to predict the onset or persistence of disorder or symptoms (Campbell & von Stauffenberg, 2009; Wahlstedt, Thorell, & Bohlin, 2008). Imaging studies of brain function have not been designed or powered to identify systematic differences in brain structure or function in different age groups, but consistencies in alterations have been seen for school-age, adolescent, and adult samples. Structural effects seem to show a degree of continuity although the one longitudinal morphometric study found that early childhood differences in striatal volume are reduced by adolescence and cerebellar differences become more prominent (Castellanos et al., 2002). However, two interesting studies of brain structure and function may challenge this view by demonstrating that the brains of ADHD children share characteristics of developmentally younger children. Shaw et al. (2007) reported that ADHD children were delayed, rather than deficient in cortical growth, especially in areas linked to executive control. Clarke, Barry, McCarthy, Selikowitz, and Brown (2002) identified a subgroup of ADHD children who they designated as having patterns of brain activity that were typical of developmentally younger children on the basis of their EEGs. Taken together, these studies suggest that developmental delays and individual differences in brain function and structure as well as associated cognitive processes are reflected in the clinical heterogeneity and variations in the developmental course of ADHD. Longitudinal studies are needed that examine neural and cognitive processes in the same children with ADHD and link changes in brain function to changing cognitive and symptom patterns across development, while also taking family context, including parenting style, into account.

Treatment

Evidence-based treatments for children with ADHD include an array of pharmacological and psychosocial approaches. FDA-approved medications include psychostimulants (i.e., methylphenidate and amphetamines) and more recently approved non-stimulant medications (i.e., atomoxetine and guanfacine). Behavioral interventions in the forms of parent management training (PMT) and contingency management in the classroom have been studied extensively. While these interventions generally provide symptom relief, at least in the short term, they also have limitations (see below). As such, efforts have been ongoing to develop novel non-pharmacological interventions for ADHD, several of which incorporate a developmental psychopathology perspective. Below, we briefly review current evidence-based medication and psychosocial treatments for ADHD and then discuss emerging interventions that show promise.

Medication

Psychostimulants are the most commonly prescribed medications for treating children with

ADHD. There are numerous preparations of both methylphenidate and amphetamine. Perhaps the biggest change in stimulant medication treatment over the past decade has been the shift from short-term preparations to those with effects lasting throughout most of the day. In addition, the approval of non-stimulant medications provides an alternative for those who do not respond well to stimulants or whose parents are concerned about their misuse. While the available non-stimulants may not be as effective as long-acting psychostimulants (Hanwella, Senanayake, & de Silva, 2011), they are helpful for many children who do not respond well to stimulants or as a supplement to stimulant treatment, and they do not raise the social concerns associated with treating children with a drug of potential abuse.

The precise mechanisms by which these medications exert their impact on ADHD symptoms are not known. Most theories posit that stimulant medications work by enhancing dopamine in the striatum (Volkow et al., 2012), although others have focused on their effect on noradrenergic alpha-2 receptors in the prefrontal cortex (Arnsten et al., 1996). Both non-stimulant medications have direct actions only on the noradrenergic system; atomoxetine selectively blocks the norepinephrine transporter (primarily in the prefrontal cortex) which has secondary effects on dopamine as well, whereas guanfacine is a highly specific alpha-2a receptor agonist.

For most children with ADHD, these medications are highly effective for reducing the core symptoms of ADHD as well as enhancing compliance and academic success and decreasing aggression (Conners, 2000; Greenhill, Halperin, & Abikoff, 1999). Stimulants are well tolerated by most children with ADHD, although a substantial number experience side effects (Swanson et al., 2007; Wigal et al., 2006). Further, many parents and teachers, especially of young children, feel uncomfortable using medication as a treatment for children with ADHD (Pisecco, Huzinec, & Curtis, 2001; Power, Hess, & Bennett, 1995) and questions about long-term medication effects remain Therefore, there is a renewed focus on psychosocial interventions for children with ADHD.

Evidence-Based Psychosocial Interventions

Many parents of children with ADHD prefer psychosocial interventions prior to or instead of medication. This is particularly the case in preschool children, where the American Academy of Pediatrics (Wolraich et al., 2011) recommends such interventions prior to the initiation of medication. Evidence-based psychosocial interventions typically employ a behavior modification model implemented through PMT and/or school-based contingency management programs. Studies of PMT have shown improvements in ADHD symptoms (Anastopoulos, Shelton, DuPaul, & Guevremont, 1993; Sonuga-Barke, Daley, Thompson, Laver-Bradbury, & Weeks, 2001), oppositional problems and impairment (Erhardt & Baker, 1990; Pisterman et al., 1992), and parent functioning (Anastopoulos et al., 1993; Pisterman et al., 1992; Sonuga-Barke et al., 2001). However, PMT is generally more effective for decreasing oppositional and defiant behaviors than core ADHD symptoms. Contingency management in the classroom has been shown to improve classroom behavior and academic productivity as reflected in teacher reports, classroom observations, and academic tests (Fabiano et al., 2007; Pelham, Wheeler, & Chronis, 1998). While behavioral interventions are effective, benefits often do not generalize to other settings, they are difficult to implement, and they may be less effective than stimulant medications (MTA Cooperative Group, 1999).

Limitations of Current Treatments

Although currently employed pharmacological and psychosocial treatments can be effective in reducing symptoms of ADHD and comorbid conditions, a substantial proportion of treated children continue to exhibit clinically significant levels of ADHD symptoms and associated impairment (Swanson et al., 2001). ADHD children usually function better following treatment, yet they remain deviant relative to peers in social and academic functioning. Furthermore, treatment-related

gains are rarely maintained beyond the termination of active treatment, and both psychopharmacological (Molina et al., 2007, 2009) and behavioral interventions (Molina et al., 2007; Pelham & Fabiano, 2008) have minimal impact on long-term outcomes of children with ADHD. While it could be argued that ADHD is a chronic condition that requires long-term treatment, perhaps throughout much of the life span, long-term adherence to both medication and behavioral interventions is generally poor (MTA Cooperative Group, 2004). For behavioral interventions to provide lasting benefits, parents and teachers need to implement highly intensive interventions over long periods of time, but this is extremely challenging. Thus, despite short-term benefits of these evidence-based treatments, the lack of "normalization" for many children, the limited generalization of treatment effects, poor long-term adherence, and the lack of evidence for improved long-term outcomes are problematic.

Developmental Psychopathology Perspectives on Treatment for ADHD

Unlike static or fixed deficit models, the developmental psychopathology perspective views ADHD as a manifestation of neurodevelopmental liability, mediated by changes in brain structure and function in response to multiple genetic and environmental risk and resilience factors (Rutter, 2000, 2006). As such, the goal of treatment is to reduce environmental risk and enhance resilience and protective processes. While there may be several potential treatment targets for accomplishing these goals, ongoing research has largely focused on two: the improvement of parent–child relationships and the facilitation of neural development. These approaches often target younger children, when brains and behavioral patterns may be more "plastic" or amenable to change and because, theoretically, relatively modest effects early on can have substantial cascading effects on the long-term trajectory (Halperin et al., 2012).

Several developmentally sensitive early interventions include a more traditional PMT component which provides guidance in the provision of structure and rule-based reinforcement. Incorporated into the intervention are strategies for promoting parental warmth and improving the quality of the parent–child relationship (Bor, Sanders, & Markie-Dadds, 2002; Sonuga-Barke et al., 2001; Thompson et al., 2009). In contrast to PMT with older children, these interventions with preschoolers yield evidence of persisting benefits beyond the termination of active treatment.

In addition, as the trajectory of ADHD is likely mediated by brain structure and function, several novel interventions focus on promoting neural development through the employment of computer-based training (Klingberg et al., 2005; Shalev, Tsal, & Mevorach, 2007), targeted cognitive skill development (Thompson et al., 2009), physical exercise (Berwid & Halperin, 2012), and play (Halperin et al., 2013; Tamm et al., 2012). Play-based interventions are noteworthy in that they aim to facilitate neurodevelopment within a context that promotes improved parent–child relationships (Halperin & Healey, 2011). While the impact of these approaches on brain development has not been systematically evaluated, preliminary data suggest that behavioral improvements last at least several months beyond the termination of active treatment.

Summary and Conclusions

Much progress has been made in describing the developmental course of ADHD from preschool age to early adulthood and recognizing that the clinical picture is likely to emerge from a heterogeneous set of correlated and interacting genetic and environmental risk factors. In addition, there is growing evidence that subgroups of children with ADHD show different patterns of cognitive and motivational deficits, some of which appear to be linked to delays in brain maturation. Specific comorbidities also vary widely, although the majority of children with ADHD have some comorbid condition. Thus, ADHD is best conceptualized as a final common manifestation of multiple neurobiological risks that may be exacerbated or ameliorated by experiences in the

family and school setting. Symptom patterns and severity of impairment are strongly associated with family adversity and parenting competence and are likely to reflect both general risks for disorder (e.g., parental psychopathology, family conflict, harsh parenting) and risks specific to ADHD (e.g., paternal ADHD). Treatment programs that begin early and are aimed at modifying the parent–child relationship and children's cognitive and attentional processing appear promising.

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