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Attention Deficit Hyperactivity Disorder (ADHD): Controversy, Developmental Mechanisms, and Multiple Levels of Analysis

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Abstract

Controversy abounds regarding the symptom dimensions of attention problems, impulsivity, and hyperactivity, developmentally extreme and impairing levels of which compose the diagnostic category of attention deficit hyperactivity disorder (ADHD). I highlight causal factors, underlying mechanisms, developmental trajectories, and female manifestations of ADHD, integrating the psychobiological underpinnings of this syndrome with contextual factors related to its clinical presentation, impairments, and soaring increases in diagnosed prevalence. Indeed, despite strong heritability, ADHD is expressed via transactional patterns of influence linked to family-, school-, peer-, neighborhood-, and policy-related factors. Moreover, intervention strategies must take into account both pharmacologic and behavioral modalities if the goal is to enhance competencies, rather than symptom reduction per se. A comprehensive understanding of ADHD mandates multiple levels of analysis—spanning genes, neurotransmission, brain pathways, individual skill levels, family socialization, peer relationships, and educational and cultural forces—which must be integrated and synthesized to surpass reductionist accounts, reduce stigma, and maximize the impact of prevention- and intervention-related efforts.

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INTRODUCTION

The neurodevelopmental condition called, in recent decades, attention deficit hyperactivity disorder (ADHD) spans the cognitive, behavioral, and affective domains of (*a*) attentional processing and executive function (EF), (*b*) response inhibition and impulsive behavior, and (*c*) overactive motor output. It is difficult to imagine a more controversial diagnostic entity than ADHD has become in the late twentieth and early twenty-first centuries (Hinshaw & Scheffler 2014). Indeed, rates of diagnosed prevalence have soared in the United States, while debates rage over the use of stimulant medication to control the behavior of fidgety, possibly bored schoolchildren and enhance the performance of success-seeking adults. The condition has become a fulcrum point related to highly debated issues—for example, overreliance on biological models of causation, faulty educational systems, and the role of the pharmaceutical industry in fueling expanded use of medication treatments both nationally and internationally.

In the relatively limited space afforded to authors of *Annual Review of Clinical Psychology* articles, I aim to present core facts and debunk relevant myths, integrate data on the neurobiological and psychosocial factors related to the etiology and maintenance of this form of problematic behavior, discuss crucial issues related to ADHD in girls and women, and highlight the essential need for integrative models of both causation and intervention strategies. Throughout, I emphasize processes related to developmental psychopathology (see Cicchetti 2016, Hinshaw 2017) with the goal of fostering appreciation for the dynamic interplay of risk and protective factors related to ADHD and its impairments across the life span. Indeed, like all forms of mental disorder, ADHD incorporates developmental extremes of key spectra of behavior, cognition, and affect. Additionally, this diagnostic syndrome is subject to equifinality, whereby multiple causal forces may converge on parallel symptom displays, and multifinality, given that early markers are not inevitably associated with later impairment (Cicchetti & Rogosch 1996). Optimal treatments involve combinations of pharmacologic and psychosocial modalities that reduce core symptom domains, promote essential competencies, and enhance resilient outcomes (Hinshaw & Arnold 2015).

At the outset, I highlight that ADHD far transcends its stereotypic presentation as problems of fidgeting and distractibility in middle-class, elementary school–aged boys who are parented permissively and who contend with stifling classrooms. In reality, ADHD symptoms and impairments often reveal themselves during the preschool years and, more often than not, extend into adulthood. The core symptoms are expressed in a wide range of social and academic contexts

(particularly those that emphasize routine or are particularly challenging), and they are linked with a wide range of impairments, including marked problems with interpersonal relationships; high risk for accidental injury; and liability for major issues with substance use, risk-taking behavior, unplanned pregnancy, and self-harm across the life span. The constituent behavior patterns afflict females as well as males and are salient for diverse socioeconomic and ethnic groups. Causal factors involve clear neurobiological mechanisms interacting and transacting with maladaptive environmental forces. In short, when diagnosed accurately, ADHD is all too real and debilitating in its developmental consequences, spanning diverse personal, familial, and cultural contexts. The clinical reality of ADHD, as well as its often-severe ramifications, is unmistakable.

FACTS AND CONTROVERSY

The constituent behavioral dimensions underlying ADHD comprise (*a*) inattentive/disorganized and (*b*) hyperactive/impulsive patterns (Am. Psychiatr. Assoc. 2013). These behavioral dimensions are associated with, yet partially independent of, such externalizing patterns as oppositionality and aggression (Ahmad & Hinshaw 2016, Hinshaw 1987). Diagnosis is made when these symptoms lie at the far end of the normative continuum and yield impairment in essential life functions. There is no magic symptom-related cutoff point beyond which ADHD absolutely exists and short of which it does not. Indeed, like nearly all forms of psychopathology, the constituent behaviors are spectrum-related phenomena; dimensional accounts are usually superior to categorical models with respect to scientific validity.

These patterns of attention and behavior came to the notice of the educational and medical communities over two centuries ago, at the end of the Enlightenment, when educational attainment became a universal ideal and when, subsequently, compulsory schooling for children swept through Europe and the United States (see Barkley 2015). Given the strongly heritable nature of ADHD-related symptoms, it is quite possible that the goal of universal education revealed the propensities for a subset of youth to show core problems in adapting to a culture of increasingly high academic expectations (Hinshaw & Scheffler 2014). In the United States, diagnosis transcends racial and ethnic categories (Visser et al. 2014) and has noteworthy prevalence in girls and women.

Belying the myth that ADHD is an exclusively US phenomenon, the prevalence of ADHD among children and adolescents is strikingly similar around the world, at least in nations with compulsory education (Polanczyk et al. 2007, 2014; see also Faraone et al. 2003). Modal rates include 5–7% of youth. The factors that matter most in explaining cross-national variation in prevalence rates are methodological and clinical ones, such as the specific diagnostic classification used by a given nation [e.g., the International Classification of Diseases (World Health Organ. 2004) versus the *Diagnostic and Statistical Manual of Mental Disorders* (DSM)] and whether parent report alone, versus parent-plus-teacher report, is mandated for assigning a diagnosis (Polanczyk et al. 2007). Indeed, one key puzzle is the presence of far higher diagnosed prevalence in a few selected nations, like the United States, potentially related to such environmental forces as educational policies and pharmaceutical advertisements (see discussion in the section titled Surging US Prevalence: What Are the Reasons?). Overall, ADHD exists far beyond first-world, affluent societies, as its symptoms and consequences are felt worldwide.

Indeed, the largely consistent rate of ADHD diagnosis around the globe provides circumstantial evidence for the contention that the underlying symptom domains reflect a neurobiological propensity for inattentive, unfocused, and impulsive behavior patterns that emerges when children are placed in classroom settings, attempting to attain skills (e.g., literacy) for which the human brain clearly did not evolve. From this perspective, the confluence of biological vulnerability with psychosocial and cultural forces produces the phenomenon termed ADHD, with

compulsory education serving as the triggering social factor. All-biological or all-cultural perspectives are therefore reductionist and short-sighted.

At their extremes, problems with inattention and hyperactivity/impulsivity often yield devastating consequences. Core impairments include academic underachievement (regardless of the presence of co-occurring learning disorders), emotion dysregulation, social ineptness, high risk for accidental injury, and a cascading set of associated problems throughout the life span. Indeed, prospective longitudinal investigations reveal that ADHD symptoms typically incur major negative consequences for years to come, in domains—such as problematic substance use, propensity for self-injury, engagement in risky behaviors, display of poor health-related habits, and major problems with consistent employment—that are essential for individuals, families, and even national economies (Hinshaw & Scheffler 2014). In addition to the direct expenditures for assessment and treatment per se, the impairments related to ADHD incur massive long-term indirect costs linked to juvenile justice, special education, and substance abuse treatment during childhood and adolescence, as well as rampant employment-related problems throughout adulthood. In the United States alone, such costs are measurable in amounts of hundreds of billions of dollars annually (Hinshaw & Scheffler 2014). The burden related to ADHD therefore spans personal attainment, key relationships, health-related outcomes, and major outlays across multiple societal systems of education and care.

Yet ADHD continues to receive derision, ridicule, and stigmatization. Media portrayals often emphasize its triviality, its exclusively sociocultural nature (e.g., troubles of normal-range youth in response to demands of poorly organized or unresponsive classrooms), and the ways in which increasing numbers of adults attempt to game the system to gain accommodations in higher education or on the job (for elaboration, see Hinshaw & Scheffler 2014). Underlying these depictions is the stereotype that ADHD comprises a set of socially triggered behavior patterns linked to faulty parenting, poor schooling, or current societal values related to rampant competition in educational and vocational settings. Moreover, critics contend, these alleged social triggers are masked when an exclusively biological model places the locus of the problem on individual, brain-based pathology (Conrad & Bergey 2014). Other critiques center on the use of stimulant medication as the core intervention for ADHD (see Safer 2016 for recent trends in medication for ADHD), abetted by arguments that drug manufacturers deploy misleading, overzealous advertisements motivated by driving sales rather than promoting psychosocial or multimodal treatments (Schwarz 2016). In the United States—along with New Zealand, the only other nation that allows direct-to-consumer pharmaceutical advertising—the high rates of advertisements for treatments for mental health conditions only fuel such contentions.

Perhaps the most heated source of controversy pertains to escalating rates of diagnosis over recent years. In fact, the diagnosed prevalence of ADHD for children and adolescents in the United States has risen by 41% in the past decade, such that 11% of all youth between the ages of 4 and 17 years have by now received this diagnosis, according to parental report from large, representative national surveys. Indeed, for boys beyond grade school, the rate of lifetime diagnosis now approximates one in five (Visser et al. 2014). Recent data from Israel reveal that the diagnostic rate there has also risen dramatically in the past decade, to an overall rate of one in seven (i24 News 2016). In the section titled Surging US Prevalence: What Are the Reasons?, I return to information on social and cultural factors that may help to explain such large increases in the diagnosed prevalence of ADHD, which appears to far outstrip its true prevalence, as well as major regional variation in rates of diagnosis.

In short, it can be difficult to separate fact from fiction in negotiating both the scientific literature and popular press related to ADHD, particularly given the huge amount of relevant articles, books, and websites that continue to accumulate. The goal of this article is to place

key arguments on sound scientific footing. For book-length compendia on this issue, the reader is referred to Banaschewski et al. (2018) and Barkley (2015); for a state-of-the-art chapter, the reader is referred to Nigg (2017).

ETIOLOGY AND UNDERLYING MECHANISMS

Causal Factors

A thorough explanation of risk factors and vulnerabilities for ADHD could easily span a book-length account (see Nigg 2006 for a fine example; see also Thapar et al. 2013). Indisputable evidence exists for the substantial heritability of ADHD in childhood and adolescence, regarding both categorical taxa and underlying symptom dimensions. Most estimates center on values near 0.75 (e.g., Burt 2009). With clinically diagnosed cases, the heritability appears to be even higher, approaching 0.90 (Larsson et al. 2014). Thus, ADHD is far more heritable than major depression, falling in the range of other highly heritable conditions like schizophrenia and bipolar disorder and approaching that of autism spectrum disorders. Notably, estimates of the heritability of ADHD in adults appear substantially lower. Yet an informative review (Brikell et al. 2015) reveals that the key reason for this apparent discrepancy pertains to the predominant use of self-report ratings of ADHD symptoms as the basis for most adult estimates. With cross-informant ratings or clinical diagnoses, adult heritability figures are nearly as high as those for youth.

It is essential to emphasize, however, that heritability signifies the proportion of variance of a given trait or condition ascribed to genes versus environmental influences, within a given population at a given point in time. It does not signify that any single genes are responsible for the condition; indeed, for all psychiatric conditions with measurable heritability, combinations of a number of genes acting in concert generate vulnerability. Moreover, substantial heritabilities do not signify that environments lack importance for shaping individual trajectories. Furthermore, fascinating work in genomics reveals shared genetic vulnerability across a range of major psychiatric disorders (Cross-Disord. Group Psychiatr. Genet. Consort. 2013). Moreover, heritabilities may not be uniform across socioeconomic spectra, as clearly shown with respect to IQ scores (Turkheimer et al. 2003). Finally, rising heritability estimates across the lifespan for many key traits or disorders reveal that genes and environments are engaged in active interplay throughout development, exemplifying the important processes of (*a*) gene–environment correlation and (*b*) gene–environment interaction (Beauchaine et al. 2017, Rutter et al. 2006). It is clearly the case that the genetic liability for various ADHD-related symptom clusters is potentiated by a range of environmental and cultural factors (Beauchaine & Hinshaw 2016). Epigenetic forces are highly likely to come into play, as exemplified by a recent report that individuals with ADHD who were exposed prenatally to acetaminophen for several weeks underwent differential patterns of gene methylation than did those exposed for shorter time periods (Gervin et al. 2017; for suggestive additional data related to ADHD, see Wilmot et al. 2016).

One risk factor for ADHD is low birth weight (Nigg 2006). In fact, the lower the weight at birth, the higher is the risk for ADHD-related symptoms, as well as for several additional learning and motor problems. In addition, evidence is building that exposure to prenatal toxins—including alcohol and, potentially, nicotine—can and does spur ADHD-related behavior patterns. In the case of alcohol, a mother's consistently high levels, or binges, can precipitate fetal alcohol syndrome, typically involving facial dysmorphisms and intellectual disability, yet lesser amounts may trigger fetal alcohol effects, which include core ADHD symptoms (Doyle et al. 2017). In the case of nicotine, more complex interactions between genetic propensity and direct toxic effects may be involved (Thapar et al. 2009).

During childhood, exposure to lead is implicated in ADHD-related symptoms (Nigg 2006) as well as compromised intellectual functioning. Recent evidence indicates that variation in an iron metabolism gene moderates the association between blood lead levels and ADHD symptoms (Nigg et al. 2016), suggesting the importance of gene-by-environment effects in the etiology of at least some cases of ADHD. Limited but growing evidence implicates toxic chemical exposures from pesticides or phthalates in ADHD (Marks et al. 2010); again, the most salient effects may appear in individuals with high genetic vulnerability. Even extremes of psychosocial deprivation can result in severe levels of inattention and overactivity, as shown by investigations of Eastern European orphans who spent early years in horribly deprived settings (for an early overview, see Rutter 1998). In such cases, however, ADHD-linked symptoms are typically embedded in a clinical picture of highly maladaptive attachments (e.g., displays of indiscriminant friendliness), signifying the complex pathways that can eventuate in clinically significant levels of the core symptoms.

A common stereotype is that ADHD results from overly permissive or other kinds of maladaptive parenting styles. Except in cases of clear neglect or other forms of maltreatment, little evidence supports this contention. At the same time, bidirectional and reciprocal effects are clearly operative (see Bell 1968). Thus, parents of children with difficult temperaments and/or early signs of impulsive, irritable behavior tend to respond with unsuccessful attempts to manage such behavior patterns (Beauchaine & McNulty 2013). The development of coercive parenting styles (Patterson 1982) is highly likely to increase the child's initial behavioral propensities and promote antisocial activity (or, more often in girls, self-harm). Thus, socialization influences, though reactive or maintaining, are still highly important. In addition, given the strongly heritable nature of ADHD-related symptoms, it is likely that the biological parents of a diagnosed child will share propensities for problems in attentional and impulse control, planning and judgment, and emotion regulation. The result, too often, can be a fully transactional cycle of genetic vulnerability fueled by discordant, even explosive, family interactions.

Can positive parenting styles protect children with ADHD? Hinshaw et al. (1997) found that boys with ADHD whose parents showed a strongly authoritative parenting style, incorporating high warmth plus strong limits, had unexpectedly high rates of social competence in terms of positive peer sociometric appraisals. Intriguingly, the typically developing comparison boys in this research program showed no such protective effect (for an additional example of positive parenting practices related to outcomes of young children with ADHD, see Healey et al. 2011). Of course, as with all family studies lacking genetically informative designs, it could be argued that shared genes comprise the third variable driving both positive parenting practices and the child's social competence. Yet landmark investigations by Harold et al. (2013a,b) utilizing adoptive families, in which passive gene–environment correlation was removed from the picture, revealed that (*a*) early ADHD-related child behaviors induced hostile parenting responses, and (*b*) such parenting practices independently predicted the maintenance of the children's behavior patterns years later. In short, despite the strongly heritable nature of ADHD behavior patterns, family socialization influences are extremely salient.

Beyond parenting, interactions and transactions between impulsive child styles and such contextual forces as unsupportive classrooms, peer rejection, and toxic neighborhood environments can also serve to propel a pernicious developmental course (e.g., Beauchaine & McNulty 2013, Jennings & Perez 2017; for an example of the protective influence of friendships, see Cardoos & Hinshaw 2011). Trait impulsivity, characterized by the preference for immediate rewards and exemplified by high risk taking as development unfolds, is strongly heritable. Children demonstrating this characteristic tend to reside in less structured and stimulating schools and homes, seek high-risk contexts, and, in turn, be propelled to behavioral extremes by the responses they receive from peers and adults in these settings, exemplifying the processes of passive, active, and evocative

gene–environment correlation (Beauchaine et al. 2017). In short, escalating transactional processes characterize the propensity for vulnerable youth to show cascading problems—such as conduct problems, substance abuse, and self-harm—as they develop, exemplifying multidirectional ontogenic process models of the development of psychopathology and comorbidities (Beauchaine & McNulty 2013, Beauchaine et al. 2016, Owens & Hinshaw 2016).

Mechanisms

This section discusses underlying processes and mechanisms related to ADHD. First, does ADHD involve deficits in attention? This is a deceptively complex question, given (*a*) the several forms of attention that exist (e.g., covert attention, selective attention, sustained attention, and attentional capacity, each with different neurological underpinnings; see Gazzaniga et al. 2014) and (*b*) research revealing that, except for the apparently preserved functions of covert attention, individuals with ADHD may well show deficits in several of these forms (Barkley 1997) Still, it is mistaken to think that people with ADHD have inherent and cross-situationally consistent attention-related deficits. Instead, evidence supports the contention that ADHD can sometimes manifest as hyperfocus—the inability to detach attention from a particularly compelling stimulus (e.g., a videogame)—meaning that ADHD is better conceptualized as a deficit in the regulation of attention to varying environmental demands. In fact, an overriding finding is that ADHD is associated with high levels of intraindividual variability in attentional (as well as other cognitive) processing (see Kofler et al. 2013). In other words, ADHD-related performance is erratic and inconsistent. Neuroimaging research suggests strongly that individuals with ADHD show intrusions of resting-state and default-mode daydreaming neural networks when attention-focused networks should be engaged (see Raichle & Snyder 2007). Furthermore, in a fascinating recent investigation, both youths and adults with ADHD-related symptoms appeared to show, rather than daydreaming or mind-wandering per se, a blank thought pattern during attentional lapses (Van den Driessche et al. 2017). This provocative area of research goes beyond the constraints of the present review but is well worth considering with respect to the underlying neurobiology of ADHD.

Second, a core extension of this line of reasoning is that ADHD comprises problems, beyond problems with attention itself, with a range of higher-order EFs, including response inhibition, planning, working memory, interference control, and error correction (see Brown 2013). As a result, difficulties with time management and organizational skills also characterize many individuals with ADHD. Recent, compelling work (Karalunas et al. 2017) reveals that, over and above other EFs or other potential endophenotypes, developmental changes in working memory were correlated with changes in ADHD symptom trajectory over time, highlighting the importance of working memory for ADHD. In addition, Nigg et al. (2017) recently showed that a polygenic risk index (summing across several vulnerability alleles) predicted ADHD, as mediated by both working memory and arousal regulation variables, again demonstrating the complexity of causal pathways to ADHD. Even though the EF model may help to explain the wide variety of performance issues incurred by individuals with ADHD, a significant percentage of people with the diagnosis do not exhibit EF-related performance deficits as measured by objective neuropsychological tests (Willcutt et al. 2005). The underlying mechanisms of ADHD in these cases may have to do more with motivational processes, as discussed later in this section, or other potential cognitive factors. Once again, equifinality is operative with respect to ADHD.

Modifying the EF model, Barkley (1997) contended that fundamental deficits in response inhibition comprise the core cognitive and neuropsychological issue, at least for those individuals marked by high levels of impulsivity, although not for those with the more purely inattentive presentation of the disorder. In other words, if individuals cannot, for crucial milliseconds, suppress

a previously rewarded, prepotent response, they will not be able to engage any of the other EFs needed for optimal performance in school, at work, or within relationships. From this perspective, then, deficits in response inhibition, characterizing trait impulsivity, are viewed as prior to problems with other forms of EF in explaining ADHD.

A third major contention is that the core deficit involves insufficient intrinsic motivation. In short, the heritable underlying mechanism comprises insufficient arousal, related to hypodopaminergic functioning, leading to a constant need for stimulation, an aversion to delayed rewards, and a need for high levels of reinforcement to motivate performance (for elaboration, see Beauchaine & McNulty 2013; for strong neurobiological evidence along these lines, see Volkow et al. 2009, 2010). As a result, difficult and/or tedious tasks are anathema to vulnerable individuals, who may require behavioral contingencies and/or dopamine-enhancing medications like stimulants to enhance behavioral and cognitive performance.

The perceptive reader will have noted the potential for integration across these seemingly disparate mechanistic accounts. Indeed, extending earlier calls for recognizing both top-down, or executive, and bottom-up, or motivational, accounts of ADHD, Sonuga-Barke et al. (2010) propose several differing, yet interrelated, pathways to ADHD (see also Sjowall et al. 2013, Thorell 2007). Once again, disparate underlying mechanisms are highly salient.

Can neurobiological findings provide coherence? A fascinating program of research from Shaw and colleagues (for initial findings, see Shaw et al. 2006, 2007) reveals that children with ADHD show a delay in the maximum thickness of the prefrontal cortex of approximately three or more years, from 6 to over 9 years of age. Moreover, the expected thinning of this cortical area is also delayed during adolescence, and cortical size shows substantial correlations with relevant ADHD symptoms (Shaw et al. 2011). In addition, a plethora of functional imaging investigations implicate frontostriatal connectivity as highly related to ADHD symptom patterns. Even so, Castellanos & Proal (2012) caution that multiple areas and pathways are likely to be implicated in ADHD-related behaviors, far beyond the frontostriatal model per se.

The key lesson from this necessarily brief overview is the necessity of invoking multiple levels of analysis to begin an adequate account of ADHD and its manifestations and impairments. The strongly heritable nature of the core symptom dimensions clearly implicates substantial, yet complex, genetic vulnerability, with a number of neurotransmitter systems (including but not limited to dopaminergic pathways) involved. Early in development, those children with high trait impulsivity—who are likely to have shown difficult temperament and poor effortful control (Rothbart 2007) in the initial years of life—begin to encounter coercive, ineffective discipline styles, fueling an escalation of hard-to-manage behaviors (for the development of the theory of coercive family processes, see Patterson 1982). In contrast, the strongest behavioral correlate and predictor of academic underachievement is inattention, rather than trait impulsivity. Teachers and parents alike may become frustrated by or develop low expectations for children with substantial inattention and disorganization, fueling additional transactional patterns. Overcrowded schools, ever-earlier demands for academic performance, high-risk neighborhoods, and varying cultural expectations for conformity and attainment comprise even higher levels of analysis in terms of the interactive processes that are involved in the development of ADHD.

Models such as the Research Domain Criteria (see Cuthbert & Insel 2013, Insel et al. 2010) comprise a twenty-first-century attempt to transcend the static diagnostic categories of the DSM by encompassing multiple domains of cognitive and motivational functioning embedded within a multiple-levels-of-analysis approach ranging from basic neural circuits to higher-order psychosocial processes. This model is highly reminiscent of the calls from developmental psychopathologists, for over a generation, to take into account bidirectional and transactional processes (Achenbach 1982; Cicchetti 1984, 1990; Sroufe & Rutter 1984).

DEVELOPMENTAL PATHWAYS AND COMORBIDITY

During the preschool years, it is more difficult to detect inattention than the more overt displays of impulsive, often oppositional behavior that typically characterize early markers of ADHD (see Curchack-Lichtin et al. 2014). Still, as noted above, early signs of inattention are a potent predictor of later underachievement (Hinshaw 1992), meaning that reports from preschool teachers are an essential complement to parent reports of such behavior patterns. At this developmental stage, high rates of accidental injury characterize children with ADHD—and continue to do so throughout the lifespan. Life at home is often challenging for parents and child alike, with coercive discipline patterns all too likely to provide maintaining and propelling forces for hyperactive and oppositional behaviors (see Beauchaine & McNulty 2013, Hinshaw & Scheffler 2014).

Can ADHD be accurately diagnosed during the preschool years, before the start of formal elementary education? The answer is a qualified "yes," if assessments are thorough and evidence based (see Am. Acad. Pediatr. 2011). Indeed, the American Academy of Pediatrics guidelines are predicated on the supposition that accurate, early identification may prevent years of impairment and suffering later in the life course. The more difficult question is whether even earlier indicators, during infancy and toddlerhood, are valid. Given the developmental normativeness of dysregulated and obstreperous behaviors in many young boys, the risk for false-positive diagnostic errors is great. A major challenge is to ascertain whether early markers of difficult temperament, as well as other indicators of trait impulsivity, can accurately predict clinical levels of ADHD.

The elementary school years comprise the period when most youth with ADHD come to clinical attention. Core impairments include academic performance issues (see review in Barkley 2015); a strong propensity for peer rejection, which can occur quite quickly, particularly when impulsivity characterizes the behavioral presentation of ADHD (Erhardt & Hinshaw 1994; see also Hoza et al. 2005); continued parenting stress and family discord (e.g., Gordon & Hinshaw 2017a,b); and the emergence of comorbid psychiatric disorders—particularly externalizing conditions like oppositional defiant and conduct disorders, as well as learning disabilities, and anxiety- and mood-related conditions. The impairments, as well as the challenges for families and teachers alike, are often considerable.

By adolescence, with the increasing demands of secondary school for organization and independence, ADHD-related challenges with EFs can be quite costly in terms of academic independence and performance. Indeed, the vast majority of children with ADHD continue to show high levels of symptoms and impairments throughout adolescence and even beyond (see Biederman et al. 2010a). Moreover, the progression of comorbidities for the most symptomatic youth includes elevated risk for delinquency (particularly when earlier signs of aggression have been present), substance abuse (particularly for boys), and self-injury and suicidal behavior (particularly for girls, as discussed in the next section). Key references for these comorbidities include the work of Molina et al. (2009) and Lee & Hinshaw (2004), as well as the reviews of Barkley (2015) and Hinshaw & Scheffler (2014). Clearly, given the many challenges of the adolescent years in general, the kinds of impairments and comorbidities linked to ADHD often become more severe.

Despite the prevailing belief, a few decades ago, that ADHD (or, as it was then called, hyperactivity or hyperkinesis) vanished before adulthood, a host of longitudinal evidence reveals that, in a majority of cases, symptom levels—particularly inattention and problems with impulse control, as motor overactivity per se typically transmogrifies into mental, as opposed to physical, restlessness—and related impairments remain high (for early accounts, see Huessy 1974, Weiss & Hechtman 1993, Wender 1995; for long-term prospective data, see Klein et al. 2012). In a thoughtful and provocative review, Asherson et al. (2016) emphasize the strong clinical importance, as well as neurobiological reality, of ADHD during the adult years. Interpersonal issues,

emotion dysregulation, and job-related performance decrements continue to plague many adults with ADHD.

Two lessons emerge from this whirlwind tour of ADHD-related symptoms and impairments across the life span. First, what is often characterized as comorbidity—technically signifying the joint presence of two or more independent disorders in the same individual at the same time (Caron & Rutter 1991)—may in fact be an artifact of overlapping symptoms within existing nosologies or may even reflect a developmental unfolding of increasingly severe complications that result from a given vulnerability. In other words, the extraordinarily high levels of apparent comorbidity between ADHD and a wide range of additional psychiatric conditions (for a seminal review, see Angold et al. 1999; see also Newcorn et al. 2004 for information on the impact of comorbidity on developmental outcomes) could actually reflect, in a number of cases, unfolding ontogenic processes that emanate from transactions between strongly heritable trait impulsivity and challenging, even toxic, family, school, peer, and neighborhood environments (Ahmad & Hinshaw 2017, Beauchaine & Hinshaw 2016, Beauchaine & McNulty 2013). Such unfolding processes often exemplify heterotypic continuity, the progression of developmentally unfolding manifestations of gene–environment correlations and/or interactions into different behavioral manifestations of an underlying trait (see, for example, Dodge & Rutter 2011).

In other words, it is not immediately apparent that trouble with paying attention and regulating classroom behavior during kindergarten and the early elementary grades would necessarily lead into serious substance use problems, placement in juvenile hall, or escalating patterns of self-destructive behavior. Yet these kinds of longitudinal progressions characterize many children who display early ADHD. Descriptive, too-often static classification systems like the DSM are not well equipped to comprehend such essential developmental paths (see Hinshaw 2017 for elaboration). The field is too often left with a range of multiply diagnosed individuals for whom underlying causal mechanisms may be obscured.

Second, to understand this kind of unfolding process, a multiple-levels-of-analysis approach is essential (Cicchetti 2008). Again, the strongly heritable trait of impulsivity, reflecting products of genetic and epigenetic processes, yields highly maladaptive outcomes when the development of structural and functional brain regions and pathways fails to meet age-related expectations (see Shaw et al. 2006, 2007; Castellanos & Proal 2012). These outcomes are particularly likely when difficult parent–child interactions, unhealthy peer relationships, and unequipped school settings potentiate and further shape the behavioral manifestations of underlying biological propensities. In short, as emphasized throughout this review, ADHD lies at the confluence of genetic vulnerability and environmental potentiation.

GIRLS AND WOMEN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER

A generation ago, clinical wisdom strongly suggested that ADHD rarely existed in girls. It is in fact true that, as with all other neurodevelopmental disorders—including autism spectrum disorders, aggressive conduct problems, and Tourette's disorder—boys show a higher prevalence than do girls (Lahey et al. 1994, Novik et al. 2006, Willcutt 2012). This gender-related disparity presumably results from, among other factors, males' greater genetic vulnerability as well as their propensity to respond negatively to a number of early life stressors. Population-based data reveal that the male:female sex ratio for ADHD in childhood and adolescence approximates 2.5:1, which is lower than is the case for autism or serious aggression but higher than for most learning disorders. Still, these statistics indicate that ADHD can and does exist in millions of females in the United States and beyond.

By adulthood, however, the sex ratio narrows, signaling that (*a*) women are more revealing of relevant symptoms than men; (*b*) women tend to present with inattentive forms of the condition, which are more likely to persist than those marked exclusively by impulsivity and hyperactivity; and/or (*c*) potential adult-onset cases of ADHD are more likely to exist in females (for selected literature on this latter, controversial topic, see Agnew-Blais et al. 2016, Moffitt et al. 2015).

A relevant conceptual issue is the gender paradox (see Eme 1979, 1992). The contention of this paradox is that, for the sex or gender with lower prevalence of a given condition—such as males in regards to major depression—the disorder, when it exists, will be more severe, requiring a greater genetic vulnerability or accumulation of other risk factors to lead to its onset (for relevant information regarding ADHD, see Gaub & Carlson 1997, Gershon 2002). Despite this theoretical interest, however, the vast majority of the research literature on ADHD pertains to boys and men. Over twenty years ago, our research group made a conscientious effort to understand ADHD in girls, including its development into adulthood. The relevant investigation, called the Berkeley Girls with ADHD Longitudinal Study, has contributed to the literature on girls and women with ADHD (see also Biederman et al. 2010b).

Details of sample ascertainment, along with initial findings, were discussed by Hinshaw (2002), as well as Blachman & Hinshaw (2002) and Zalecki & Hinshaw (2004). In short, we investigated girls with carefully diagnosed ADHD—both the inattentive presentation and the combined (inattentive plus hyperactive/impulsive presentation)—as a part of naturalistic, ecologically valid summer programs when they were in elementary school, along with an age- and ethnicity-matched comparison group of typically developing girls. From our baseline assessments and from data collected during the summer programs, we determined that the ADHD sample displayed statistically and clinically significant deficits across parent, teacher, staff, peer, and objective-test informants, spanning every domain measured (e.g., academic and peer-related impairments, relational aggression, friendship quality, use of special educational services, self-perceptions, family functioning), even with strict statistical adjustment for demographic variables and IQ (we deployed these covariates in our follow-up data analyses, discussed below in this section, as well). Thus, we found ADHD in girls to be associated with a plethora of real-life problems. In addition, their EFs, measured via objective neuropsychological tests, were significantly worse than those of the comparison girls, with effect sizes in the medium range (Hinshaw et al. 2002).

All of our prospective assessments have yielded retention rates nearing 95%, removing large attrition rates as sources of bias. By our initial, 5-year follow-up, when the girls were in their early-to-mid-teenage years, significant impairments persisted in all domains we investigated, including EFs, as well as signs of disordered eating (Hinshaw et al. 2006, 2007; Mikami et al. 2008). Thus, ADHD was not a transitory phenomenon for the affected girls, as its symptoms and impairments clearly lasted into adolescence. In fact, even in cases for which clinical symptoms dipped below clinical thresholds for diagnosis, impairments typically persisted. Additionally, whereas adolescent outcomes varied considerably across the ADHD sample, distressingly few girls showed clearly resilient functioning and positive adjustment (Owens et al. 2009).

When we subsequently followed the sample into early adulthood, fascinating yet clinically distressing patterns crystallized. As expected, academic, peer-related, self-concept-relevant, familial, and neuropsychological impairments persisted (see Hinshaw et al. 2012, Miller et al. 2012a). Except for a few selected outcomes, including antisocial behavior and peer rejection (for which girls with early impulsivity showed worse outcomes), few effects emerged when we attempted to predict impairment from the childhood designation of ADHD types (now termed presentations). In other words, girls with both the combined and inattentive forms of ADHD were at high risk for nearly every measure of impairment we examined, including EF impairment. Moreover, predictions from childhood EF deficits to key young-adult functional outcomes were robust (Miller et al. 2012b,

2013). Somewhat surprisingly, risk for substance use problems was not above that of the normative comparison group, and the eating-related pathology evident during adolescence for the girls with ADHD no longer remained a significant area of concern, given relatively high rates of binge eating and body-image distortion among the comparison young women (Hinshaw et al. 2012).

In addition to repeating key measures—essential for longitudinal research—we measured new domains of outcome during our young-adult follow-up. First, the girls with childhood ADHD were at high risk for experiencing intimate partner violence (Guendelman et al. 2016a). Second, striking findings emerged for the outcome of self-harm, including both nonsuicidal self-injury (NSSI)—including cutting, burning, and self-mutilation without the intent of ending one's life—and actual suicide attempts. As detailed by Hinshaw et al. (2012) and Swanson et al. (2014), girls who had been diagnosed in childhood with the combined presentation of ADHD—that is, those with noteworthy hyperactivity/impulsivity in addition to inattention—showed far higher rates of both NSSI and suicide attempts than both those with the inattentive presentation and those in the comparison group. Indeed, 51% of the girls with the combined presentation of ADHD were engaging in moderate to severe NSSI, and over 22% had made at least one suicide attempt, over twice as many as the girls with the inattentive presentation and the comparison girls in the case of NSSI and three times as many in the case of suicidal behavior. In these results, early impulsivity, rather than inattention, was the key risk factor.

Moreover, Guendelman et al. (2016b) found that, among the girls with ADHD who had also experienced maltreatment earlier in life—physical abuse, sexual abuse, or neglect (or some combination)—fully one-third had made a suicide attempt by our 10-year follow-up. These results are parallel to those for another highly heritable condition, bipolar disorder, for which the presence of childhood maltreatment predicts comorbid disorders, a worse course, and heightened risk for suicide attempts (see Brown et al. 2005). In both instances, heritable risk is accentuated by trauma with respect to clinically important outcomes such as attempted suicide.

Additional investigations have examined adolescent mediators of the predictive association between childhood ADHD and young-adult self-injury. Swanson et al. (2014) discovered that, during early-to-mid-adolescence, comorbid externalizing behavior patterns, in addition to deficits in response inhibition (revealed from an objective neuropsychological test), partially mediated the risk for severity of NSSI by early adulthood. Yet only comorbid internalizing behavior patterns (e.g., anxiety, depression) mediated the risk for suicide attempts. Also, in the domain of peer relationships, Meza et al. (2016) found that peer victimization (physical and/or verbal, as reported by participants) partially mediated the link between early ADHD-related cognitive and behavioral patterns and NSSI. Yet peer rejection (as reported by participants' teachers) partially mediated the link to subsequent suicide attempts. In short, behavioral and emotional, neuropsychological, and peer-related factors play key roles in pathways to self-injury for the vulnerable population of girls with ADHD.

Regarding our 16-year follow-up, conducted when participants were in their mid-to-late 20s, space allows only headline coverage (see Owens et al. 2017). Most saliently, even for cases in which relevant symptoms abated to the point where ADHD was no longer detectable, impairments persisted in important domains of functioning. For example, regardless of the persistence of ADHD symptoms, risk for unplanned pregnancy was substantially higher in the girls diagnosed with ADHD years before (nearly 44%) than in the comparison group (10%). In addition, markers of educational attainment (objective test scores as well as years of education and highest degree attained) were well behind those of the comparison sample regardless of ADHD persistence. Yet for most other outcomes, including comorbid psychopathology, self-injury, and occupational functioning, the worst impairments were evident for the young women whose ADHD-related symptoms had persisted over time. In all, adult impairments were substantial.

Consistent with the ontogenic process perspective, Owens & Hinshaw (2016) also found that a childhood measure of neurocognitive vulnerability, indexed from EF deficits plus teacher-reported cognitive problems, reliably predicted the presence, 16 years later, of conjoint internalizing and externalizing symptoms, over and above ADHD behavior patterns per se. In addition, in keeping with a multiple-levels-of analysis approach, processes measured during adolescence and early adulthood—particularly low self-control and poor delay of gratification (intraindividual level), peer problems (social level), and low educational attainment (school level)—mediated the links from early neurocognitive vulnerability to comorbid psychopathology in adulthood. Parenting stress factors (family level) played a moderating role, such that the individual- and school-level mediator paths were strongest in the presence of low family distress. Once again, equifinal pathways appear to exist—and ascribing predictive effects of early ADHD to any one level of analysis would fail to do justice to the complexity of the multilevel processes involved.

In sum, girls with ADHD often show a difficult developmental course. Risk for self-injury—intensified by the presence of early maltreatment and mediated, during adolescence, by comorbidities, deficits in response inhibition, and maladaptive peer relationships—is substantial. Persisting academic and vocational problems, as well as strong likelihood of unplanned pregnancy, are other core outcomes. Multiple levels of analysis are needed to comprehend relevant developmental pathways.

SURGING US PREVALENCE: WHAT ARE THE REASONS?

If we switch gears to consider issues of social policy, we must ask the question as to what might explain the rapid expansion of diagnosed prevalence of ADHD in the United States since the turn of the twenty-first century. Much of the basis for this claim emanates from the National Survey of Children's Health (NSCH), a periodic survey of large, representative samples of the nation's families. By the early 2000s, questions about the diagnosis of ADHD and its treatment with medication had been included (Visser et al. 2010). In brief, parents are asked whether their child has either currently or ever been diagnosed with ADHD [or attention deficit disorder (ADD)] or whether a professional has told them that their child has that condition. Among all 4–17-year-olds in the United States, the rate of "ever diagnosed" climbed 41% from 2003 to 2012, with one in nine children receiving that designation by the latter date (Visser et al. 2014). Indeed, as noted above, among boys older than elementary school age, overall rates approached 20%, signifying an alarming rate of one in five.

Of course, these figures may overstate the true prevalence of ADHD. In the absence of unequivocal biological markers for any form of mental disorder, true prevalence is impossible to know. The best, evidence-based diagnostic processes—which include thorough developmental histories and use of normed rating scales from adult informants—yield worldwide estimates of 5–7% of the youth population. Thus, the rate of diagnosed prevalence in the United States has surged to nearly double those rates.

In terms of ADHD's prevalence across the past century, space precludes a comprehensive review, but evidence exists that, once hyperactivity or hyperkinesis became a viable diagnosis in the 1960s, rates of diagnosis slowly but steadily climbed. A sharp increase in diagnosis occurred during the early-to-mid-1990s, linked to three policy-related shifts (for detailed coverage, see Hinshaw & Scheffler 2014). First, the federal special education law was renamed as the Individuals with Disabilities Education Act and re-authorized at the beginning of the 1990s, with the specific inclusion of ADHD as an "other health-impaired condition" for which accommodations could be sought. Second, Medicaid was re-authorized, including ADHD as a condition for which one could potentially be reimbursed for assessment and treatment—however, for the latter, only medication

treatment is reimbursed. Third, a Supreme Court decision on Supplemental Security Income led to the inclusion of ADHD, if accompanied by documented, severe impairments, as a covered condition. The key conclusion is that, if a given diagnosis can lead to accommodations and/or benefits, it will be sought.

In their discussion of forces outside the United States that are alleged to spur ever-higher diagnosis of psychiatric conditions like ADHD, Conrad & Bergey (2014) posit that the concepts of medicalization and globalization are central. Indeed, they discuss efforts from pharmaceutical firms (see also Schwarz 2016), the growth of advocacy groups that pressure government insurers to cover medication treatment, and the increased online presence of ADHD—including symptom checklists and algorithms for self-diagnosis.

Not only has diagnosed prevalence surged in the United States, as well as abroad (see Hinshaw et al. 2011), but major variation is readily apparent across regions and states (for an international example, see Madsen et al. 2015). In the United States, such variation is dramatic, as nearly threefold differences in rates of diagnosed prevalence across regions and states exist. Specifically, the South and Midwest show far higher rates of ADHD diagnosis (and, in general, of medication treatment for ADHD) than the Far West (Visser et al. 2014). In states like North Carolina, Arkansas, and Indiana, an alarming rate of nearly one in three adolescent boys has been diagnosed with ADHD at some point. Yet in California and Nevada, rates are far lower, consistent with averages in the rest of the world.

The search for relevant factors to explain such discrepancies has a robust history in a research area termed small-area variation (Wennberg & Gittelsohn 1973). Their formulation addressed variability in diagnosis and especially treatment of medical conditions, positing that such variation was influenced far less by actual disease distribution than by physician beliefs about specific indications for treatments for the condition in question. One potential explanation for the discrepancies in ADHD diagnosis would be demographic factors, such as ethnic variation, which have been related to diagnosis rates (with Hispanic families traditionally low with respect to ADHD diagnosis). Yet adjusting for ethnic differences across states and regions did little to alter the dramatic differences in rates of ADHD diagnosis (Fulton et al. 2015, Hinshaw & Scheffler 2014). That is, despite the far greater concentration of Hispanic families in California (a low-diagnosis state) than in North Carolina (an extremely high-diagnosis state), adjusting statistically for this demographic difference still left nearly twice as many diagnosed youth in the North Carolina. Our research team also examined whether such well-established factors as the regional or state density of health professionals might underlie the marked difference in ADHD diagnoses, as it does for other mental health and physical health conditions. Yet concentrations of pediatricians or child specialists was not significantly associated with youth ADHD diagnoses in the NSCH.

A shift in focus to educational policy proved revelatory. Specifically, changes in US policy in recent decades provided the opportunity for a natural experiment related to the provision of incentives to schools and school districts regarding student scores on high-stakes standardized testing (Fulton et al. 2015). In brief, following marked concern over diminishing standardized test scores in the United States, which began in earnest in the 1980s—and which often focused on public schools with large numbers of low-income youth—many states began to implement consequential accountability legislation. This legislation made public school districts accountable for their students' levels of achievement, such that in the absence of gains, negative consequences would ensue (e.g., newspaper accounts, cuts in public funding to given districts). Such direct, output-focused incentives and punishments had the goal of more immediate and dramatic test score increases than previous input-focused policies (e.g., lowering of classroom size).

By the early 2000s, 30 US states had enacted such consequential accountability legislation, with the highest concentration in the South, which had already shown high rates of ADHD

diagnosis at the time of the first NSCH in 2003. Fortuitously for our research design, at just this time, the educational reform package called No Child Left Behind (NCLB) became law, with implementation starting in the 2002–2003 school year—precisely the initial year for inclusion of NSCH's ADHD-related questions. Via this legislation, the remaining 20 states (plus the District of Columbia) were immediately mandated to implement consequential accountability.

Of course, our research team did not randomly assign consequential accountability to the states in question, but with fixed-effects statistical models and rigorous covariates, we had an intriguing contrast in place. In a follow-up 4 years later, as we had hypothesized, for the most impoverished youth in the 21 states with NCLB-mandated accountability beginning in 2002–2003 (i.e., youth concentrated in public, Title I–backed schools), rates of ADHD diagnoses surged compared to those in the states that had enacted such legislation previously. Indeed, by the second wave of the NSCH in 2007, for children in families within 200% of the federal poverty level, rates of ADHD diagnoses escalated by nearly 60%, compared to a 10% increase for comparable children in those states that had enacted consequential accountability some years before. No such effect emerged between these two groups of states for either (*a*) middle-class and more affluent youth or (*b*) those in private schools, as such schools are not accountable under NCLB.

What are the relevant mechanisms resulting in these findings? First, school districts would, in all likelihood, be incentivized to refer their lowest-scoring youth for ADHD-related assessment to facilitate medication and perhaps educational interventions. Second, and more nefariously, districts might push for ADHD diagnoses of low-achieving youth, given that a special education designation would remove that child's scores from the district's overall average. Evidence exists that, before it was banned several years later, precisely this gaming of the system was practiced in some locales (see also Hinshaw & Scheffler 2018).

Of course, the originators of NCLB had no interest in ADHD, as this legislation was an attempt to lift school achievement nationwide. Thus, the ramifications linked to ADHD comprise what are called unintended effects or unintended consequences. As a follow up, it is important to note that, between 2007 and 2012 (the second and third waves of the NSCH survey data), the Obama administration had begun to dismantle NCLB and replace it with a different set of incentives for high-performing schools. Not surprisingly, the dramatic difference in rates of increase of ADHD diagnoses for poor versus wealthier children vanished during this time period (Fulton et al. 2015).

Finally, additional state legislation in the United States at the beginning of the twenty-first century has also affected rates of ADHD diagnosis. For example, as elaborated by Fulton et al. (2015), several states implemented laws designed to curtail the rights of schools to insist on medication treatment for youth with ADHD. Analysis of the NSCH database revealed that, in such states, rates of ADHD diagnosis remained nearly flat from 2003 to 2012, whereas in the remaining states, rates surged. Once again, policy appears to be a significant factor in explaining variation in ADHD diagnostic prevalence.

Overall, educational practices and policies play an important role in explaining differences in rates of ADHD diagnosis for children of different social classes and in driving ever-higher rates of diagnosed prevalence. As reviewed above, academic performance pressures may constitute a precipitating factor related to increases in the rates of diagnosis of ADHD through the unintended consequences of consequential accountability statutes. At the same time, other laws—directly intended to reduce ADHD medication pressures—result in lowered rates of ADHD diagnosis.

Does evidence exist for any actual increase in the true prevalence of ADHD? Nigg (2006) posited that the increased presence of neonatal intensive care units, which have greatly increased survival rates of low-birth-weight infants, may in fact increase the true prevalence of conditions like ADHD. Still, increases in diagnosed prevalence, linked to educational policies or other social forces, appear to be far greater. I highlight once again that non-evidence-based diagnostic

assessments (e.g., a few minutes in a pediatrician's office) are undoubtedly linked to these phenomena. That is, false-positive diagnoses may well emerge from evaluations that fail to include rating scales, thorough developmental histories, differential diagnoses, appropriate use of cognitive and achievement tests, and the like. Overly quick and cursory assessments can also trigger underdiagnosis related to ADHD, i.e., when the clinician in question fails to obtain ecologically valid data from the individual's school, social, or vocational settings and concludes, on the basis of an informal office assessment, that the individual could not exhibit ADHD. Overall, if more stringent diagnostic standards were taught, accepted, and reimbursed, much of the critique of current diagnostic practices related to ADHD could be eliminated—and, I posit, school accountability legislation would probably not result in increased ADHD diagnoses for disenfranchised children.

TREATMENT STRATEGIES

An entire review could be devoted to the controversial and essential issues related to intervention for ADHD. In this highly selective overview, the vast literature in this area is barely touched on.

Although many forms of treatment for ADHD are touted, only two truly evidence-based forms of intervention exist, each having received scrutiny in literally hundreds of controlled trials: (*a*) medication, chiefly stimulants but also noradrenergic agents, and (*b*) behavioral (for youth) and cognitive behavioral (for adults) forms of psychosocial treatment. For children and adolescents, behavioral intervention chiefly involves management interventions with parents, consultation with teachers, and structured forms of social skills training with youth themselves. The overall goals are to provide extrinsic rewards for successive approximations of important academic, behavioral, and social skills. For adults, extremely promising work reveals that organizational and time-management skills as well as emotion regulation can be learned via cognitive behavioral intervention strategies (e.g., Solanto 2011), although the data are far skimpier than those for children and adolescents regarding traditional behavioral interventions. A recent meta-analysis summarizes the voluminous controlled research on pharmacologic and psychosocial interventions for ADHD (Catalá-López et al. 2017).

Among potentially promising forms of intervention, neurofeedback has not, in recent trials, compared favorably to careful control conditions (e.g., sham feedback; see Schönenberg et al. 2017). Dietary interventions, formerly viewed as a panacea before controlled trials yielded far more pessimistic findings, may yield some improvements in some cases, particularly with respect to restriction of dyes and additives, though not in the same range of effect size as medications or behavioral interventions (see Nigg et al. 2012). Relatively recent controlled trials of aerobic exercise show promising results (Cerrillo-Urbina et al. 2015). Specific cognitive training—most saliently, to enhance working memory—has been advocated, but recent reviews suggest poor transfer of skills to real-world tasks (e.g., Mawjee et al. 2015, Melby-Lurvåg & Hulme 2013). There are simply not enough data regarding mindfulness interventions, practices of martial arts, or exposure to green environments, despite advocacy for these treatments. More dubious forms of intervention, including chiropractic treatments, cerebellar stimulating exercises, blue-green algae, and homeopathy, and other non-evidence-based interventions, are best avoided.

Stimulant medications provide reduction of relevant symptoms in a clear majority of cases, as attested by a vast literature of controlled trials, yielding medium, large, or very large effect sizes on average. They are generally superior to noradrenergic medications; both classes are superior to placebo (Catalá-López et al. 2017). Even large-scale, relatively long-term investigations attest to this finding (MTA Coop. Group 1999). Indeed, medication treatment of ADHD is more successful, on average, than pharmacologic intervention for any other child or adolescent psychiatric condition. Side effects can be a real concern but are often managed with adjustments to dose levels and their timing.

Yet placebo-controlled medication interventions cannot last for years. Despite the inherent problems in investigating outcomes for any class of interventions based on naturalistic investigations—in which various selection biases may well exist—accumulating evidence from prospective interventions reveals the lack of long-term sufficiency of medications as a sole treatment for ADHD (e.g., Swanson et al. 2017). Indeed, many, if not most, youth with ADHD stop taking medication during the teen years, and longitudinal investigations reveal no conclusive evidence that receipt of medications during childhood or adolescence slows trajectories toward substance use disorders or antisocial behavior (Molina et al. 2009, 2013). Yet population-based studies reveal that, during periods of receipt of ADHD medications, risk for substance abuse and serious accidents is reduced, often substantially (e.g., Chang et al. 2014, Quinn et al. 2017). In the long run, pharmacologic intervention alone is rarely adequate for complex, comorbid cases or for enhancing the skills and competencies so clearly needed to counter the long-range impairments linked to ADHD. Indeed, in a reconsideration of findings from trials such as the Multimodal Treatment Study of Children with ADHD, Hinshaw & Arnold (2015) have emphasized the need to intervene with parents, schools, and even wider communities; to emphasize skill building as much as symptom reduction; and to gear intervention toward amelioration of key life impairments. In short, combination treatments appear optimal for most individuals with ADHD if the objectives are to go beyond symptom reduction per se. Moreover, a number of comorbid conditions (e.g., anxiety disorders, depression, disruptive behavior disorders, learning disabilities) require interventions that far exceed ADHD medications.

Huge controversy surrounds the use of stimulant medications as performance enhancers for the general population. In brief, despite continued advocacy for cognitive enhancement (neuroenhancement) of people without ADHD via stimulant medications (for a recent argument, see Lyon 2017), Smith & Farah (2011) and, in an experimental investigation, Ilieva et al. (2013) contend that the effects of stimulants on actual cognitive enhancement (beyond simple alertness) are not strong. Moreover, and the risk for developing dependence on stimulants in the general population is considerable. These issues keep the topic ensnared in controversy.

The positive effects of behavioral interventions take longer to occur than do those of stimulant medications, and behavioral interventions require considerable effort on the part of parents, teachers, and individuals with ADHD themselves. Cognitive behavioral treatments for adults also require time and effort. Yet skill gains and reductions in problem behaviors have clearly been documented (see Fabiano et al. 2009), and debate continues as to whether medication, rather than psychosocial alternatives, should be the first-line intervention for ADHD. Except for preschool-aged children, medication is the default indication in the United States; however, elsewhere, the consensus is that medication should be tried later (e.g., Nat. Inst. Health Clin. Excel. 2009). Finally, as noted above, combinations of medication and behavioral interventions appear to offer the best chance of enhancing competencies and producing normalization of functioning (see also Hinshaw et al. 2000). Yet research on community-based interventions reveals that pediatric practices are often suboptimal due to a lack of psychosocial or behavioral treatment options (Epstein et al. 2014).

CONCLUSIONS

The global, impairing, costly, and controversial topic of ADHD mandates multilevel efforts with respect to scientific research, provision of evidence-based clinical services, and integrative dialog regarding policy endeavors (Singh 2008). Critics who contend that ADHD is exclusively a social construct—a child- or patient-blaming label to mask social ills—are as shortsighted as those who focus exclusively on the pathology of particular neural pathways related to deficient attention or poor impulse control, without due consideration of the kinds of social and educational contexts in which self-regulation is expressed. The need for integrative perspectives on ADHD in particular

and developmental psychopathology in general has never been greater (see Hinshaw 2015, 2017; Hyde 2015; Mash & Barkley 2014; Nigg 2017).

Furthermore, without increased advocacy for utilization of evidence-based standards for assessment and diagnosis, the diagnosed prevalence of ADHD is highly likely to continue to outpace true prevalence, especially in high-performance societies. Such a continuing trend will expose many individuals to unneeded and potentially harmful treatments—and it will paradoxically fuel the stigmatization that already exists related to ADHD in particular and mental disorders more generally (Hinshaw & Stier 2008, Martinez & Hinshaw 2016).

Indeed, how could a diagnostic category revealing such rapid increases in prevalence as ADHD—and one that receives the publicity that it does—still be stigmatized? For one thing, people with ADHD often behave inconsistently and erratically, probably leading many in the general public to believe that misbehavior is intentional. At a larger level, when such a condition becomes linked in the public's mind with overdiagnosis and the desire for accommodations (for both children, linked to educational supports, and adults, linked to the attaining of medications), it may well lose credibility as a legitimate disorder.

This article has emphasized a multiple-levels-of-analysis approach to all phenomena related to ADHD. Indeed, knowledge is expanding rapidly on fronts ranging from molecular genetics and epigenetic processes, to brain networks and connectivity, to temperament and the unfolding of heterotypically continuous behavior patterns, and to a host of socialization forces in homes, schools, cultures, and nations. The clear need is for scientists and clinicians to span and integrate across such levels—no easy task, but one that is essential for future scientific efforts and clinical care.

In the end, both enhanced public knowledge regarding the neurobiological validity of ADHD and humanization of those with the condition are crucial. Indeed, the impairments linked to ADHD are sufficiently devastating that children, adolescents, and adults dealing with this syndrome require the best of evidence-based assessment, intervention, and support. It is incumbent on those involved in scientific, clinical, and preventive efforts to insist on sound scientific standards, respectful and multilevel dialogue, thorough diagnostic evaluations, and well-disseminated clinical and preventive efforts. Without progress on these fronts, impairments and social costs will only grow.

SUMMARY POINTS

1. ADHD is a controversial yet all too real clinical condition marked by developmentally extreme and impairing symptoms of inattention and hyperactivity/impulsivity. The burden of ADHD spans underattainment in academics and underperformance in vocational endeavors, compromised relationships with family members and peers, suboptimal health-related outcomes, and major outlays across multiple societal systems of education and health care. ADHD is typically a long-standing behavioral disorder, with impairments persisting into the adult years.
2. A multiple-levels-of-analysis perspective is essential for understanding causal factors and developmental pathways. The symptom dimensions related to ADHD are highly heritable; other biological factors (e.g., prenatal substance use by mothers, low birth weight, environmental toxins) are relevant for etiology, as well. Yet discordant family interactions, as well as poor fit with educational environments, can and do maintain symptom patterns and promote an unfolding spiral of low achievement, externalizing behavior patterns, and—by adolescence and beyond—risk for substance use, self-injury, vocational problems, and lowered independence.

3. Underlying mechanisms include dysregulated attentional capacities, deficits in executive functioning (particularly working memory and response inhibition), and low intrinsic motivation (including excessive delay aversion). Because of the presence of equifinality, it is possible that distinct—or even overlapping—mechanisms underlie ADHD across vulnerable individuals.
4. Girls and women can and do present with ADHD, and their impairments are considerable. Indeed, their developmental course may well include heterotypically continuous pathways to significant self-injury—accentuated in the presence of internalizing and externalizing comorbidities, deficits in response inhibition, and maltreatment.
5. The diagnosed prevalence of ADHD in the United States has been rising precipitously in recent years, apparently well beyond its true prevalence and at rates above those of most of the rest of the world. Increased recognition of the condition is clearly a factor, but policy changes deeming that an ADHD diagnosis can garner needed services are also relevant. Furthermore, an unintended consequence of consequential accountability legislation, designed to boost school achievement test scores, appears to be an increase in ADHD diagnoses for public school children in the lowest socioeconomic strata.
6. Medication (usually stimulants) and behavioral or cognitive behavioral treatments are the core evidence-based interventions for ADHD. Multimodal treatment, involving combinations of carefully monitored medication and behavioral intervention, is usually optimal for promoting competencies as well as reducing problem behaviors.

FUTURE ISSUES

1. Despite the considerable heritability of ADHD, the particular genes contributing to vulnerability are proving elusive, as is the case with all mental disorders. Moreover, the particular kinds of gene–environment interplays that are relevant to particular symptoms and impairments remain largely unknown.
2. The heterogeneity inherent in the symptom presentations, underlying mechanisms, and developmental outcomes related to ADHD developmental signifies that future research is needed to untangle the separable and combined pathways to this syndrome.
3. Manifestations of and mechanisms related to ADHD in females and in adults remain less well identified than in males and in youth.
4. Promotion of evidence-based assessment and treatment procedures is a major priority. At the same time, better translational science is needed to approach the kinds of precision intervention that are so urgently needed.

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