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Attention-Deficit Hyperactivity Disorder (ADHD): Does New Research Support Old Concepts?

Lydia Mary Furman, MD

Objective: To examine the evidence for and against the classification of attention-deficit hyperactivity disorder (ADHD) as a valid disease entity, as defined by the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*), criteria. *Data Sources:* Sources included but were not limited to published literature on ADHD accessed via PubMed (http://www.ncbi.nlm.nih.gov/PubMed/). *Study Selection:* Peer-reviewed research, review articles, consensus statements, "white papers," and proceedings of professional meetings were used. *Data Extraction:* Focused on evidence base and scientific validity of conclusions. *Data Synthesis:* Evidence for a genetic or neuroanatomic cause of ADHD is insufficient. Experimental work shows that executive function deficits do not explain ADHD. The psychometric properties of widely used ADHD rating scales do not meet standards expected for disease identification. *Conclusions:* ADHD is unlikely to exist as an identifiable disease. Inattention, hyperactivity, and impulsivity are symptoms of many underlying treatable medical, emotional, and psychosocial conditions affecting children.

Keywords: ADHD; attention-deficit hyperactivity disorder; stimulant

Attention-deficit hyperactivity disorder (ADHD) is now practically a household word. Estimates suggest that anywhere from 2.4 to 4.4 million children aged 4 to 17 years in the United States may meet published criteria for ADHD, yet this disease has no established biological cause or objective diagnostic test.[1-3] Critics have challenged the validity of the diagnosis.[4-8] Roughly 1 in 25 children in the United States has been prescribed stimulant medications, with a steadily increasing price tag; in 2003, $2.4 billion dollars were spent on ADHD drugs in the United States.[9] The crux of this problem has been highlighted by publication of the 3-year outcomes of the National Institutes of Mental Health sponsored Multimodal Treatment Study of Children with Attention Deficit Hyperactivity Disorder, which enrolled 579 ADHD-diagnosed children.[10-15] Although neither blinded nor placebo controlled, the study reported at 36 months that all treatment groups *with and without stimulant medication* were improved from baseline and did not differ significantly on any measure of outcome, and that children receiving (as compared with not receiving) stimulant medications showed significant symptom deterioration from 24 to 36 months and higher delinquency ratings at 24 and 36 months.[10-15] These unexpected outcomes are not easily explained by the orthodox paradigm of ADHD as a neurobehavioral disease best treated with stimulants. The results give pause to thoughtful clinicians and suggest the need for more rigorous and transparent diagnostic and therapeutic methods.

Evidence for an Etiology of ADHD

A *genetic cause* for ADHD is postulated. A prominent ADHD researcher states, "Family studies have identified a 2- to 8-fold increase in the risk for ADHD in parents and siblings of children with ADHD. Various twin and adoption studies have also highlighted the highly genetic nature of ADHD."[16] Jay Joseph has elegantly unraveled the evidence behind the rhetoric and points out that not only does "familial" not distinguish between "nature" (genes) and "nurture" (environmental factors), but the logic behind family, twin, and adoption studies is fundamentally flawed.[17-20] Most ADHD reviews confuse "familial" with "genetic," and trivialize the potential role of nongenetic factors with short lists such as "food additives/diet, lead contamination, cigarette and alcohol exposure, maternal smoking during pregnancy, and low birth

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weight."[16] In fact, nongenetic familial factors are powerful and difficult to measure and include the effects of culture, religion, learning, parenting, and socioeconomic adversity.

Twin studies that purport to demonstrate a genetic cause for ADHD are scientifically untenable. Studies are based on the "equal environment assumption," which assumes that, contrary to evidence, (*a*) the only difference between monozygotic and dizygotic twins is greater genetic similarity between the former than the latter and (*b*) monozygotic and dizygotic twin pairs share the same behavior-influencing environment. An extended literature documents that monozygotic as compared with dizygotic twins do not experience equal environments; rather, monozygotic twins share greater psychological and physical closeness, are treated more similarly by their parents, and more report "extreme closeness" (65% vs 19%) and being "inseparable as children" (73% vs 19%) than dizygotic twins.[21,22] No studies report on ADHD-diagnosed twins who are reared apart. Greater concordance between monozygotic than dizygotic twins for the diagnosis of ADHD does not distinguish between the roles of genes and family factors or lead to the conclusion that ADHD is genetic.

Methodologic problems with adoption studies have been elucidated, again by Joseph.[17-20] Researchers propose that the effects of genes and environment can be differentiated by comparing children with (and without) ADHD who are living with their own parents versus with adoptive parents. However, it is well appreciated that parents seeking to adopt are screened for mental health problems whereas biologic parents are not, and most children in adoptive care have endured traumatic experiences or emotional upset. Thus, neither adoptive and biological parents nor their children are comparable with regard to nongenetic factors. No adoption study uses blinded diagnosticians to identify children with ADHD, and no study has assessed the biological relatives of adoptees. These scientific limitations preclude meaningful contribution to an understanding of ADHD.

Psychiatric geneticists initially embraced genome scans and candidate gene studies as ways to identify a genetic cause of ADHD. It is clear that genome-wide scans have yielded negative results.[23] Candidate molecular gene research has focused primarily on neurotransmitters affected by ADHD medications. This literature is largely inaccessible to those not schooled in epidemiologic analysis of molecular genetic studies, creating reliance on reviews that are excessively enthusiastic and frankly misleading, describing results as having "produced substantial evidence implicating several genes in the etiology [of ADHD]."[23] Such a summary sidesteps several scientific issues.[24-27] A methodologic white paper on gene–disease associations cautions, "Regarding the strength of association, many of the genetic variants so far identified as influencing susceptibility to common diseases are associated with a low relative and absolute risk. Therefore exclusion of noncausal explanations for association is crucial."[25(p307)] This task has not been undertaken for ADHD.

Waldman and Gizer[26] outline areas for future research, illuminating difficulties with current studies. Individual study replicability has been poor, with both positive and negative results for each candidate gene. The most obvious explanation is small sample size with low statistical power. Multiple studies have sought to replicate findings of an association of the dopamine D4 and D5 receptor genes (DRD4 and DRD5), the dopamine transporter gene (DAT), the dopamine β-hydroxylase gene (DBH), the serotonin transporter and receptor 1B genes (5-HTT and HTR1B), and the synaptosomal-associated protein 25 gene (SNAP25) with ADHD. Meta-analyses have produced mixed results, for example, regarding whether or not the dopamine transporter gene DAT is related to ADHD.[28,29] The validity of meta-analysis for observational molecular genetics studies is debated, because the technique combines results of studies that may be disparate in design and subject ascertainment and exclusion.[26] Sample pooling is preferable because it combines data from individuals. However, family-based studies show pooled odds ratios that are barely significant (eg, dopamine D4 receptor gene 1.16 [1.03-1.13] and the dopamine transporter gene 1.13 [1.03-1.24]), whereas case–control studies, which show slightly higher odds ratios, are weakened by inherent susceptibility to the effects of population stratification.[23,30]

It is difficult to extrapolate a causal role for single markers in a candidate gene to ADHD as a whole, because individual genes are unlikely to act directly and independently of surrounding genes. It is also difficult to link candidate genes to specific measurable qualities of ADHD. This search for an "endophenotype" (a simplified phenotype of a more complex disorder that is closer to the biological cause or candidate gene) has not yielded an objective measure or mechanism.[31] Finally, studies of candidate genes have ignored the role of individual characteristics such as age, gender, age of onset, and gene–environment interactions, which are known to affect rates of ADHD diagnosis and have played a key role in other medical genetics stories (eg, breast cancer and BRCA1).[26] Swanson et al note,

> The existing studies of genetic and environmental factors do not meet the standards for modern molecular genetic studies . . . [which] emphasize that gene–gene and gene–environment interactions are likely to be present and require large sample sizes to detect and describe.[32(p53)]

Given the extraordinary variability of children labeled as ADHD, many of whose symptoms change over time, and the lack of any measurable endophenotype, the likelihood that any of the candidate molecular genes has a causal role in ADHD is as small as the very low pooled odds ratios would indicate, and it is misleading and inaccurate to state that any substantive "genetic cause" of ADHD has been identified.[33]

The evidence for a neuroanatomic cause/locus for ADHD has been similarly misrepresented. Studies of neuroanatomy are compromised by small numbers; use of "controls" with other neurologic diagnoses; inclusion of subjects who are not medication naive; failure to account for confounders, including prenatal and perinatal factors and other psychiatric diagnoses; and use of a cross-sectional rather than longitudinal approach (which is critical because myelination continues into early adulthood).[34] Leo and Cohen[35] have provided a critical review of studies on the neuroanatomy of ADHD, and they conclude that imaging of the neural circuitry of learning is at best a scientific goal for the future, not a current accomplishment. Executive function, deficits of which are proposed by Barkley as central to ADHD, is localized to the prefrontal cortex and frontostriatal regions, yet the most careful and methodologically acceptable study of children with and without ADHD did not find a significant difference in these regions after controlling for brain volume; rather, a difference in cerebellar volume was noted.[36,37] Other studies of overall and region-specific cerebellar volumes showed inconsistent rather than confirmatory results.[38] It is highly likely that complex brain functions recruit neural networks throughout the cortex and are not mapped identically in all individuals.[39-41]

The original unifying *neuropsychological theory* postulated for ADHD was a deficiency in executive function, specifically in inhibitory control.[36] A recent study comparing 75 boys with "severe" ADHD with 70 matched controls, however, found no group differences on executive function inhibitory control tests.[42] Meta-analyses have demonstrated that executive function dysfunction is "neither necessary nor sufficient to have a causal role in ADHD."[43(p1336)] No single executive function task defines all children with ADHD or ADHD subtype. Meta-analyses show low to moderate effect sizes across studies (d = 0.4-0.7; d = 0.6-0.8) and overlapping performance distributions, with some ADHD children testing as normal on all tests.[43,44] One meta-analysis found that only 16% to 51% of children with ADHD were impaired on any 1 of 5 typical tests of executive function and that 21% of children with ADHD, compared with 53% of controls, failed none of multiple tests of executive function.[44] Another meta-analysis of 83 studies found significant differences between groups on all 13 executive function tasks, but significant group differences were not found in 35% of comparisons (59 of 168).[43] "Clearly the strong predictions of the executive function deficit hypothesis of ADHD are not supported. The cognitive literature is thus incompatible with the assumption of pathophysiological homogeneity—of a single core deficit [for ADHD]."[39(p119)]

It is not surprising that more children diagnosed with ADHD than controls show impairment on tests of executive function. Because an ADHD diagnosis requires impairment in 2 settings, and in most cases 1 setting is school, children who have academic and educational problems are being compared with those who do not. It is also not surprising that children with academic problems have nonidentical results on neurocognitive testing.

Other neuropsychological theories of ADHD include executive function "subset" theories (working memory manipulation problems, "hot" [affect] driven rather than "cool" [abstract] executive function deficits), the theory of optimal stimulation/arousal deficit, reward response deficit theories, and the cognitive-energetic model.[39,45-50] A recent scholarly attempt to clarify the relationship between language disorders, spatial working memory manipulation deficits, and ADHD is confounded by significant group differences in intelligence quotients, by absence of significant group differences in ADHD Conners's Rating Scale scores, and by use of outcome measures (tests of verbal memory) that are also components of tests that measure intelligence quotient.[49] Almost all samples of children with ADHD as compared to controls have significantly lower mean full-scale intelligence quotient (mean differences of 10 points are typical) and significantly higher rates of reading and language disorder; whether these differences should be statistically controlled for is debated.[36,49] Additionally, neurocognitive testing studies typically use small sample sizes and exclude children with intelligence quotients less than 80 and children with psychiatric diagnoses, limiting the ability to generalize results.

Neuropsychological research on ADHD has largely ignored environmental and personality factors, which have been important to understanding of other childhood pathologies. Test results are analyzed without consideration for emotional factors. Investigators use reward points for task success as a proxy for affect, motivation, and task saliency.[51] In "How emotions inform judgement and regulate thought," Clore and Huntsinger[52] review the importance of affect (feelings) to cognition and cognitive testing. Test anxiety, self-esteem, and interest in task on the day of testing are also not evaluated and are likely to differentially affect performance and response variability.[53]

Other Causes of ADHD Symptoms

Factors associated with the diagnosis of ADHD include lower socioeconomic level; family conflict; punitive parenting methods; parental affective disorders, such as maternal depression and anxiety; parental substance abuse; parental disruptive, antisocial, and criminal behavior; increased and early TV viewing; and intellectual disability.[54-65] In a prospective longitudinal study of a national sample of Canadian children aged 2 to 7 years that controlled for relevant confounders, statistically significant predictors of high and persistent hyperactivity included male sex, maternal depression, hostile parenting, and maternal prenatal smoking.[65] Enduring associations between environmental, psychosocial, and parenting influences and the diagnosis of ADHD do not prove causality, but should not be ignored.

The very common behaviors described in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*), criteria for ADHD can be conceptualized as *symptoms* of childhood mental, emotional, and cognitive problems rather than as a neurobehavioral disease. This approach explains the remarkable heterogeneity of children whose behavior is diagnosed as ADHD. Children who meet criteria for ADHD may have one or more urgent and treatable conditions, including

1. Ongoing or past physical or sexual abuse, ranging from punitive parenting to explicit abuse;
2. Mental retardation, cognitive limitations, or one or more specific learning disabilities;
3. Hypervigilance and apprehension because of an unsafe or unpredictable environment at home or school;
4. Psychiatric diagnoses, including depression and anxiety;
5. Emotional and developmental difficulties because of conflicts or life stresses that would benefit from psychotherapy; and
6. A mismatch between parental or educator expectations and child behavior and performance—this may be due to developmentally inappropriate or child-inappropriate expectations.

Children with apparently "pure" attentional problems whose grades improve with stimulant treatment may have short-term improvement without long-term benefit, and the child's apparent improvement (or worsening) can mask need for treatment of an underlying problem. A mainstream ADHD researcher noted that the "costs of [ADHD] treatment reflect dramatic underutilization of psychosocial treatments" and recommended the use of behavioral treatments, including educational interventions and parent education before medication.[66] In a list of 10 "Limitations of Pharmacological Interventions When Used Alone" included are "removes incentives for parents and teachers/schools to work on other treatments," "does not affect several important variables (eg, academic achievement, concurrent family problems, peer relationships)," and "uniform lack of evidence for beneficial long-term effects."[66]

The Parent Trap

Clinicians may be reluctant to explore causes for symptoms diagnosed as ADHD. Without obvious psychosocial stressors, with an intelligence quotient above 80 and parents who are involved and caring (and often professionals), it may seem untenable that a child's behaviors could be anything but a "brain disease." It is falsely assumed that the only other possibility is that the child's difficulties are the parents' fault.

This unhelpful and fallacious dichotomous approach prevents children from obtaining needed treatment. It also fails to engage the parents in the supportive role to which they are optimally suited; they know the child best and are best positioned to alter home care in ways that can help the child. The simplistic concept of a "neurotransmitter deficiency" is well outdated, and even generalized "behavior treatments" that may not address the individual child's needs show some efficacy in decreasing symptoms.[67,68] Therapy that is tailored to the individual child's difficulties and includes parental support has not received sufficient attention.

Comorbidities or Etiologies?

The range of "comorbidities" described in ADHD includes oppositional defiant disorder (30% to 60%); conduct disorder (9% to 19%); mood disorders, including depression (18% to 60%); anxiety disorders (23% to 34%); and learning disorders (10% to 90%).[10,69-76] The significant degree of overlap between ADHD and oppositional defiant disorder and conduct disorder suggests that the same children are being identified: "Almost all children younger than 12 years of age who meet criteria for ODD [oppositional defiant disorder] or CD [conduct disorder] will almost always meet criteria for ADHD."[76(p526)] Depression and anxiety may be difficult to identify in children, both have documented strong continuity in adulthood, and neither condition is treated with stimulant medications.[77-85] In fact, children with major affective disorders including depression may have dysphoria and worsening with stimulants, whereas children with anxiety plus ADHD diagnosis are much less likely to have response to stimulants.[11,81,82,86-88] An increasing number of neuropsychologists are exploring the overlap between learning disabilities and ADHD.[48,49] Although stimulants cause motoric slowing and improved attention and performance on rote tasks for both control and ADHD-diagnosed individuals, they do not improve reading ability, knowledge acquisition, or knowledge application.[89-96] Because early and intensive treatment of learning disabilities improves educational outcomes, the use of stimulant medications as first-line treatment for academic failure is worrisome.[97-99] "Comorbidities" mimic ADHD, may be difficult to diagnose accurately, and have poor outcomes without appropriate therapy. It is likely that "comorbidities" produce symptoms mistakenly diagnosed as ADHD.

The Rating Scales—Searching for Diagnostic Validity

Children aged 6 years and older are diagnosed with ADHD if they are identified as having 6 or more hyperactive/impulsive or inattentive behaviors from a checklist in the *DSM-IV* and the behaviors occur "to an extent that is disruptive and inappropriate for developmental level,"

cause "clinically significant impairment" in 2 settings, and were present for more than 6 months with onset before age 7 years.[100] In practice, many more children of younger ages are identified, and many clinicians identify children who do not strictly meet the criteria. However, the validity of this behavior-driven diagnostic method is debated. Horwitz and Wakefield[101] examine this clinical problem as it applies to the *DSM-IV* diagnosis of depression.[101] In his review of their book, McHugh notes that this approach "may obscure important distinctions between a patient with a mental disorder and a person who is responding naturally to life circumstances." This concern applies equally to the diagnosis of ADHD.[102] A highly reliable diagnostic method may repeatedly identify the same individual(s), yet does not create a meaningful or coherent diagnostic category.

Snyder et al[103] reviewed the accuracy of ADHD rating scales using American Academy of Neurology evidence standards. Eleven scales, including the widely used Conners's Rating Scale–Revised, were eliminated because of major design flaws such as use of the same sample for development and validation of the tool (Conners's Rating Scale-Revised), use of the evaluated scale as the clinical standard, and convergent validity with no prior validation of either scale. Thirteen scales could be evaluated, none met all standards, and a pooled mean accuracy of 69% (±7%) for 9 studies with 2228 participants was reported. Not evaluated were the Vanderbilt ADHD rating scales, which have been widely promoted by the American Academy of Pediatrics in their ADHD Toolkit.[104] The forms were partially funded by McNeil Consumer and Specialty Pharmaceuticals, whose parent pharmaceutical company manufactures Concerta, a sustained release stimulant medication for ADHD.[105]

Investigators developing the Vanderbilt ADHD Parent Rating Scale recruited parents from an urban K–12 school with 6171 students and screened with teacher ratings that identified 1536 (23%) as having ADHD.[106,107] Teachers had no information on longevity of symptoms, 2 setting behaviors, or age of onset of symptoms, as required by *DSM-IV* for diagnosis. Parents of these 1536 students received anonymous letters requesting participation, of whom 288 (18.7%) responded and 241 (15.7%) completed 3 interviews that were compared with teacher evaluations. The responding parents differed from nonresponders in that significantly more of their children were receiving stimulant medications. During the 2-year study children were not interviewed, observed, or directly assessed at any time. Investigators used the ADHD section of the Diagnostic Interview Schedule for Children (DISC-IV) to validate the Vanderbilt ADHD Parent Rating Scale, even though "no formal validity testing has been performed" for this section of the DISC-IV.[108] They found good concurrent validity (0.79)—not unexpectedly because the same 18 questions are used on both scales—but very low interrater reliability between teachers and parents and low test–retest reliability. The investigators concluded that the Vanderbilt ADHD Parent Rating Scale has "good psychometric properties in a high risk population." Alternately, using Snyder's evaluative caveats, one would conclude that the Vanderbilt ADHD Parent Rating Scale does not have good psychometric properties because (*a*) it underwent testing with a small prescreened population whose diagnosis was not defined by *DSM-IV* criteria or interview, and (*b*) convergent validity was demonstrated with the DISC-IV without prior validation of either scale.

Development of the Vanderbilt ADHD Diagnostic Teacher Rating Scale involved teachers of 8257 children (year 1) and 4323 children (year 2) in a suburban school system (6.9% African American, 17.2% low income).[109-111] Internal consistency for the scale was high, but the authors report,

> It was not possible to obtain a precise measure of the presence of AD/HD by which to compare the scale to a "gold standard" . . . The teachers' responses to the question about the child having been diagnosed with AD/HD provided an approximation . . . One limitation of this study is that all information was obtained from teacher reports, which does not allow for an independent determination of the diagnoses.[110(pp149-150)]

Thus, validation of the Vanderbilt ADHD Diagnostic Teacher Rating Scale was compromised by use of a population that did not meet standardized *DSM-IV* criteria for ADHD, which is demographically at lower risk for ADHD than the general population, and by use of the same informants for both the clinical diagnosis and rating scale development.

The problem of parent–teacher rating scale discrepancy is not easily dismissed because *DSM-IV* requires impairment in 2 settings. In evaluating the Vanderbilt forms, Leslie et al[112] reported a discrepancy rate such that 40% of children no longer met criteria for diagnosis with both raters. Wolraich et al[107] found teacher–parent concordance so low that diagnostic rates decreased among all subtypes of ADHD, leading the authors to suggest that criteria be relaxed. Other studies show similar results.[113-115] Knowing whether a behavior is "inappropriate for developmental level" requires knowledge of "appropriate" for developmental level, and persistent discrepancies may reflect the work of untrained informants (parents and teachers) using subjective criteria. Scales do not include objective measures or child interview and do not adjust for any child characteristic (eg, age, intelligence quotient, gender). Because a child's behavior depends on setting-specific structure, expectations, and adult guidance, a home–school discrepancy is not surprising.

Rating scales are called "objectives" because quantitative information is generated. Missing from the evaluation of most children labeled as ADHD are "projectives," or tests that use a free response and require interpretation. Examples include the Children's Apperception Test, which presents a

child with 10 pictures to describe. Projectives evaluate personality structure and dynamics and assess coping and defense mechanisms and can identify possible underlying reasons for attentional or behavioral problems, such as anxiety, depression, or areas of emotional conflict that can respond to appropriate therapy.

Medications

Few clinicians who attempt to treat ADHD do so without prescribing stimulant medications. Both older short-acting preparations and newer more expensive sustained release preparations of mixed amphetamine salts and methylphenidate are marketed, in addition to the non-stimulant atomoxitine. No published evidence exists that demonstrates better comparative effectiveness of any of these pharmacologic treatments for ADHD.[3] Choice of medication is anecdotal and physician driven.

Side effects of treatment are infrequently studied prospectively. Rates range from 5% to 25% for anorexia, listlessness, nausea, somnolence, and mood swings, with at least 1 side effect reported in 22% of children in a large study.[116] Side effects of higher morbidity and lower frequency include tics, hallucinations, and bizarre behavior. Few studies examine the opinions of the child who is receiving the medication, but when opinion is sought, 12.7% to 18.8% of children reported that they feel worse on stimulants.[117]

Few ADHD studies were actually designed to monitor growth, and long-term studies that continue through the pubertal growth spurt to adult height have not been performed. Clinicians face a significant challenge interpreting results because most studies are performed by researchers funded by pharmaceutical firms that manufacture the studied medications, and results revealing growth decrements are summarized with reassuring language that minimizes findings.[118,119] For example, growth decrements in a prospective study of 0.23 cm and 1.23 kg after 21 months in osmotic-release methylphenidate treated as compared with untreated children are described as "clinically insignificant."[120] The Multimodal Treatment Study of Children with Attention Deficit Hyperactivity Disorder documented average growth of 2.0 cm and 2.7 kg *less* in newly medicated as compared with never medicated children at 36 months, without evidence of growth rebound.[121] This information was obtained prospectively and appears solid. Longer-term studies also show measurable effects of stimulants on height and weight gain.[122]

Whether the reported rate of sudden death in children receiving amphetamine and methylphenidate products (0.3-0.2/100 000 patient years) actually differs from baseline rates of sudden death in childhood is not known because of limitations in the reliability of spontaneous report data.[3,123] Elevations of blood pressure (3.6 mm Hg systolic, 2.5 mm Hg diastolic) and resting heart rate (3.4 beats per minute) during 2 years of stimulant treatment are described as "insignificant"; however, because long-term studies have not been performed, and prehypertension is causally linked to cardiovascular mortality, this conclusion may be premature.[124-126]

Conflict of Interest

Pharmaceutical firms that manufacture ADHD medications play a large role in promotion of ADHD as a disease requiring medication. Pharmaceutical firms fund informational brochures from professional organizations such as the American Academy of Pediatrics, funded the development of the Vanderbilt ADHD rating scales in the American Academy of Pediatrics "ADHD Toolkit," contribute substantively to parent support groups, including Child and Adults with Attention-Deficit/Hyperactivity Disorder (26.11% of its $1 169 000 budget for 2006-2007), and fund continuing medical education, speakers, and physician researchers.[104,105,127-129] Over half of the principal investigators participating in the National Institutes of Mental Health Multimodal Treatment Study of Children with Attention Deficit Hyperactivity Disorder reported multiple financial disclosures due to pharmaceutical funding received as speakers, consultants, and researchers.[13-15] Thirteen of the 21 individuals who created the *DSM-IV* criteria for diagnosis of ADHD have financial ties to manufacturers of ADHD medications.[130,131]

There is evidence from the fields of economics and psychology that self-interest bias "does not appear to be strategic or deliberate,"[132(p110)] yet is pervasive, and "It takes extraordinarily little to bias an individual's interpretation and processing of information."[133(p42)] There is a growing awareness that acceptance of gifts from pharmaceutical firms is unethical, that pharmaceutical sponsorship of "research" may contribute significantly to publication bias, and that physicians who accept fees to perform as consultants may not be serving the best interests of their patients.[134-141] Physicians should consider the possibility that extensive pharmaceutical funding has essentially controlled research and treatment for children with symptoms of hyperactivity and inattention and has driven an explosion in the number of children who must be diagnosed as ADHD.

Summary

It is critical for unbiased clinicians to consider the possibility that ADHD is not a neurobehavioral disease but rather a constellation of symptoms that require attention (no pun intended). Children and adolescents manifesting hyperactivity, impulsivity, or inattention may have treatable medical, emotional, or psychosocial conditions that require urgent care. Stimulant medications are costly, have no proven

long-term efficacy, and may mask problems without benefiting the child. Parents, educators, and physicians are urged to reevaluate their thinking on this controversial topic.

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