Attention-Deficit/Hyperactivity Disorder in Adults

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ATTENTION-DEFICIT/HYPERactivity disorder (ADHD) is a prevalent disorder estimated to affect 3% to 9% of school-aged children and approximately 4% of adults worldwide.[1-3] Although in the past it was thought that ADHD did not continue beyond adolescence, long-term controlled follow-up studies have shown that the disorder persists in a sizable number of adults who had been diagnosed as having ADHD in childhood.[4]

Longitudinal studies in ADHD youth show that symptoms of hyperactivity and impulsivity may decay, but inattention tends to persist.[5] Studies of clinically referred adults with ADHD show that about half have clinically important levels of hyperactivity and impulsivity and up to 90% have prominent attentional symptoms.[6] Like some youth with ADHD, adults with ADHD tend to have additional cognitive deficits, specifically executive function deficits, which include problems encoding and manipulating information and difficulties with organization and time management.[7]

Adults with ADHD typically have childhood histories reflecting school dysfunction, including deficits in educational performance, discipline problems, and high rates of repeated grades, tutoring, placement in special classes, and reading disabilities.[8] School problems faced by children with ADHD often continue or worsen in college, resulting in academic underachievement, low grade point averages, lower completion rates, and more time to complete degrees.[2] Adults with ADHD tend to have lower socioeconomic status, lower rates of professional employment, more frequent job changes, more work difficulties, and high rates of spousal separation and divorce.[9] Similarly, adults with ADHD have more speeding violations, driver's license suspensions, and automobile collisions, and they perform poorly in driving simulators.[3,10] Adults with addictions (eg, alcohol or other drug abuse, tobacco, gambling), repeated traffic violations (speeding, failure to renew license), and recurrent life failures (occupational, financial, academic)—especially in the context of a family history of ADHD—should be screened for ADHD.

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Diagnosis of ADHD in Adults

Attention-deficit/hyperactivity disorder can be diagnosed reliably in adults who currently have symptoms of ADHD (as defined in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*[11] and who, on careful questioning, give a history of such symptoms since childhood.

According to the *DSM-IV* definitions, a diagnosis of ADHD requires that patients must meet all criteria in established sections B through E and must have a minimum of 6 symptoms listed in sections A1 (inattention) or A2 (hyperactivity and impulsivity). These symptoms not only must have persisted for at least 6 months but they must also be "to a degree that [they are] maladaptive and inconsistent with developmental level."[11]

For inattention, those symptoms are

a. Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities;
b. Often has difficulty sustaining attention in tasks or play activities;
c. Often does not seem to listen when spoken to directly;
d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions);
e. Often has difficulty organizing tasks and activities;
f. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework);
g. Often loses things necessary for tasks or activities (eg, toys, school assignments, pencils, books, or tools);

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h. Is often easily distracted by extraneous stimuli;
i. Is often forgetful in daily activities.

For hyperactivity, those symptoms are

a. Often fidgets with hands or feet or squirms in seat;
b. Often leaves seat in classroom or in other situations in which remaining seated is expected;
c. Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness);
d. Often has difficulty playing or engaging in leisure activities quietly;
e. Is often "on the go" or acts as if "driven by a motor";
f. Often talks excessively.

For impulsivity, those symptoms are

a. Often blurts out answers before questions have been completed;
b. Often has difficulty awaiting one's turn;
c. Often interrupts or intrudes on others (eg, butts into conversations or games).

The final 4 criteria B through E are

B. Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before age 7 years;
C. Some impairment from the symptoms is present in ≥2 settings (eg, school, work, home);
D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning;
E. The symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder and are not better accounted for by another mental disorder (eg, mood disorder, anxiety disorder, dissociative disorder, or a personality disorder).

Research shows that diagnosing ADHD based on the retrospective self-reports of adults is a valid method of diagnosing the disorder. Murphy and Schachar[12] reported that the consistent reporting of childhood ADHD symptoms by both adults and their parents is highly correlated ($R>0.75$). They also found strong agreement between the self-reports of adults and of their partners regarding ADHD symptoms. However, to ensure accuracy, clinicians should corroborate these self-reports and familial reports with a clinical interview because the use of written adult self-report scales—such as the ADHD rating scale and the Conners rating scale, which incorporate the *DSM-IV* criteria for ADHD—are highly valid and reliable instruments).[13,14] The Brown attention-deficit disorder and Wender-Reimherr scales are also used commonly to diagnose ADHD (and comorbidity) in adults.[14]

Psychiatric and learning problems exist simultaneously in a majority of adults with ADHD, who also manifest higher rates of anxiety disorders, depression, cigarette smoking, and substance use disorders than adults without ADHD.[9] Conversely, approximately 15% to 20% of adults with substance abuse disorders, anxiety, depressive disorders, and bipolar disorders have ADHD.[15-17] Since attentional dysfunction may be evident in a host of other disorders (eg, depression, anxiety, dementia), careful attention to the existence of longitudinal symptoms and impairments of ADHD coupled with the possibility that the manifest cognitive deficits may be related to another disorder are necessary for an accurate diagnosis. Adults presenting with diagnostic dilemmas or clinically significant co-occurring disorders such as depression, bipolar disorder, panic disorder, and substance abuse should be referred to a practitioner with experience in treating ADHD.

Genetic Susceptibility to ADHD in Adults

Family, twin, adoption, and molecular genetic studies show that genes influence the etiology of ADHD. The heritability of the disorder, about 70%, is among the highest for psychiatric disorders.[18] Family studies show that ADHD is more prevalent among the relatives of children with ADHD, and the biological children of adults with ADHD are at high risk of having ADHD themselves.[19] This high familial loading of adult ADHD suggests that biological factors may be stronger in adults than in pediatric ADHD.[20]

Studies of children and adults have found evidence for the involvement of several genes in the etiology of ADHD: the D_2 dopamine-receptor gene, the dopamine-beta-hydroxylase gene, the dopamine transporter gene, the *SNAP 25*, and the D_4 dopamine-receptor gene, and others.[21] The data for the D_4 receptor are especially compelling because the gene variant associated with ADHD is known to mediate a blunted response to the neurotransmitters norepinephrine and dopamine,[22] important neurotransmitters associated with the pathophysiology of ADHD.

Brain Anomalies in Adults With ADHD

A substantial body of literature implicates abnormalities of brain structure and function in the pathophysiology of both childhood and adult ADHD.[23-25] We have known for decades that ADHD youth show impaired performance on tasks requiring vigilance, motoric inhibition, organization, planning, complex problem-solving ability, verbal learning, and memory. A recent meta-analysis has demonstrated that a smaller but substantial literature shows similar problems in adults with ADHD.[23]

Age, learning disabilities, psychiatric comorbidity, and gender do not account for these impairments.[23] Although neuropsychological testing is not used for diagnosing ADHD in adults, such testing can help identify other problems, including disabilities, subaverage intelligence, and specific information processing deficits.

As recently reviewed,[26] current thinking suggests that a network of interrelated brain areas are involved in the attentional-executive impairments of children with ADHD. The cingulate cortex plays a role in motivational aspects of attention and in response selection and inhibition. A system mainly involving the right prefrontal and parietal cortex is activated during sustained and directed attention across sensory modalities.[26,27] The inferior parietal lobe and superior temporal sulcus are polymodal sensory convergence areas that provide a representation of extrapersonal space, which plays an important role in focusing on and selecting a target stimulus. The brain-stem

reticular activating system and the reticular thalamic nuclei regulate attentional tone and filter interference. Abnormalities involving multiple areas of the brain, including the anterior hippocampus, ventral anterior and dorsolateral thalamus, anterior cingulate, parietal cortex, and dorsolateral prefrontal cortex may play a part in problems with memory.[26,27]

Neuroimaging Studies

In the neuroimaging literature, nearly all studies using either computed tomography or magnetic resonance imaging show evidence of structural brain abnormalities in those with ADHD.[28] The most common findings are smaller volumes in frontal cortex, cerebellum, and subcortical structures.[28]

Functional imaging studies are consistent with the structural studies in implicating frontosubcortical systems in the pathophysiology of ADHD.[29] For example, in a positron emission tomography study of adult ADHD, Zametkin et al[30] found reduced global and regional glucose metabolism in the premotor cortex and the superior prefrontal cortex. Neuroimaging studies suggest that 3 subcortical structures—caudate, putamen, and globus pallidus—are part of the neural circuitry that underlies motor control, executive functions, inhibition of behavior, and modulation of reward pathways. These frontal-striatal-pallidal-thalamic circuits provide feedback to the cortex for the regulation of behavior. Adults with ADHD also demonstrate less activation of the anterior cingulate than adults without ADHD.[28] Of interest, functional imaging studies of children with ADHD show that stimulant medications do not affect brain growth adversely.[31]

Attention-deficit/hyperactivity disorder is thought to be mediated by catecholaminergic dysregulation of dopamine and norepinephrine. Although there is some disagreement about this, some studies have shown increased dopamine transporter density in the striatum.[32] This is particularly important given that the dopamine transporter in the striatum is the site of action of stimulant medications used to treat ADHD.[33]

Table. Medications Used in Adults With Attention-Deficit/Hyperactivity Disorder

Medication	Daily Dose, mg*	Daily Dosage Schedule	Common Adverse Effects
Stimulants			
Methylphenidate	20-100	Twice to 4 times	Insomnia Decreased appetite/weight loss Headaches Edginess
Amphetamine Dextroamphetamine and mixed amphetamine salts†	10-60	Twice to 3 times	Insomnia Decreased appetite/weight loss Headaches Edginess Mild increases in pulse/blood pressure
Magnesium pemoline	75-150	Once or twice	Insomnia Decreased appetite/weight loss Headaches Edginess Abnormal liver function test results
Noradrenergic agents			
Atomoxetine	40-120	Once or twice	Sleep disturbance Gastrointestinal tract distress, nausea Headache Mild increases in pulse/blood pressure
Antidepressants			
Tricyclics			
Desipramine; imipramine	100-300	Once or twice	Dry mouth Constipation Vital sign and electrocardiographic changes
Nortriptyline	50-200	Once or twice	Dry mouth Constipation Vital sign and electrocardiographic changes
Bupropion	150-450	Once or twice	Insomnia Risk of seizures (in doses >6 mg/kg) Contraindicated in bulimia

*Denotes typical daily doses, which may exceed US Food and Drug Administration–approved dosing.
†US Food and Drug Administration approved for adults with attention-deficit/hyperactivity disorder.

Treatment

Formal guidelines on the treatment of adults with ADHD are lacking. Support groups, such as Children and Adults With Attention-Deficit/Hyperactivity Disorder (information about which can be found at http://www.chadd.org), assist newly diagnosed adults by providing information about ADHD and available resources, including peer support groups. Coaching and training in organizational skills appear useful but remain unstudied. Although the efficacy of various psychotherapeutic interventions remain to be established, limited data suggest that cognitive-behavioral therapies may be useful for adults with ADHD.[34]

The benefit of pharmacotherapy for the treatment of ADHD in children has been established, but the usefulness of medication as a treatment for adults with ADHD is not well established. The medications used to treat ADHD mainly affect neurotransmission of catecholamines, including dopamine and norepinephrine. A recent review of the literature[35] identified 15 studies (N = 482 participants) of stimulants, and 28 studies of nonstimulant medications (N = 1179 participants) including noradrenergic reuptake inhibitors, antidepressants, and cholinergic agents that may be useful for the treatment of ADHD in adults (TABLE).

To date, the US Food and Drug Administration approved the follow-

ing agents for adult-use only: mixed amphetamine compounds and the noradrenergic specific reuptake inhibitor, atomoxetine. The stimulant medications—amphetamine, methylphenidate, and pemoline—block the presynaptic reuptake of dopamine and norepinephrine resulting in accumulation of norepinephrine and dopamine in the synaptic cleft.[36] Amphetamine also releases dopamine and norepinephrine directly. Atomoxetine specifically inhibits presynaptic norepinephrine reuptake resulting similarly in increased synaptic norepinephrine.[37] Placebo-controlled clinical trials with stimulants,[38-40] atomoxetine,[37] and the catecholaminergic antidepressants[41] have demonstrated significant short-term improvement in ADHD symptoms.[35] The stimulants methylphenidate and amphetamine are the most commonly used and are highly effective in a dose-dependent manner for adults with ADHD.[36-38] The stimulants have an immediate onset of action and may last from 4 to 12 hours depending on the formulation of the agent (immediate vs extended release). Longer-term trials of methylphenidate use by adults support the ongoing effectiveness and tolerability of stimulants.[35] The most common adverse effects with stimulants include edginess, insomnia, headache, and mild increases in heart rate and blood pressure necessitating monitoring.[38-40] Atomoxetine may be particularly useful when anxiety, mood, or tics occur with ADHD. Atomoxetine should be started slowly (0.5 mg/kg per day) and increased to therapeutic dosing (40-120 mg/d) over 1 month. Common adverse effects include gastrointestinal upset, mild increases in heart rate and blood pressure, and sexual dysfunction in men.[37] Other available medications shown to be effective for adults with ADHD include bupropion, desipramine, and pemoline, the latter 2 requiring serum level (desipramine) or frequent liver function test (pemoline) monitoring.[35] A limited amount of data suggests that pharmacotherapy may improve the driving skills of adults with ADHD[42] and may prevent the onset of substance abuse.[43] Although taking medication is lifelong, periodic reappraisals of the need to continue therapy are recommended. The lack of current symptoms or impairments of ADHD in the unmedicated status is one signal, for example, that medication may not be necessary any longer.

Summary

Attention-deficit/hyperactivity disorder in adults can be validly and reliably diagnosed. The clinical features are highly reminiscent of the pediatric form of the disorder. Diagnosis is based on clinical assessment using the *DSM-IV* criteria. Many adults with ADHD experience co-occurring disorders and have impaired success in academic achievement, career development, automobile driving, and interpersonal relationships. Studies of biological features support a genetic etiology for the disorder with associated neuropsychological deficits and catecholaminergic dysregulation. Emerging treatment strategies include structured psychotherapies, stimulant, and nonstimulant medications.

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I once had a sparrow land upon my shoulder for a moment, while I was hoeing in a village garden, and I felt that I was more distinguished by that circumstance than I should have been by any epaulet I could have worn.

—Henry David Thoreau (1817-1862)