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Understanding Attention-Deficit/Hyperactivity Disorder From Childhood to Adulthood

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Abstract

Attention deficit/hyperactivity disorder (ADHD) is among the most common neurobehavioral disorders presenting for treatment in children and adolescents. ADHD is often chronic with prominent symptoms and impairment spanning into adulthood. ADHD is often associated with co-occurring disorders including disruptive, mood, anxiety, and substance abuse. The diagnosis of ADHD is clinically established by review of symptoms and impairment. The biological underpinning of the disorder is supported by genetic, neuroimaging, neurochemistry and neuropsychological data. Consideration of all aspects of an individual's life needs to be considered in the diagnosis and treatment of ADHD. Multimodal treatment includes educational, family, and individual support. Psychotherapy alone and in combination with medication is helpful for ADHD and comorbid problems. Pharmacotherapy including stimulants, noradrenergic agents, alpha agonists, and antidepressants plays a fundamental role in the long-term management of ADHD across the lifespan.

Keywords

ADHD; ADD; comorbidity; treatment

INTRODUCTION AND OVERVIEW

Attention-deficit/hyperactivity disorder (ADHD) is among the most common neurobehavioral disorders presenting for treatment in children [1, 2]. It carries a high rate of comorbid psychiatric problems such as oppositional defiant disorder (ODD), conduct disorder, mood and anxiety disorders, and cigarette and substance use disorders [3]. Across the life span, the social and societal costs of untreated ADHD are considerable, including academic and occupational underachievement, delinquency, motor vehicle safety, and difficulties with personal relationships [3-56].

ADHD affects an estimated 4% to 12% of school-aged children worldwide [7] with survey and epidemiologically derived data showing that 4 to 5% of college aged students and adults have ADHD [8]. In more recent years, the recognition and diagnosis of ADHD in adults have been increasing although treatment of adults with ADHD continues to lag substantially

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Conflict of Interest Statement

Timothy Wilens, MD discloses conflicts of interest with Abbott, AstraZeneca, Eli Lilly and Co., McNeil Pharmaceuticals, Merck, the National Institutes of Health (National Institute on Drug Abuse), Novartis, and Shire. Thomas Spencer, MD discloses conflicts of interest with Cephalon, Eli Lilly and Co., GlaxoSmithKline, Janssen Pharmaceutical, McNeil Pharmaceuticals, the National Institute of Mental Health, Novartis, Pfizer, and Shire.

behind that of children [8, 9]. In contrast to a disproportionate rate of boys diagnosed with ADHD relative to girls in childhood, in adults, an equal number of men and women with ADHD are presenting for diagnosis and treatment [10].

PSYCHIATRIC COMORBIDITY

During the past decade, epidemiological studies have documented high rates of concurrent psychiatric and learning disorders among individuals with ADHD [3, 11, 1213]. Consistent with childhood studies, studies of ADHD adults have found high rates of childhood conduct disorder as well as adult antisocial disorders in these subjects [3].

Mood & Anxiety

Anxiety often confounds the diagnosis and treatment of ADHD [3, 11, 12]. High rates of the various anxiety symptoms exist in ADHD and may manifest as social, generalized or panic-like symptoms. Similarly, ADHD increases the likelihood of having a depressive disorder by at least two-fold [8, 14]. Interestingly, recent data suggest that stimulant treatment of ADHD over time may decrease the ultimate risk for anxiety and depressive disorders [15].

A growing literature reports the co-occurrence of bipolar disorder and ADHD. Systematic studies of children and adolescents indicate rates of ADHD ranging from 57% to 98% in bipolar children; and conversely, rates of bipolar disorder in 22% of ADHD children and adolescents [16]. There continues to be much controversy about the validity of the concurrent diagnoses of ADHD and severe mood instability or bipolar disorder. Whereas ADHD is characterized by the typical cognitive and hyperactive/impulsive features of the disorder, bipolar disorder (BPD) is characterized by mood instability, pervasive irritability/rage, grandiosity, psychosis, cyclicity, and lack of response to structure [17]. When individuals experience both sets of symptoms, they may suffer from both ADHD and BPD [17].

Substance Use Disorders

Combined data from retrospective accounts of adults and prospective observations of youth indicate that juveniles with ADHD are at increased risk for cigarette smoking and substance abuse (SA) during adolescence [18]. ADHD adolescents and adults become addicted to cigarette smoking at twice the rate compared to non-ADHD individuals [19, 20]. ADHD youth disproportionately become involved with cigarettes, [19] which increases the risk for subsequent alcohol and drug use [21]. Individuals with ADHD tend to have more severe substance abuse and maintain their addictions longer compared to their non-ADHD peers [19, 22-24].

Concerns of the abuse liability of stimulants and the potential kindling of substance abuse secondary to early stimulant exposure in ADHD children have been raised. [25] These concerns are based largely on data from animal studies. [25] However, the preponderance of clinical data and consensus in the field do not appear to support such a contention. For example, in a prospective study of ADHD girls followed into adolescence, a significant reduction in the risk for SA was reported in treated compared to untreated ADHD youth [26] with no increase (or decreased) SUD risk associated with stimulant treatment into adulthood [27].

DIAGNOSING ADHD

ADHD can be reliably diagnosed in children, adolescents, and adults [28]. Using the current guidelines, the child or adult patient must meet the criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)[29]. It is important to note, however, that the DSM-IV-TR criteria for ADHD symptoms were derived from youth to age 17 years and

therefore were not specifically tailored to adults and hence, may not always "fit" adults with the disorder [28, 30]. The symptoms of the disorder are categorized as follows: inattention-difficulty sustaining attention and mental effort, forgetfulness, and distractibility; hyperactivity-fidgeting, excessive talking, and restlessness; and impulsivity-difficulty waiting one's turn and frequent interruption of others. The *DSM-IV-TR* criteria also include onset by age 7, impaired functioning in at least 2 settings (home, work, school, job), and more than 6 months of duration [30]. Three subtypes of the syndrome are currently recognized: predominantly inattentive, predominantly hyperactive-impulsive, and the combined type, which is the most common and typically more severe and with more comorbidity [29, 31, 32]. Between 90 to 95% of adolescents and adults with ADHD manifest the inattention cluster of symptoms at least as a component of their disorder [31]. Of interest, the combined subtype of ADHD may simply represent a more severe and debilitating presentation of ADHD (e.g. more symptoms) and there may be relatively more stability of the subtype with development [32, 33].

To meet the diagnostic criteria for the inattentive or hyperactive-impulsive subtypes, an individual must have 6 or more of the 9 symptoms from either group of criteria (18 possible traits in all) [30]. For the combined subtype, an individual must have 6 or more inattentive symptoms and 6 or more hyperactive-impulsive symptoms. To warrant the ADHD diagnosis, symptoms must cause significant impairment. Adults diagnosed with the disorder must have had childhood onset and persistent and current symptoms, although allowance is made for incomplete persistence of full criteria (ADHD-in partial remission) or lack of clear childhood symptoms (ADHD NOS).

Of interest, whereas clinicians are concerned as to the possibility of purposely misrepresenting or over-reporting of ADHD symptoms by college students or adults, data suggest the opposite may be operant. Mannuzza et al. [34] in a prospective 16-year follow-up of children with ADHD now at a mean age of 25, found that of the 176 individuals with a well characterized past history of ADHD, only 28% of the adults through direct interviews were identified as having childhood ADHD. These data further highlight issues around the relatively poor sensitivity of recalling symptoms (and establishing the diagnosis of ADHD) by adult self-report, particularly when not anchoring symptoms in childhood.

The diagnosis of ADHD is made clinically with scales used in an ancillary manner. The patient's symptoms, severity of impairment, possible comorbidity, family history, and psychosocial stressors may be determined during the patient and/or parent interview. In pediatric evaluations, the adolescent's behavior and parent-child interaction are observed, and the child's school, medical, and neurological status are evaluated [2]. A number of diagnostic and follow-up scales are available (see www.schoolpsychiatry.org)[35]. Symptom scales used with all age groups (to assess home, school, and job performance) include, but are not limited to, the ADHD Symptom Checklist, SNAP-IV Teacher and Parent Rating Scale, Conners Rating Scales-Revised,, Brown Attention-Deficit Disorder Scales for Children, and the ADHD Symptoms Rating Scale [36]. Although these tools quantify behavior deviating from norms, they should not be used alone to make or refute the diagnosis.

Diagnosing adults involves careful querying for developmentally appropriate criteria from the *DSM-IV-TR* concerning the childhood onset, persistence, and current presence of symptoms [29]. Diagnostic aids are available for adult ADHD [3637]. For instance, the Adult Self Report Scale, Conners Adult ADHD Scales, and Brown Attention scales for adults are among instruments available to assist in the diagnosis of ADHD[3637]. For a briefer screening of adults, the World Health Organization Adult ADHD self-report scale (Figure 1) can be downloaded (www.who.org) and has been validated as a manner of identifying those at risk for ADHD who necessitate further screening [38].

Follow-up studies show that prominent symptoms and impairment related to the disorder persist into adulthood in approximately one-half of cases [39, 40]. There appears to be developmental variance in the ADHD symptom profile across the life span [31, 32, 39-41]. Longitudinally derived data in ADHD youth growing up indicate that the symptom cluster of hyperactivity and impulsivity decays over time, while the symptoms of inattention largely persist [32, 39-4131]. In support of this notion, data derived from a group of clinically referred adults with ADHD indicate that approximately half of adults endorse clinically significant levels of hyperactivity/impulsivity, but 90% endorse prominent attentional symptoms [3231].

A substantial body of literature implicates abnormalities of brain structure and function in the pathophysiology of both childhood and adult ADHD [42-4849-51]. We have known for decades that ADHD youth show impaired performance on tasks assessing vigilance, motoric inhibition, organization, planning, complex problem solving, and verbal learning and memory [52, 53]. Prominent neuropsychologically-derived executive dysfunction is associated with learning disabilities and poorer overall prognosis over time in ADHD youth [54]. Similar findings are emerging in adults with ADHD [52]. While neuropsychological testing is not used clinically to diagnose ADHD in adults, such testing aids in identifying learning disabilities, sub average intelligence, and specific information processing deficits.

PATHOPHYSIOLOGY AND GENETICS

Neurobiology

ADHD has been conceptualized as a disorder affecting “frontal” circuitry due to associated deficits in executive cognitive functioning. Structural imaging studies have documented diffuse abnormalities in children and adults with ADHD. A large study by Castellanos and colleagues [55] reported smaller total cerebrum, cerebellum, and the four cerebral lobes that did not change over time. A structural magnetic resonance imaging (MRI) study [56] in adults with and without ADHD also revealed a smaller anterior cingulate cortex (ACC) and dorsolateral prefrontal cortex (DLPFC). The DLPFC controls working memory that involves the ability to retain information while processing new information. These differences are thought to account for deficits in goal-directed and on task behavior in ADHD. The ACC is thought to be a key region of regulation involving the ability to focus on one task and choose between options.

Investigators have also examined the developmental pattern of cortical maturation in ADHD. Shaw and colleagues [57] reported a delay in cortical thickness among ADHD patients. The pattern of brain development, from sensorimotor to associative areas, was similar in children with and without ADHD. However, the age of peak development was delayed in those with ADHD. Using the same measure of cortical thickness data in adults, Makris and associates [58] have shown that cortical thickness is not normalized and that the areas of the brain that are affected in children with ADHD remain affected in adulthood. In this study the DLPFC, parietal areas, and ACC had thinner measures of cortical thickness in adults with ADHD than in adults without ADHD.

Functional magnetic resonance imaging (fMRI) has been used to examine brain activity during selective cognitive challenges in individuals with ADHD. One study that measures brain activity using a neuropsychological test (go/no-go) found that both youth and adults with ADHD showed attenuated activity in the frontostriatal regions of the brain that are key for inhibitory control and for attention (prefrontal cortex and caudate) [59]. Adults with ADHD also activated non-frontostriatal regions (ACC, parietal areas) moreso than controls. The amount of brain activation observed correlated closely with the degree of efficiency on the task in both children and adults with ADHD.

The results of fMRI studies were reviewed by Casey and Durston [60] who hypothesized that top-down and bottom-up control systems were affected in ADHD. They speculated that bottom-up neural systems detect the regularities and irregularities in the environment to activate the frontal brain systems to alter behavior. These systems are key regulators of maintaining sustained attention vs. shifting attention due to sensory input. Casey and Durston [60] posited that the striatum regulates *what* to expect (type of task), the cerebellum regulates *when* to expect it (timing of task), and the parietal lobe alerts one to novel or newer competing stimuli.

Interestingly, medication may normalize some of these functional deficits. Bush and colleagues published a study showing that 7 weeks of treatment with methylphenidate normalized activation in the ACC [61]. Those receiving medication showed increases in activation of the ACC and DLPFC at follow-up as compared to baseline and to those receiving placebo treatment. Hence, those areas of the brain that were underactive in adults without treatment normalized with treatment.

The neurobiology of ADHD is strongly influenced by genetic factors. As highlighted in a special issue of Science dedicated to the human genome project, ADHD is among the most recognized genetic-based disorders in psychiatry [62]. Family studies of ADHD have shown that the relatives of ADHD children are at high risk for ADHD, comorbid psychiatric disorders, school failure, learning disability and impairments in intellectual functioning [63]. Additional lines of evidence from twin, adoption and segregation analysis studies suggest that the familial aggregation of ADHD has a substantial genetic component. Twin studies find greater similarity for ADHD and components of the syndrome between monozygotic twins compared with dizygotic twins [64, 65]. Faraone and colleagues [66] in a meta-analysis of the various studies reported on the mean heritability of ADHD. Heritability refers to the amount of genetic influence for a particular condition. A coefficient of 1 indicates an entirely genetically influenced phenomenon, while a 0 indicates no genetic influence. Depression, anxiety, panic, and even Asthma had mean heritability rates below 50%. In contrast, two of the most biologically related psychiatric disorders, schizophrenia and autism, are heritable at ~75%. ADHD falls in this higher range as well, with work by Rietveld and associates showing a mean heritability rate of 75% [67].

As with many complex neuropsychiatric conditions, multifactorial causation is thought to be involved in ADHD; an additive effect of multiple vulnerability genes interacting with environmental influences. Pooled analyses reveal that there is not one single gene associated with ADHD [66]. The disorder is thought to result from a combination of small effects from a number of genes (polygenetic). Some of the candidate genes that have been identified thus far relate to synthesis, packaging, release, detection and recycling of dopamine or catecholamines including the post-synaptic DRD4, dopamine transporter, and SNAP 25 genes; as well as others related to other neurotransmitters such as serotonin. Clearly, more work is necessary in disentangling the relationship of candidate genes in producing specific phenocopies of ADHD, as well as response prediction to psychosocial and pharmacological intervention.

TREATMENT

The management of ADHD includes consideration of two major areas: non-pharmacological (educational remediation, individual and family psychotherapy) and pharmacotherapy [2]. Support groups for children and adolescents and their families, as well as adults with ADHD, provide an invaluable and inexpensive environment in which individuals are able to learn about ADHD and resources available for their children or themselves. Support groups can be accessed by calling an ADHD hotline or a large support group organization (i.e.

Children and adults with ADHD-CHADD, Adults with ADHD-ADDA,), or by accessing the internet.

Specialized educational planning based on the child's difficulties is necessary in a majority of cases [68]. Since learning disorders co-occur in one-third of ADHD youth, ADHD individuals should be screened and appropriate individualized educational plans developed. Parents should be encouraged to work closely with the child's school guidance counselor who can provide direct contact with the child as well as serve as a valuable liaison for teachers and school administrators. The school's psychologist can be helpful in providing cognitive testing as well as assisting in the development and implementation of the individualized education plan. Educational adjustments should be considered in individuals with ADHD with difficulties in behavioral or academic performance. Increased structure, predictable routine, learning aids, resource room time, and checked homework are among typical educational considerations in these individuals. Similar modifications in the home environment should be undertaken to optimize the ability to complete homework. For youth, frequent parental communication with the school about the child's progress is essential.

PSYCHOSOCIAL TREATMENTS

Clinicians have at their disposal a variety of psychosocial interventions for ADHD (for review see [68, 69]). Apart from traditional psychotherapy, which addresses underlying emotions, tutors are available to help children develop strategies for improving academic performance and interpersonal relations. Tutors can assist the child with skills in organization and prioritization, as well as act as mentors, advocates, and motivational figures.

Parent training is often conducted using the antecedent behavior consequence model, and is implemented using various methods, including small and large parent training groups, parent training with individual families, videotapes, and behavioral sessions that include children [70]. In the academic setting, virtually all children with ADHD must cope with organizational and behavioral demands and expectations. Classroom behavioral interventions often involve training the teacher in use of these methods.

Teachers can conduct individual and class-wide interventions using antecedents and/or consequence methods [71]. Antecedent interventions are based on an understanding of the range of antecedents (eg, boredom, peer provocation, unclear inconsistent rules) that precipitate behavioral problems. Antecedent/consequence interventions involve understanding antecedents to inappropriate behavior and reinforcing appropriate behavior with rewards. Consequence interventions involve the judicious use of punishment to encourage appropriate classroom behavior.

Accommodations should be considered to assist the child with ADHD. For instance, other behavioral strategies can be used in the classroom setting to facilitate attention [72]. These include placing the child with ADHD in proximity to the teacher, eliminating environmental distractions, and arranging seating in traditional rows rather than clusters. Lessons that involve novelty and stimulation in easy and repetitive tasks rather than new or difficult ones have been shown to benefit the child with ADHD. Additional interventions shown to be effective in the academic setting include peer-mediated interventions and token economies.

Exciting new work has shown that cognitive therapies [73] and cognitive behavioral therapy have been shown effective in medicated adults with ADHD who manifest residual ADHD symptoms [74-77]. Social skills remediation for improving interpersonal interactions and coaching for improving organization and study skills may be useful adjuncts to treatment, although there generalizeability remains debated. Little data exists for the use of

neurofeedback, cerebellar training, attention or memory training, or ophthalmic manipulation for the treatment of core ADHD symptoms [71].

PHARMACOTHERAPY

Medications remain a mainstay of treatment for children, adolescents, and adults with ADHD (see Table 1). In fact, NIH-funded multisite studies support that medication management of ADHD is the most important variable in outcome (for core ADHD symptoms) in context to multimodal treatment at least over the first year to two of treatment [78-80]. The stimulants, noradrenergic agents, and alpha agonists comprise the available agents for ADHD. The medications used in ADHD have been observed to have pharmacological responsivity across the lifespan for school-aged children, adolescents, and adult groups with ADHD.

Stimulants

The stimulant class medications are among first line agents for pediatric and adult groups with ADHD based on their extensive efficacy and safety data [1]. The most commonly used compounds in this class include methylphenidate-based (Ritalin, Concerta, Focalin, Metadate, Daytrana and others) and amphetamine-based (Adderall, Dexedrine, Vyvanse) formulations. Stimulants are sympathomimetic drugs which increase intrasynaptic catecholamines (mainly dopamine and norepinephrine) by inhibiting the presynaptic reuptake mechanism and releasing presynaptic catecholamines [81]. Whereas methylphenidate is specific for blockade of the dopamine and noradrenergic transporter proteins, amphetamines (in addition to blocking the dopamine and noradrenergic transporter protein) release catecholaminergic stores and cytoplasmic dopamine and noradrenaline directly into the synaptic cleft (for review see [1, 81]).

Given the need to additionally treat ADHD outside of academic settings (i.e. social, homework, driving) and to reduce the need for in school dosing and likelihood for diversion, there has been a shift to the extended release preparations of the stimulants. Extended release preparations diminish afternoon wear-off and rebound and appear to manifest less abuse liability compared to their immediate-release counterparts [82, 83]. The extended release stimulants include methylphenidate (trade names: Concerta, Daytrana Patch, Focalin XR, Metadate CD, Ritalin LA) and amphetamine formulations (trade names: Adderall XR, Vyvanse). The literature suggests more similarities than differences in response to the various available stimulants [1, 84]. However, based on different mechanisms of action and individual tolerability, some patients who lack a satisfactory response or manifest adverse effects to one stimulant may respond favorably to another. Stimulants should be initiated at the lowest available dosing once daily and increased every three to seven days until a response is noted or adverse effects emerge.

Stimulants appear to work in all age groups of individuals with ADHD. For instance, a controlled multi-site study in preschoolers showed improvement in ADHD symptoms and structured tasks; however, the response was less robust with a higher side effect burden compared to other age groups [85]. There has been a great interest in the use of stimulant treatment in adults with ADHD. There have been approximately 40 studies of stimulants demonstrating moderate efficacy [86]. Currently FDA approval is only for the extended-release preparation of stimulants in adults.

Predictable short-term adverse effects include reduced appetite, insomnia, edginess, and GI upset [87]. Elevated vital signs may emerge necessitating baseline and on-drug monitoring. Although stimulants may produce anorexia and weight loss, their effect on ultimate height remains less certain [88, 89]. Whereas a number of studies have indicated potential growth

delay earlier in treatment, normalization appears to occur with chronic treatment. Longitudinal studies suggest that the majority of ADHD youth with tics can tolerate stimulant medications [90]; however, up to one-third of children with tics may have worsening of their tics with stimulant exposure [91]. Current consensus suggests that stimulants can be used in youth with comorbid ADHD plus tics with careful monitoring for stimulant-induced tic exacerbation.

Warnings have also highlighted potential cardiovascular adverse events. Data suggest that rates of sudden and catastrophic adverse cardiovascular effects are no higher on stimulants and nonstimulants to treat ADHD compared to the general population [92]. Based on guidelines from the American Academy of Pediatrics [93, 94], history and symptoms referable to structural heart disease should be queried prior to starting and during treatment with medications (see Figure 2) including family history of premature death, congenital heart disease, palpitations, syncopal episodes, dizziness, or chest pain [93, 94]. Blood pressure and pulse monitoring at baseline and periodically thereafter is recommended whereas ECG monitoring is optional [93, 94].

Despite lingering concerns of stimulant abuse, there is a paucity of scientific data supporting that stimulant-treated ADHD individuals systematically abuse their medication [95] and the preponderance of recent data continue to suggest reductions of cigarette smoking and substance abuse associated with treatment[19, 26]. However, data suggest that diversion of stimulants to non-ADHD youth continues to be a concern [96, 97]. Families should closely monitor stimulant medication, and college students receiving stimulants should be advised to carefully store their medication [96]. Two studies have shown less abuse liability associated with extended-release relative to immediate release MPH [82, 83].

Atomoxetine

Atomoxetine is a potent norepinephrine-specific reuptake inhibitor that has been studied in youths and adults [98, 99]. Atomoxetine has been shown to be effective in long-term use [100]. Atomoxetine has also been shown particularly useful in comorbid ADHD. In a noninferiority study in children with ADHD and tic disorder, atomoxetine reduced tic severity while improving ADHD symptoms. Children with ADHD and clinically significant anxiety responded more favorably to atomoxetine than placebo with reductions in both anxiety and ADHD scores [101]. Likewise, data in young adults with ADHD has shown that 12 week treatment with atomoxetine in recently abstinent alcoholics (4-30 days) was associated with significant reductions in ADHD and heavy drinking (not relapse) compared to placebo [102]. In clinical trials, atomoxetine is associated with nausea, GI distress, and sedation most commonly reported. Patients may rarely experience hostility, irritability, and/or suicidality. There is currently a black box warning for rare, but potentially serious, hepatitis (see http://www.strattera.com/pages/index) [103]. While routine liver function monitoring is not recommended, careful informed consent with patients and their families can enhance vigilance for warning signs and symptoms.

Antihypertensives/alpha agonists

The antihypertensives guanfacine and clonidine are alpha-adrenergic agonists; an extended-release preparation of guanfacine is FDA approved. Whereas clonidine affects alpha receptors more broadly, guanfacine appears to be more selective for the alpha 2a receptor. Improvements in both attention and hyperactivity/impulsivity have been demonstrated with the alpha agonists [104]. The alpha agonists have been used for the treatment of core ADHD as well as associated tics, oppositional defiant behavior, aggression, and sleep disturbances, particularly in younger children [105].

Multisite combination studies using alpha agonists and stimulants have been conducted in youth with ADHD and ADHD plus tics. Interestingly, all studies have shown that the combination was more effective than either agent alone in improving ADHD and/or tics [106-109110]. In these studies, no clinically meaningful adverse cardiovascular events were observed [106, 107]. Cardiovascular monitoring by ECG remains optional. Adverse effects with the alpha agonists include sedation, fatigue, mood, and the potential for rebound hypertension with abrupt discontinuation.

Several additional medications have demonstrated benefit in controlled trials, but have not been approved by the FDA for the treatment of ADHD. The antidepressant bupropion has been shown effective for ADHD in controlled trials of children [111] and adults [112, 113]. Additionally, open trials in adolescents with ADHD and depression [114] and adults with ADHD and bipolar disorder [115] have suggested a further utility for this agent. Given its utility in reducing cigarette smoking, improving mood, lack of monitoring requirements, and general tolerability, bupropion is often used as an agent for complex ADHD patients with substance abuse or a mood disorder. Adverse events include activation, irritability, insomnia, and in rare cases, seizures.

The tricyclic antidepressants (TCAs) such as imipramine are effective in controlling abnormal behaviors and improving cognitive impairments associated with ADHD, but less so than the majority of stimulants [116]. The TCAs are particularly useful when other FDA approved agents fail and/or when oppositionality, anxiety, tics, sleep, or depressive symptoms co-occur within ADHD. Unwanted side effects include sedation, weight gain, dry mouth, and constipation. Blood levels should be measured periodically and, since TCAs prolong the cardiac repolarization, ECG monitoring is recommended but not required to screen for arrhythmia risk. TCAs can be fatal in overdose and need to be stored carefully, particularly if toddlers are in the family.

Modafinil is currently approved as treatment for narcolepsy and has been shown effective in pediatric, but not adult, trials of ADHD [117]. Modafinil has not been approved by the FDA for the treatment of ADHD due to safety concerns (rare but potentially serious erythema multiforme).

SUMMARY

In summary, ADHD is a prevalent world-wide, heterogeneous disorder that frequently persists through adolescence into adult years. ADHD continues to be diagnosed by careful history with an understanding of the developmental presentation of normal behavior and symptoms of the disorder. ADHD has been reconceptualized as a more chronic condition with approximately one-half of children continuing to exhibit symptoms and impairment of the disorder into adulthood [39, 40].. Most individuals with ADHD have a comorbid disorder: including oppositional, conduct, anxiety, or mood disorders [3, 11, 12].. In addition, ADHD carries with it significant impairment in academic, occupational, social, and intrapersonal domains necessitating treatment. Converging data strongly support a neurobiological and genetic basis for ADHD with catecholaminergic dysfunction as a central finding.

Psychosocial interventions such as educational remediation, structure/routine, and cognitive-behavioral approaches should be considered in the management of ADHD. Contemporary work exhibiting improved outcomes associated with specific cognitive therapies in adults with ADHD has been demonstrated. An extensive literature supports the effectiveness of pharmacotherapy not only for the core behavioral symptoms of ADHD but also improvement in linked impairments. Similarities between pediatric and adult groups in the presentation, characteristics, neurobiology, and treatment response of ADHD support the continuity of the disorder across the lifespan.

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REFERENCES

1. Greenhill LL, Pliszka S, Dulcan MK, et al. Practice parameter for the use of stimulant medications in the treatment of children, adolescents, and adults. Journal of the American Academy of Child and Adolescent Psychiatry. Feb; 2002 41(2 Suppl):26S–49S. [PubMed: 11833633]
2. Clinical practice guideline: treatment of the school-aged child with attention-deficit/hyperactivity disorder. Pediatrics. Oct; 2001 108(4):1033–1044. [PubMed: 11581465]
3. Biederman J, Monuteaux M, Mick E, et al. Young Adult Outcome of Attention Deficit Hyperactivity Disorder: A Controlled 10 year Follow-Up Study. Psychological Medicine. 2006; 36:167–179. [PubMed: 16420713]
4. Swanson J, Lerner M, Gupta S, Shoulson I, Wigal S. Development of a new once-a-day formulation of methylphenidate for the treatment of ADHD: Proof of concept and proof of product studies. Archives of General Psychiatry. 2003; 60(2):204–211. [PubMed: 12578439]
5. Barkley R. Major life activity and health outcomes associated with attention-deficit hyperactivity disorder. Journal of Clinical Psychiatry. 2002; 63(Supp 12):10–15. [PubMed: 12562056]
6. Wilens, T.; Spencer, T. Attention-Deficit/Hyperactivity Disorders, Lifetime Course and Strategies for Intervention. In: Howlin, P.; Charman, T.; Ghaziuddin, M., editors. The SAGE Handbook of Developmental Disorders. SAGE Publications; London: 2010.
7. Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. The American Journal of Psychiatry. Jun; 2007 164(6):942–948. [PubMed: 17541055]
8. Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: Results from the national comorbidity survey replication. American Journal of Psychiatry. 2006; 163(4):716–723. [PubMed: 16585449]
9. Centers for Disease Control and Prevention (CDC). Mental health in the United States. Prevalence of diagnosis and medication treatment for attention-deficit/hyperactivity disorder-United States, 2003. Morbidity and Mortality Weekly Report. 2005; 54:842–847. [PubMed: 16138075]
10. Biederman J, Faraone SV, Monuteaux M, et al. Gender effects of attention deficit hyperactivity disorder in adults, revisited. Biological Psychiatry. 2004; 55(7):692–700. [PubMed: 15038997]
11. Anderson JC, Williams S, McGee R, Silva PA. DSM III disorders in preadolescent children. Prevalence in a large sample from the general population. Archives of General Psychiatry. 1987; 44:69–76. [PubMed: 2432848]
12. Bird HR, Gould MS, Staghezza BM. Patterns of diagnostic comorbidity in a community sample of children aged 9 through 16 years. Journal of the American Academy of Child and Adolescent Psychiatry. 1993; 32(2):361–368. [PubMed: 8444766]
13. Abikoff H, McGough J, Vitiello B, et al. Sequential Pharmacotherapy for Children With Comorbid Attention-Deficit/Hyperactivity and Anxiety Disorders. J Am Acad Child Adolesc Psychiatry. May; 2005 44(5):418–427. [PubMed: 15843763]
14. Jensen PS, Shervette RE, Xenakis SN, Richters J. Anxiety and depressive disorders in attention deficit hyperactivity disorder with hyperactivity: New findings. American Journal of Psychiatry. 1993; 150:1203–1209. [PubMed: 8328565]
15. Biederman J, Monuteaux MC, Spencer T, Wilens TE, Faraone SV. Do stimulants protect against psychiatric disorders in youth with ADHD? A 10-year follow-up study. Pediatrics. Jul; 2009 124(1):71–78. [PubMed: 19564285]
16. Faraone SV, Biederman J, Wozniak J, Mundy E, Mennin D, O'Donnell D. Is comorbidity with ADHD a marker for juvenile-onset mania? Journal of the American Academy of Child and Adolescent Psychiatry. 1997; 36(8):1046–1055. [PubMed: 9256584]
17. Wilens T, Biederman J, Wozniak J, Gunawardene S, Wong J, Monuteaux M. Can Adults with Attention-Deficit Hyperactivity Disorder be Distinguished from those with Comorbid Bipolar

Disorder: Findings from a Sample of Clinically Referred Adults. Biological Psychiatry. 2003; 54(1):1–8. [PubMed: 12842302]

18. Wilens T, Biederman J. Alcohol, drugs, and attention-deficit/hyperactivity disorder: A model for the study of addictions in youth. Journal of Psychopharmacology. 2006; 20(4):580–588. [PubMed: 16174669]
19. Wilens TE, Vitulano M, Upadhyaya H, et al. Cigarette smoking associated with attention deficit hyperactivity disorder. J Pediatr. Sep; 2008 153(3):414–419. [PubMed: 18534619]
20. Kollins SH, McClernon FJ, Fuemmeler BF. Association between smoking and attention-deficit/hyperactivity disorder symptoms in a population-based sample of young adults. Arch Gen Psychiatry. Oct; 2005 62(10):1142–1147. [PubMed: 16203959]
21. Biederman J, Monuteaux M, Mick E, et al. Is cigarette smoking a gateway drug to subseqeunt alcohol and illicit drug use disorders? A controlled study of youths with and without ADHD. Biological Psychiatry. 2006; 59:258–264. [PubMed: 16154546]
22. Wilens T, Biederman J, Mick E. Does ADHD Affect the course of substance abuse? Findings from a sample of adults with and without ADHD. American Journal on Addictions. 1998; 7:156–163. [PubMed: 9598219]
23. Levin FR, Evans SM. Diagnostic and treatment issues in comorbid substance abuse and adult attention-deficit hyperactivity disorder. Psychiatric Annals. 2001; 31(5):303–312.
24. Wilson JJ, Levin FR. Attention-deficit/hyperactivity disorder and early-onset substance use disorders. J Child Adolesc Psychopharmacol. Oct; 2005 15(5):751–763. [PubMed: 16262592]
25. Vitiello B. Long-term effects of stimulant medications on the brain: possible relevance to the treatment of attention deficit hyperactivity disorder. Journal of Child and Adolescent Psychopharmacology. 2001; 11(1):25–34. [PubMed: 11322742]
26. Wilens TE, Adamson J, Monuteaux MC, et al. Effect of prior stimulant treatment for attention-deficit/hyperactivity disorder on subsequent risk for cigarette smoking and alcohol and drug use disorders in adolescents. Archives of Pediatrics and Adolescent Medicine. Oct; 2008 162(10):916–921. [PubMed: 18838643]
27. Biederman J, Monuteaux MC, Spencer T, Wilens TE, Macpherson HA, Faraone SV. Stimulant therapy and risk for subsequent substance use disorders in male adults with ADHD: a naturalistic controlled 10-year follow-up study. American Journal of Psychiatry. May; 2008 165(5):597–603. [PubMed: 18316421]
28. Barkley R, Biederman J. The case against a specific age of onset criterion for attention deficit hyperactivity disorder. American Journal of Psychiatry. 1997
29. Association, AP. Diagnostic and Statistical Manual of Mental Disorders: Fourth Edition Text Revision (DSM-IV-TR). 4th ed.. American Psychiatric Association; Washington, DC: 2000.
30. APA. Diagnostic and Statistical Manual of Mental Disorders IV. 4th ed.. American Psychiatric Association Press; Washington, D.C.: 1994.
31. Wilens T, Biederman J, Faraone S, Martelon M, Westerberg D, Spencer T. Presenting ADHD Symptoms, Subtypes, and Comorbid Disorders in Clinically Referred Adults with ADHD. Journal of Clinical Psychiatry. 2009; 70(11):1557–1562. [PubMed: 20031097]
32. Millstein RB, Wilens TE, Biederman J, Spencer TJ. Presenting ADHD symptoms and subtypes in clincially referred adults with ADHD. Journal of Attention Disorders. 1997; 2(3):159–166.
33. Lahey BB, Pelham WE, Loney J, Lee SS, Willcutt E. Instability of the DSM-IV Subtypes of ADHD from preschool through elementary school. Archives of General Psychiatry. Aug; 2005 62(8):896–902. [PubMed: 16061767]
34. Mannuzza S, Klein RG, Moulton JL 3rd. Young adult outcome of children with “situational” hyperactivity: a prospective, controlled follow-up study. Journal of Abnormal Child Psychology. Apr; 2002 30(2):191–198. [PubMed: 12008657]
35. Hospital, MG. School Psychiatry Program & Madi Resource Center. http://www2.massgeneral.org/schoolpsychiatry/ [Accessed August 12, 2010]
36. Adler, L.; Cohen, J. Diagnosis and evaluation of adults with ADHD. In: Spencer, T., editor. Psychiatric Clinics of North America. Vol. 27. Saunders Press; Philadelphia, P.A.: 2004. p. 187-201.

37. Kooij JJS, Boonstra AM, Swinkels SH, Bekker EM, de Noord I, Buitelaar JK. Reliability, validity, and utility of instruments for self-report and informant report concerning symptoms of ADHD in adult patients. Journal of Attention Disorders. Jan; 2008 11(4):445–458. [PubMed: 18083961]
38. Kessler RC, Adler L, Ames M, et al. The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. Psychological Medicine. Feb; 2005 35(2):245–256. [PubMed: 15841682]
39. Mick E, Faraone SV, Biederman J, Spencer T. The course and outcome of ADHD. Primary Psychiatry. 2004; 11(7):42–48.
40. Biederman J, Faraone S, Mick E. Age dependent decline of ADHD symptoms revisited: Impact of remission definition and symptom subtype. American Journal of Psychiatry. 2000; 157:816–817. [PubMed: 10784477]
41. Hart EL, Lahey BB, Loeber R, Applegate B, Frick PJ. Developmental change in attention-deficit hyperactivity disorder in boys: A four-year longitudinal study. Journal of Abnormal Child Psychology. 1995; 23(6):729–749. [PubMed: 8609310]
42. Martinussen R, Hayden J, Hogg-Johnson S, Tannock R. A meta-analysis of working memory impairments in children with attention-deficit/hyperactivity disorder. Journal of American Academy of Child and Adolescent Psychiatry. Apr; 2005 44(4):377–384.
43. Barkley RA. Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. Psychological Bulletin. 1997; 121(1):65–94. [PubMed: 9000892]
44. Seidman LJ. Neuropsychological functioning in people with ADHD across the lifespan. Clinical Psychology Review. Aug; 2006 26(4):466–485. [PubMed: 16473440]
45. de Zeeuw P, Aarnoudse-Moens C, Bijlhout J, et al. Inhibitory performance, response speed, intraindividual variability, and response accuracy in ADHD. Journal of the American Academy of Child and Adolescent Psychiatry. Jul; 2008 47(7):808–816. [PubMed: 18520957]
46. Sergeant JA, Geurts H, Oosterlaan J. How specific is a deficit of executive functioning for attention-deficit/hyperactivity disorder? Behavioural Brain Research. 2002; 130(1-2):3–28. [PubMed: 11864714]
47. Sonuga-Barke E, Dalen L, Remington B. Do executive deficits and delay aversio make independent contributions to preschool attention-deficit/hyperactivity disorder symptoms. Journal of the American Academy of Child and Adolescent Psychiatry. 2003; 42(11):1335–1342. [PubMed: 14566171]
48. Shaw P, Lalonde F, Lepage C, et al. Development of cortical asymmetry in typically developing children and its disruption in attention-deficit/hyperactivity disorder. Arch Gen Psychiatry. Aug; 2009 66(8):888–896. [PubMed: 19652128]
49. McAlonan GM, Cheung V, Chua SE, et al. Age-related grey matter volume correlates of response inhibition and shifting in attention-deficit hyperactivity disorder. Br J Psychiatry. Feb; 2009 194(2):123–129. [PubMed: 19182173]
50. Cole WR, Mostofsky SH, Larson JC, Denckla MB, Mahone EM. Age-related changes in motor subtle signs among girls and boys with ADHD. Neurology. Nov 4; 2008 71(19):1514–1520. [PubMed: 18981373]
51. Ivanov I, Bansal R, Hao X, et al. Morphological abnormalities of the thalamus in youths with attention deficit hyperactivity disorder. Am J Psychiatry. Apr; 2010 167(4):397–408. [PubMed: 20123910]
52. Hervey AS, Epstein J, Curry JF. The neuropsychology of adults with attention deficit hyperactivity disorder: A meta-analytic review. Neuropsychology. 2004; 18(3):485–503. [PubMed: 15291727]
53. Seidman, L.; Doyle, A.; Fried, R.; Valera, E.; Crum, K.; Matthews, L. Neuropsychological functioning in adults with attention-deficit/hyperactiity disorder. In: Spencer, T., editor. Adult ADHD, Psychiatric Clinics of North America. Vol. 27. Elsevier Science; 2004. p. 261-282.
54. Biederman J, Monuteaux M, Seidman L, et al. Impact of Executive Function Deficits and ADHD on Academic Outcomes in Children. Journal of Consulting and Clinical Psychology. 2004; 72(5): 757–766. [PubMed: 15482034]
55. Castellanos FX, Lee PP, Sharp W, et al. Developmental trajectories of brain volume abnormalities in children and adolescents with attention-deficit/hyperactivity disorder. Journal of the American Medical Association. 2002; 288(14):1740–1748. [PubMed: 12365958]

56. Seidman LJ, Valera EM, Makris N, et al. Dorsolateral prefrontal and anterior cingulate cortex volumetric abnormalities in adults with attention-deficit/hyperactivity disorder identified by magnetic resonance imaging. Biological Psychiatry. Nov 15; 2006 60(10):1071–1080. [PubMed: 16876137]
57. Shaw P, Eckstrand K, Sharp W, et al. Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation. Proceedings of the National Academy of Sciences. Dec 4; 2007 104(49):19649–19654.
58. Makris N, Biederman J, Valera EM, et al. Cortical thinning of the attention and executive function networks in adults with attention-deficit/hyperactivity disorder. Cerebral Cortex. Jun; 2007 17(6): 1364–1375. [PubMed: 16920883]
59. Epstein JN, Casey BJ, Tonev ST, et al. ADHD- and medication-related brain activation effects in concordantly affected parent-child dyads with ADHD. The Journal of Child Psychology and Psychiatry. Sep; 2007 48(9):899–913.
60. Casey BJ, Durston S. From behavior to cognition to the brain and back: what have we learned from functional imaging studies of attention deficit hyperactivity disorder? American Journal of Psychiatry. Jun; 2006 163(6):957–960. [PubMed: 16741192]
61. Bush G, Spencer TJ, Holmes J, et al. Functional magnetic resonance imaging of methylphenidate and placebo in attention-deficit/hyperactivity disorder during the multi-source interference task. Arch Gen Psychiatry. Jan; 2008 65(1):102–114. [PubMed: 18180434]
62. McGuffin P, Riley B, Plomin R. Toward behavioral genomics. Science. 2001; 291:1232–1249. [PubMed: 11233447]
63. Faraone S, Biederman J. Genetics of attention-deficit hyperactivity disorder. Child and Adolescent Psychiatric Clinics of North America. 1994; 3(2):285–302.
64. Goodman R, Stevenson J. A twin study of hyperactivity: II. The aetiological role of genes, family relationships and perinatal adversity. Journal of Child Psychology and Psychiatry. 1989; 30(5): 691–709. [PubMed: 2793957]
65. Levy F, Hay D, McStephen M, Wood C, Waldman I. Attention-deficit hyperactivity disorder: A category or a continuum? Genetic analysis of a large-scale twin study. Journal of the American Academy of Child and Adolescent Psychiatry. 1997; 36(6):737–744. [PubMed: 9183127]
66. Faraone, SV. Genetics of Adult Attention Deficit Hyperactivity Disorder. In: Spencer, T., editor. Psychiatric Clinics of North America. Vol. 27. Saunders Press; Philadelphia, PA: 2004. p. 303-321.
67. Rietveld MJ, Hudziak JJ, Bartels M, van Beijsterveldt CE, Boomsma DI. Heritability of attention problems in children: longitudinal results from a study of twins, age 3 to 12. J Child Psychol Psychiatry. Mar; 2004 45(3):577–588. [PubMed: 15055376]
68. Pelham W, Wheeler T, Chronis A. Empirically supported psychosocial treatments for attention deficit hyperactivity disorder. Journal of Clinical Child Psychology. 1998; 27(2):190–205. [PubMed: 9648036]
69. Chronis AM, Jones HA, Raggi VL. Evidence-based psychosocial treatments for children and adolescents with attention-deficit/hyperactivity disorder. Clinical Psychology Review Aug. 2006; 26(4):486–502.
70. van den Hoofdakker BJ, van der Veen-Mulders L, Sytema S, Emmelkamp PM, Minderaa RB, Nauta MH. Effectiveness of behavioral parent training for children with ADHD in routine clinical practice: a randomized controlled study. Journal of American Academy of Child and Adolescent Psychiatry. Oct; 2007 46(10):1263–1271.
71. Barkley, R. Attention-Deficit/Hyperactivity Disorder: A Handbook for Diagnosis and Treament. 3rd ed.. Guilford Press; New York, NY: 2005.
72. Abikoff H. Cognitive training in ADHD children; Less to it than meets the eye. Journal of Learning Disabilities. 1991; 24:205–209. [PubMed: 1875155]
73. McDermott, SP.; Wilens, TE. Cognitive therapy for adults with ADHD. In: Brown, T., editor. Subtypes of Attention Deficit Disorders in Children, Adolescents, and Adults. American Psychiatric Press, Inc; Washington, DC: 2000. p. 569-606.

74. Safren SA, Otto M, Sprich S, Winett C, Wilens T, Biederman J. Cognitive-behavioral therapy for ADHD in medication-treated adults with continued symptoms. Behavior Research and Therapy. 2005; 43(7):831–842.
75. Solanto MV, Marks DJ, Mitchell KJ, Wasserstein J, Kofman MD. Development of a new psychosocial treatment for adult ADHD. Journal of Attention Disorders. May; 2008 11(6):728–736. [PubMed: 17712167]
76. Toplak ME, Connors L, Shuster J, Knezevic B, Parks S. Review of cognitive, cognitive-behavioral, and neural-based interventions for Attention-Deficit/Hyperactivity Disorder (ADHD). Clin Psychol Rev. Jun; 2008 28(5):801–823. [PubMed: 18061324]
77. Solanto MV, Marks DJ, Wasserstein J, et al. Efficacy of Meta-Cognitive Therapy for Adult ADHD. Am J Psychiatry. Aug; 2010 167(8):958–968. [PubMed: 20231319]
78. Hechtman L, Abikoff H, Klein RG, et al. Academic Achievement and Emotional Status of Children With ADHD Treated With Long-Term Methylphenidate and Multimodal Psychosocial Treatment. Journal of American Academy of Child and Adolescent Psychiatry. Jul; 2004 43(7): 812–819.
79. MTA Cooperative Group. Moderators and mediators of treatment response for children with attention-deficit/hyperactivity disorder: the Multimodal Treatment Study of children with Attention-deficit/hyperactivity disorder. Archives of General Psychiatry. 1999; 56(12):1088–1096. [PubMed: 10591284]
80. MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. The MTA Cooperative Group. Multimodal Treatment Study of Children with ADHD. Archives of General Psychiatry. 1999; 56(12):1073–1086. see comments. [PubMed: 10591283]
81. Wilens T. Mechanism of Action of Agents used in ADHD. Journal of Clinical Psychiatry. 2006; 67(Suppl 8):32–37. [PubMed: 16961428]
82. Spencer T, Biederman J, Ciccone P, et al. A PET Study Examining Pharmacokinetics, Detection and Likeability, and Dopamine Transporter Receptor Occupancy Of Short and Long-Acting Orally Administered Formulations of Methylphenidate in Adults. American Journal of Psychiatry. 2006; 163(3):387–395. [PubMed: 16513858]
83. Parasrampuria DA, Schoedel KA, Schuller R, et al. Do formulation differences alter abuse liability of methylphenidate? A placebo-controlled, randomized, double-blind, crossover study in recreational drug users. Journal of Clinical Psychopharmacology. Oct; 2007 27(5):459–467. [PubMed: 17873677]
84. Greenhill, L.; Osman, B. Ritalin: Theory and Practice. Mary Ann Liebert; New York: 1999.
85. Greenhill L, Kollins S, Abikoff H, et al. Efficacy and Safety of Immediate-Release Methylphenidate Treatment for Preschoolers With ADHD. Journal of American Academy of Child and Adolescent Psychiatry. Nov; 2006 45(11):1284–1293.
86. Wilens TE. Pharmacotherapy of ADHD in adults. CNS Spectr. May; 2008 13(5 Suppl 8):11–13. [PubMed: 18567133]
87. Barkley RA, McMurray MB, Edelbrock CS, Robbin K. Side effects of methylphenidate in children with attention deficit hyperactivity disorder: A systemic, placebo-controlled evaluation. Pediatrics. 1990; 86(2):184–192. [PubMed: 2196520]
88. Safer D, Allen R, Barr E. Depression of growth in hyperactive children on stimulant drugs. New England Journal of Medicine. 1972; 287(5):217–220. [PubMed: 4556640]
89. MTA Cooperative Group. National institue of mental health multimodal treatment study of ADHD follow-up: Changes in effectiveness and growth after the end of treatment. Pediatrics. 2004; 113:762–769. [PubMed: 15060225]
90. Gadow K, Sverd J, Sprafkin J, Nolan E, Grossman S. Long-term Methylphenidate therapy in children with comorbid Attention-Deficit Hyperactivity Disorder and Chronic Multiple Tic Disorder. Archives of General Psychiatry. 1999; 56(4):330–336. [PubMed: 10197827]
91. Castellanos FX, Giedd JN, Elia J, et al. Controlled stimulant treatment of ADHD and comorbid tourette's syndrome: Effects of stimulant and dose. Journal of the American Academy of Child and Adolescent Psychiatry. 1997; 36(5):589–596. [PubMed: 9136492]

92. Rappley MD, Moore JW, Dokken D. ADHD drugs and cardiovascular risk. The New England Journal of Medicine. May 25; 2006 354(21):2296–2298. author reply 2296-2298. [PubMed: 16729375]

93. Gutgesell, H.; Atkins, D.; Barst, R., et al. Cardiovascular monitoring of children and adolescents receiving psychotropic drugs. American Heart Association, Inc.; 1999. p. 979-982.

94. Perrin JM, Friedman RA, Knilans TK. Cardiovascular monitoring and stimulant drugs for attention-deficit/hyperactivity disorder. Pediatrics. Aug; 2008 122(2):451–453. [PubMed: 18676566]

95. Wilens TE, Gignac M, Swezey A, Monuteaux MC, Biederman J. Characteristics of adolescents and young adults with ADHD who divert or misuse their prescribed medications. Journal of American Academy of Child and Adolescent Psychiatry. Apr; 2006 45(4):408–414.

96. Wilens TE, Adler LA, Adamson J, et al. Misuse and diversion of stimulants prescribed for ADHD: a systematic review of the literature. Journal of American Academy of Child and Adolescent Psychiatry. Jan; 2008 47(1):21–31.

97. McCabe SE, Knight JR, Teter CJ, Wechsler H. Non-medical use of prescription stimulants among US college students: prevalence and correlates from a national survey. Addiction. Jan; 2005 99(1): 96–106. [PubMed: 15598197]

98. Michelson D, Faries D, Wernicke J, et al. Atomoxetine in the treatment of children and adolescents with attention-deficit/hyperactivity disorder: a randomized, placebo-controlled, dose-response study. Pediatrics. 2001; 108(5):E83. [PubMed: 11694667]

99. Michelson D, Allen AJ, Busner J, et al. Once-daily atomoxetine treatment for children and adolescents with ADHD: A randomized, placebo-controlled study. American Journal of Psychiatry. 2002; 159:1896–1901. [PubMed: 12411225]

100. Michelson D, Buitelaar JK, Danckaerts M, et al. Relapse Prevention in Pediatric Patients with ADHD Treated with Atomoxetine: A Randomized, Double-Blind, Placebo-Controlled Study. Journal of American Academy of Child and Adolescent Psychiatry. 2004; 43(7):896–904.

101. Geller D, Donnelly C, Lopez F, et al. Atomoxetine treatment for pediatric patients with attention-deficit/hyperactivity disorder with comorbid anxiety disorder. Journal of American Academy of Child and Adolescent Psychiatry. Sep; 2007 46(9):1119–1127.

102. Wilens TE, Adler LA, Weiss MD, et al. Atomoxetine treatment of adults with ADHD and comorbid alcohol use disorders. Drug Alcohol Depend. Jul 1; 2008 96(1-2):145–154. [PubMed: 18403134]

103. Lilly USA L. Strattera (atomoxetine HCl) - Important Safety Information. http://www.strattera.com/pages/index.aspx [Accessed August 12, 2010]

104. Sallee F, McGough J, Wigal T, Donahue J, Lyne A, Biederman J. Guanfacine Extended Release in Children and Adolescents With Attention-Deficit/Hyperactivity Disorder: A Placebo-Controlled Trial. J. Am. Acad. Child Adolesc. Psychiatry. Feb; 2009 48(2):155–165. [PubMed: 19106767]

105. Connor DF, Fletcher KE, Swanson JM. A meta-analysis of clonidine for symptoms of attention-deficit hyperactivity disorder. Journal of the American Academy of Child and Adolescent Psychiatry. 1999; 38(12):1551–1559. [PubMed: 10596256]

106. Kurlan R. Methylphenidate to treat ADHD is not contraindicated in children with tics. Movement Disorders. Jan; 2002 17(1):5–6. [PubMed: 11835432]

107. Hazell PL, Stuart JE. A randomized controlled trial of clonidine added to psychostimulant medication for hyperactive and aggressive children. Journal of American Academy of Child and Adolescent Psychiatry. Aug; 2003 42(8):886–894.

108. Palumbo DR, Sallee FR, Pelham WE Jr. Bukstein OG, Daviss WB, McDermott MP. Clonidine for attention-deficit/hyperactivity disorder: I. Efficacy and tolerability outcomes. Journal of American Academy of Child and Adolescent Psychiatry. Feb; 2008 47(2):180–188.

109. Spencer TJ, Greenbaum M, Ginsberg LD, Murphy WR. Safety and effectiveness of coadministration of guanfacine extended release and psychostimulants in children and adolescents with attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol. Oct; 2009 19(5):501–510. [PubMed: 19877974]

110. Wilens, T.; Youcha, SH.; Lyne, A.; Grannis, K.; Children, A.; Findling, RL. A multisite placebo-controlled trial of morning or evening dosed extended-release guanfacine in combination with psychostimulants in children and adolescents; Paper presented at: Scientific Meetings of the Society of Biological Psychiatry; 2010; New Orleans: May. 2010

111. Conners CK, Casat CD, Gualtieri CT, et al. Bupropion hydrochloride in attention deficit disorder with hyperactivity. Journal of American Academy of Child and Adolescent Psychiatry. 1996; 35(10):1314–1321.

112. Wilens TE, Spencer TJ, Biederman J, et al. A controlled clinical trial of bupropion for attention deficit hyperactivity disorder in adults. American Journal of Psychiatry. 2001; 158(2):282–288. [PubMed: 11156812]

113. Wilens T, Haight BR, Horrigan JP, et al. Bupropion XL in Adults with ADHD: A Randomized, Placebo-Controlled Study. Biological Psychiatry. 2005; 57(7):793–801. [PubMed: 15820237]

114. Daviss WB, Bentivoglio P, Racusin R, Brown KM, Bostic JQ, Wiley L. Bupropion sustained release in adolescents with comorbid attention-deficit/hyperactivity disorder and depression. J Am Acad Child Adolesc Psychiatry. Mar; 2001 40(3):307–314. [PubMed: 11288772]

115. Wilens T, Prince J, Spencer T, et al. An Open Trial of Bupropion for the Treatment of Adults with Attention Deficit Hyperactivity Disorder and Bipolar Disorder. Biological Psychiatry. 2003; 54(1):9–16. [PubMed: 12842303]

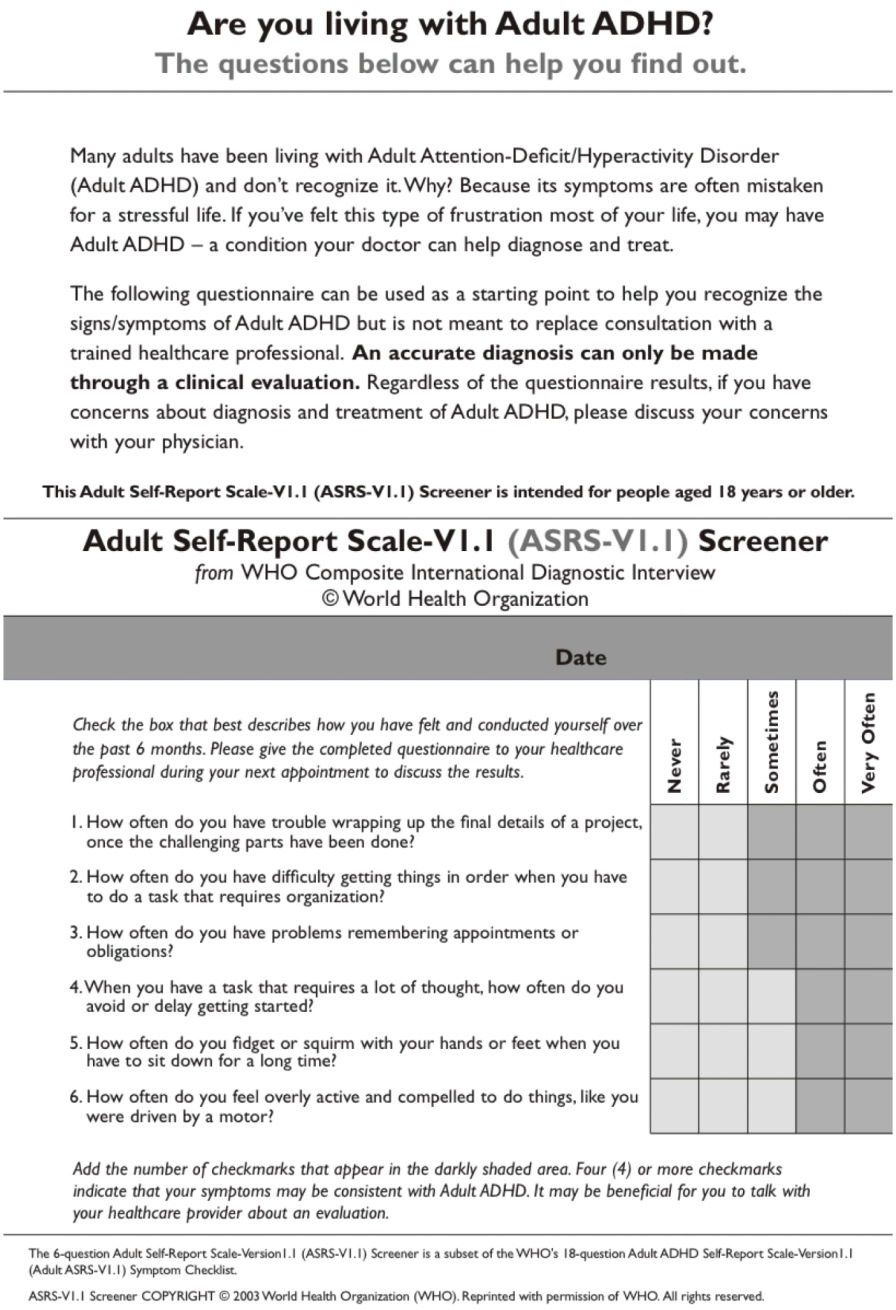
116. Spencer, T.; Biederman, J.; Wilens, T. Pharmacotherapy of attention-deficit/hyperactivity disorder: A life span perspective. In: Dickstein, L.; Riba, M.; Oldham, J., editors. Review of Psychiatry. Vol. 16. American Psychiatric Press; Washington, DC: 1998. p. IV-87-IV-127.

117. Biederman J, Pliszka SR. Modafinil improves symptoms of attention-deficit/hyperactivity disorder across subtypes in children and adolescents. J Pediatr. Mar; 2008 152(3):394–399. [PubMed: 18280848]

Summary

Attention-deficit/hyperactivity disorder is a heterogenous disorder that is prevalent worldwide and frequently persists from adolescence into adult years. Attention-deficit/hyperactivity disorder continues to be diagnosed by careful history with an understanding of the developmental presentation of normal behavior and symptoms of the disorder. It has been reconceptualized as a more chronic condition, with approximately half of children continuing to exhibit symptoms and impairment into adulthood.[39, 40] Most individuals with ADHD have a comorbid disorder, including oppositional, conduct, anxiety, or mood disorders.[3, 11, 12] In addition, ADHD carries with it significant impairment in academic, occupational, social, and intrapersonal domains necessitating treatment. Converging data strongly support a neurobiological and genetic basis for ADHD, with catecholaminergic dysfunction as a central finding.

Psychosocial interventions such as educational remediation, structure/routine, and cognitive behavioral approaches should be considered in the management of ADHD. Contemporary work exhibiting improved outcomes associated with specific cognitive therapies in adults with ADHD has been demonstrated. Extensive literature supports the effectiveness of pharmacotherapy not only for the core behavioral symptoms of ADHD but also improvement in linked impairments. Similarities between pediatric and adult groups in the presentation, characteristics, neurobiology, and treatment response of ADHD support the continuity of the disorder across the lifespan.



Are you living with Adult ADHD?

The questions below can help you find out.

Many adults have been living with Adult Attention-Deficit/Hyperactivity Disorder (Adult ADHD) and don't recognize it. Why? Because its symptoms are often mistaken for a stressful life. If you've felt this type of frustration most of your life, you may have Adult ADHD – a condition your doctor can help diagnose and treat.

The following questionnaire can be used as a starting point to help you recognize the signs/symptoms of Adult ADHD but is not meant to replace consultation with a trained healthcare professional. **An accurate diagnosis can only be made through a clinical evaluation.** Regardless of the questionnaire results, if you have concerns about diagnosis and treatment of Adult ADHD, please discuss your concerns with your physician.

This Adult Self-Report Scale-V1.1 (ASRS-V1.1) Screener is intended for people aged 18 years or older.

Adult Self-Report Scale-V1.1 (ASRS-V1.1) Screener

from WHO Composite International Diagnostic Interview
© World Health Organization

Date

Check the box that best describes how you have felt and conducted yourself over the past 6 months. Please give the completed questionnaire to your healthcare professional during your next appointment to discuss the results.	Never	Rarely	Sometimes	Often	Very Often
1. How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?					
2. How often do you have difficulty getting things in order when you have to do a task that requires organization?					
3. How often do you have problems remembering appointments or obligations?					
4. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?					
5. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?					
6. How often do you feel overly active and compelled to do things, like you were driven by a motor?					

Add the number of checkmarks that appear in the darkly shaded area. Four (4) or more checkmarks indicate that your symptoms may be consistent with Adult ADHD. It may be beneficial for you to talk with your healthcare provider about an evaluation.

The 6-question Adult Self-Report Scale-Version1.1 (ASRS-V1.1) Screener is a subset of the WHO's 18-question Adult ADHD Self-Report Scale-Version1.1 (Adult ASRS-V1.1) Symptom Checklist.

Figure 1. ADHD Screener

MGH CARDIOVASCULAR SCREEN

Cardiovascular History ***A.) Personal History***	Yes	No	Comment
1.) Congenital or acquired cardiac disease	○	○	
2.) Coronary artery disease	○	○	
3.) Chest pain	○	○	
4.) Palpitations	○	○	
5.) Shortness of breath	○	○	
6.) Dizziness	○	○	
7.) Syncope	○	○	
B.) Family History (<30 years of age)			
1.) History of early MI	○	○	
2.) History of cardiac death	○	○	
3.) History of significant arrthymias?	○	○	
4.) History of long QT syndrome	○	○	
C.)Objective			
1.) Baseline (off medication) blood pressure and heart rate within normal limits	○	○	

If positive on an item, recommend referral to P.C.P or pediatric cardiology for further assessment prior to initiating medication.

References:

1. "American Academy of Pediatrics/American Heart Association clarification of statement on cardiovascular evaluation and monitoring of children and adolescents with heart disease receiving medications for ADHD: May 16, 2008." J Dev Behav Pediatr **29**(4): 335.
2. "ECG's before stimulants in Children." The Medical Letter. 2008
3. Gutgesell, H., D. Atkins, et al. (1999). "AHA scientific statement: Cardiovascular monitoring of children and adolescents receiving psychotropic drugs." Journal of the American Academy of Child and Adolescent Psychiatry **38**(8): 979-982.
4. Vetter, V. L., J. Elia, et al. (2008). "Cardiovascular Monitoring of Children and Adolescents With Heart Disease Receiving Stimulant Drugs. A Scientific Statement From the American Heart Association Council on Cardiovascular Disease in the Young Congenital Cardiac Defects Committee and the Council on Cardiovascular Nursing." Circulation.
5. Wilens, T., T. Spencer, et al. (2006). "Stimulants and Sudden Death: What is a Physician to do?" Pediatrics **118**(3): 1215-9.

Figure 2. CV Screener

TABLE 1
Medications Used in the Treatment of ADHD

Generic class (Brand name)	DAILY DOSE (MG/KG)	DAILY DOSAGE SCHEDULE	TYPICAL DOSING SCHEDULE**	COMMON ADVERSE EFFECTS
Stimulants				
Amphetamine	0.3-1.5			-Insomnia
Short-acting (Dexedrine-tablets)		Twice or three times	5-30 mg BID to TID	-Decreased appetite, weight loss -Tic exacerbation -Depression, anxiety
Intermediate-acting (Adderall, Dexedrine spansules)		Once or twice	5-30 mg BID	-Rebound phenomena (short acting preparations) -Increased blood pressure/ pulse
Extended-release (Adderall-XR; Vyvanse)		Once	10-70 mg QD	
Methylphenidate				-Insomnia
Short acting (Ritalin, Metadate; Focalin)	0.5.0-2.0 (< 1 mg for d-MPH or patch)	Twice to four times	5-40 mg BID to QID	-Decreased appetite, weight loss -Tic exacerbation -Depression, anxiety
Intermediate-acting (Ritalin SR, Metadate SR)		Once or twice	10-60 mg QD to BID	-Rebound phenomena (short acting preparations) - Increased blood pressure/ pulse
Extended-release (Concerta; Metadate CD; Focalin XR; Daytrana Patch)		Once	10-90 mg QD	
Noradrenergic Agents				
Atomoxetine (Strattera)	1.0-2.0	Once or twice	25-140 mg QD	-GI Upset, nausea -Sedation, insomnia -Agitation
Alpha Agonists				
Guanfacine (Intuniv [Extended-release; Tenex*])	30-100 mcg/kg	Twice	0.5-1 mg TID 1-4 mg daily	-Similar to clonidine but less sedation
Clonidine* (Catapress)	3-10 mcg/kg	Twice or three times	0.05-0.1 mg TID	-Sedation, dry mouth, depression -Confusion (with high dose) -Bradycardias, syncope -Rebound hypertension
Modafinil*		Once or twice	100-400 mg QD	-Insomnia -Weight loss -Increased blood pressure/pulse
Antidepressants*				
Tricyclics (TCAs)* e.g., Imipramine, Desipramine, Nortriptyline (NT)	2.0-5.0 (1.0-3.0 for NT)	Once or twice	25-300 mg QD (25-150 mg QD for NT)	-Dry mouth, constipation -Weight loss -Vital sign and ECG changes

Generic class (Brand name)	DAILY DOSE (MG/KG)	DAILY DOSAGE SCHEDULE	TYPICAL DOSING SCHEDULE**	COMMON ADVERSE EFFECTS
Bupropion* (Wellbutrin short acting and sustained release-SR, XL)	1.0-6.0	Once to three times	75-100 mg TID 150-200 BID (SR); 150-450 XL	-Irritability, insomnia -Risk of seizures -Contraindicated in bulimics

* Denotes not FDA approved for ADHD at this time

** Denotes typical clinical dosing of these compounds; not reflective of FDA approved indications or dosing