ABSTRACT

Once believed to be a childhood syndrome, attention-deficit/hyperactivity disorder (ADHD) is increasingly recognized as a disorder that continues into adulthood. The Diagnostic and Statistical Manual of Mental Disorders, fourth edition, definitions for ADHD suggest that it may persist into adulthood, but they fail to differentiate between childhood and adult manifestations of the disorder. This article reports on the findings of several longitudinal studies of children with ADHD into adulthood. The findings suggest that while many symptoms and impairments are similar, they manifest differently in adults, primarily as a result of maturity and changes in lifestyle. In this article, adult ADHD symptoms are described, and clinical trial results of the efficacy of off-label use of drugs for adult ADHD are reviewed. Preliminary efficacy results of atomoxetine (an investigational drug currently under Food and Drug Administration review) to treat adult ADHD are also reported. (Advanced Studies in Medicine. 2002;2(25):902-905)

DIAGNOSIS AND CLINICAL FEATURES

Until recently, attention-deficit/hyperactivity disorder (ADHD) was seldom diagnosed in adults, despite medical evidence supporting its existence. The persistence into adulthood of ADHD symptoms such as impulsivity, inattention, and difficulty regulating physical activity has been reported in a number of studies dating back to the mid 1970s. Nonetheless, the early emphasis on hyperactivity as a core component of ADHD, a trait that we now know typically diminishes with age, overshadowed the continuation of the cognitive symptoms into adulthood.

Even though awareness of adult ADHD historically has been limited, growing medical evidence in this area and revised Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) diagnostic criteria for childhood ADHD have spawned more widespread recognition of this syndrome. The third edition (DSM-III) designated an attention deficit disorder classification, describing it as residual for adults, but remained somewhat vague about adult symptoms. The revised third edition of DSM (DSM-III-R) stated that approximately one third of children with ADHD showed continuing signs into adulthood, but did not code this as a separate category. The fourth edition of DSM (DSM-IV) states that “symptoms attenuate during late adolescence and adulthood, although a minority experience the full complement of symptoms of ADHD into midadulthood,” thereby acknowledging the persistence of ADHD diagnosis within the adult population.

DSM-IV defines 3 ADHD subtypes: predominantly inattentive type, predominantly hyperactive-
impulsive type, and combined type. Overall diagnostic criteria for ADHD include onset by age 7 years, impairment from symptoms in at least 2 settings, and significant impairment in social, academic, or occupational functioning. Although DSM-IV suggests continuation of symptoms into adulthood, it does not specifically define the syndrome in adults. Diagnostic criteria also suggest that those diagnosed with the inattentive type have 6 or more inattentive symptoms present for more than 6 months, and that those with hyperactive type have 6 or more of the symptoms for hyperactive subtype. To be diagnosed with the combined subtype, a person must have 6 or more inattentive symptoms and 6 or more hyperactive symptoms.

For those with the inattentive subtype, symptoms may include difficulty sustaining attention in tasks or play and lack of close attention to details in schoolwork or on the job.

One key point for adults with the disorder is that the outward restlessness and hyperactivity that occurs in children is instead manifested as internal restlessness. Whereas a child may be running or climbing too much and feeling “on the go,” adults may choose occupations where getting up and down is an essential component of the job, eg, sales representatives or stock brokers.

**Childhood vs Adult ADHD**

ADHD is generally thought to be a genetically transmitted, neurobiological disorder of dopaminergic and noradrenergic pathways with a high genetic rate (~50% concordance rates in first-degree relatives). Existing prevalence and natural history data suggest that the prevalence of ADHD in children is 6% to 9%. Somewhere between one third and two thirds of adults continue to manifest their childhood ADHD symptoms, meaning that 2% to 6% (most commonly 4%) of the general adult population has ADHD.

However, these data are based upon longitudinal studies begun at a time when the classification of ADHD did not differentiate between hyperactive and inattentive subtypes. Therefore, because we now know that hyperactivity symptoms diminish when ADHD persists into adulthood, it is likely that the use of older definitions of ADHD have resulted in a substantial underrepresentation of overall adult prevalence. While adult presentation of ADHD can occur, adult-onset ADHD is not a valid diagnosis and most likely represents another condition. By DSM-IV definition, ADHD begins in childhood; diagnostic criteria state that evidence of the condition must be demonstrated by age 7 years.

As children mature into adulthood, the DSM-IV diagnostic threshold (at least 6 symptoms of hyperactivity/impulsivity and/or inattention) often manifests differently. The aimless restlessness that children feel becomes a more purposeful kind of restlessness in adulthood. For example, symptoms of hyperactivity in children (eg, fidgeting, excessive talking) frequently manifest in adults with ADHD as a tendency for overworking, typically in jobs that require an abundance of physical activity. In adulthood, symptoms of impulsivity can lead to more serious consequences, because adults with ADHD generally have a low frustration tolerance that can lead to high job and relationship turnover, explosive or irritable episodes, and reckless driving. Common adult manifestations of inattention include poor time management and difficulty completing and changing tasks. When possible, adults often attempt to compensate for such shortcomings by enlisting support staff to assist with organizational tasks.

One key point for adults with the disorder is that the outward restlessness and hyperactivity that occurs in children is instead manifested as internal restlessness. Whereas a child may be running or climbing too much and feeling “on the go,” adults may choose occupations where getting up and down is an essential component of the job, eg, sales representatives or stock brokers.

**Related Impairments**

**Educational Outcomes**

According to evidence gleaned from self-reports and high-school transcripts, adults with ADHD experience more grade retention (Milwaukee Young Adult Outcome Study [MKE]: 42%, ADHD vs 13%, control), are more often suspended (MKE: 60%, ADHD vs 19%, control), and have a higher expulsion rate (MKE: 14%, ADHD vs 6%, control) and drop-out rate (MKE: 32%, ADHD vs 0%, control). On average, those with ADHD had lower grade-point averages (MKE: 1.7, ADHD vs 2.6, control). In addition, fewer adults with ADHD enter college (MKE: 22%, ADHD vs 77%, control) and, among those with ADHD who do, they have a lower matriculation rate (5%, ADHD vs 35%, control).
Employment Problems

Employment problems have been reported in adults with ADHD, leading 35% of these adults to become self-employed by the time they are between ages 30 and 40 years. Specifically, adults with ADHD are more likely to be fired (MKE: 55%, ADHD vs 23%, control; mean 1.1 jobs vs 0.3) and they change jobs more often (MKE: 2.7 jobs, ADHD vs 1.3, control, within 2-8 years of leaving high school). In addition, they display more ADHD/oppositional defiant disorder symptoms on the job (as rated by current supervisors [MKE]) and garner lower work performance ratings (as reported by current supervisors [MKE]).

Motor Vehicle Driving Risks

Adults with ADHD are at significantly higher risk for motor vehicle accidents, according to assessments based upon self-report, driving records, lab testing, driving simulators, and behind-the-wheel tests. Interestingly when placed on driving simulators, ADHD patients tended to accelerate into critical incidents rather than breaking away from them (conversation with RA Barkley, MD [2002]).

Sexual/Reproductive Risks

Assessed through self-reports, it appears that sexual/reproductive risks are higher in patients with ADHD. They begin sexual activity earlier (15 years, ADHD vs 16 years, control), have many more sexual partners (18.6, ADHD vs 6.5, control), and stay with each partner for less time than adults without ADHD. They are also less likely to use contraception and have a far greater risk of teen pregnancy (38%, ADHD vs 4%, control). Fifty-four percent of adults with ADHD do not have custody of their offspring. Adults with ADHD are also at a higher risk for contracting sexually transmitted diseases (16%, ADHD vs 4%, control).

Validity of Adult ADHD Diagnosis

As described by Faroane and colleagues, the validity of an adult ADHD diagnosis is not established by a single assessment, but by a pattern of consistent evidence in several domains. Validators of the diagnosis include multiple reports describing adults with clinical features correlating to childhood ADHD. Both children and adults show a family history of ADHD and a characteristic profile of neuropsychologic deficits. Neuroimaging analysis shows comparable brain abnormalities in both children and adults. The course and outcome of impairments are similar in both groups, with both syndromatic and symptomatic persistence. Based upon the limited clinical data available, both groups appear to respond to treatment similarly. Moreover, numerous clinical correlates have been identified in children and adults, specifically, antisocial, depressive, and anxiety disorders.

Adult ADHD Drug Trials

The medications that have shown to be effective in adults are similar to those that have been examined in children. The main medications that have been studied are the stimulants (methylphenidate, dextroamphetamine, mixed amphetamine salts, and pemoline) and antidepressants. To date, the medical literature has reported only 9 controlled trials of off-label use of stimulants in 272 adults. However, no medications are specifically approved by the FDA for the treatment of adult ADHD. Existing evidence has shown that stimulants are effective; however, response rates in adults have been somewhat more inconsistent than response rates in trials with children. In the Spencer mixed amphetamine trial, 70% of subjects receiving the active compound showed improvement in ADHD symptoms compared with 7% of those taking placebo.

Off-label use of nonstimulants for adult ADHD has assessed the efficacy of essentially 3 classes of drugs: those that affect norepinephrine and serotonin (tricyclic antidepressants and venlafaxine), those that affect norepinephrine and dopamine (bupropion), and those that affect norepinephrine alone (atomoxetine). Monoamine oxidase inhibitors, nicotinic agonists, and antihypertensives have all been studied in relatively small trials. The tricyclic antidepressants generally have not been commonly used in adults because of concerns about their side-effect profile. Selective serotonin reuptake inhibitors appear to have little effect on core ADHD symptoms, although they may benefit those patients with comorbid depressive disorders.
Clinical investigation of the efficacy of atomoxetine, a norepinephrine reuptake inhibitor currently undergoing FDA review, has suggested its efficacy in the adult population. An initial double-blind, placebo-controlled, crossover study of adults with ADHD (N = 21) demonstrated a mean reduction in the ADHD rating scale of approximately 8.5 points (vs 0.3 points for placebo, N = 21) over a 3-week period with a dose of 80 mg/day. Two additional large-scale, randomized, controlled trials of atomoxetine in adult ADHD have also been undertaken (manuscripts in preparation for publication). At a daily dose of 60 mg/day titrated to a maximum dose of 120 mg/day, the atomoxetine effects were apparent by week 4, and persisted and increased over 8 weeks of treatment, with significant effects demonstrated in both trials. In a third trial extending to 34 weeks, subjects who received atomoxetine continued to demonstrate ongoing improvement. If approved by the FDA for use in adult ADHD, atomoxetine will represent the first drug available for this indication. The theoretical advantages of atomoxetine include its relatively long duration of effect and the fact that it has been studied in once-daily dosing. Also, because atomoxetine is not a stimulant, there is the possibility of a lower risk of inducing tics and psychosis, although this has not been clinically demonstrated to date.

**Conclusion**

Although it historically has not been diagnostically validated by DSM-IV, adult ADHD is a widely prevalent syndrome. Clinical features of ADHD in children frequently continue into adulthood, although symptomatology changes with maturity. Existing medical evidence suggests that drugs useful for children with ADHD are similarly effective in the management of adults with this disorder.

The author would like to thank Julie Cohen, BA, for her assistance in the editorial preparation of this manuscript.

**References**