Neuropsychological Performance in Adults With Attention Deficit Hyperactivity Disorder

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1. INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is characterized by developmentally inappropriate levels of attention, impulsivity, and overactivity; it is estimated to affect 5–10% of children and adolescents and 3–4% of adults (1,2). ADHD was previously considered a disorder of childhood; however, follow-up studies suggest that the majority of individuals continue to exhibit ADHD symptoms throughout adolescence and adulthood. Longitudinal studies also indicate that these individuals are at greater risk for academic, social, and behavioral difficulties during childhood, adolescence, and adulthood, as well as psychiatric comorbidity (e.g., antisocial behavior, drug use, mood disorders) (3–7). Relative to what is known about ADHD in children and adolescents, less empirical information is available concerning ADHD in adults. In fact, some researchers have questioned the validity of adult ADHD and have asserted that ADHD typically remits in adulthood (8). Many others, however, disagree with this notion and attest to the persistence of ADHD throughout adolescence and adulthood (9,10). Recently Faraone et al. (11) sought to determine whether ADHD is a valid disorder in adulthood, using the validity criteria of Robins and Guze (12). Faraone et al. reviewed clinical, family, psychopharmacological, neurobiological, and adult ADHD outcome studies and concluded that adult ADHD is a valid disorder, although the authors emphasized that additional studies are needed to clarify the specific nature of ADHD in adulthood.

One factor that fuels the controversy surrounding ADHD in adulthood is that the precise etiology of ADHD is unknown. Findings from genetic, neurochemical, neuroimaging, and neuropsychological studies, however, collectively support a neurobiological basis for the disorder. For example, twin and adoption studies have demonstrated that genetic factors are etiologically important in the expression of ADHD (13), and recently Willcutt, et al. (14) reported that monozygotic twins were significantly more likely than dizygotic twins to meet the criteria for ADHD (78% and 35%, respectively). Familial studies have found that individuals with ADHD are more likely to have siblings or parents with ADHD relative to families with no history of ADHD (15). Genetic studies have found that despite shared environmental influences, ADHD is primarily influenced by genetic factors (16). Neuroanatomical, neurochemical, and neuroimaging studies collectively have supported a physiological basis for ADHD, although some findings have been inconsistent. Several studies, for example, have reported differences in size and symmetry of anatomical brain structures (e.g., corpus callosum, cerebellum, striatum)
when comparing individuals with and without ADHD, whereas other studies have not replicated these findings (17–22). Numerous neurotransmitter, neurometabolite, cerebral blood flow, and glucose metabolism studies have also reported differences between those with and without ADHD, although the mechanism responsible for these differences remains elusive (23–27).

2. NEOBIOLOGICAL THEORIES AND EXECUTIVE FUNCTIONS

Several neurobiological theories have been advanced to explain the underlying pathophysiology of ADHD and most converge on abnormalities of frontal-subcortical networks and structures. As Teeter and Semrud-Clikeman suggested (28), these theories can be classified into two groups: those that focus on abnormalities of subcortical structures and regions such as the basal ganglia, and those that focus on abnormalities of frontal and prefrontal cortices. Recent studies have also focused on the role of the right hemisphere in ADHD (29), and others have found size differences in the cerebellum of children with and without ADHD (17,30). The precise etiology of the structural and functional abnormalities implicated in ADHD is unknown but is likely resulting from interactions among genetic, physiological, and environmental factors that ultimately affect brain development and neuronal functioning. For example, evidence suggests that ADHD may be owing in part to polymorphisms in dopamine genes that modulate neurotransmission in subcortical and cortical regions (31). It is also plausible that prenatal factors such as exposure to teratogens and other risk factors result in morphological abnormalities within the frontal-subcortical region (32). These morphological abnormalities may contribute to the dysregulation of cognitive and behavioral systems that mediate the core behaviors deficient in ADHD, such as self-regulation, motor behavior, and higher-order neuropsychological processes known as executive functions (33).

Executive functions are broadly defined as higher-order cognitive abilities that allow for strategic planning, cognitive flexibility, self-regulation, goal-directed behavior, and impulse control. Neuroanatomically, executive functions have been ascribed to the frontal lobes and, more specifically, the prefrontal cortex (34). As noted by Fletcher, however, the physiological substrates that underlie executive functions are complex and likely involve intricate neural networks interconnected with numerous brain regions (35). Supporting this notion is the fact that damage to brain regions other than the prefrontal lobes, such as the basal ganglia, can result in executive function deficits. Nevertheless, the prevailing neurobiological and neuropsychological theories of ADHD focus on frontal-subcortical structures and circuitry (36). These theories arose in part from the earlier “dysfunctional frontal lobe hypothesis” of ADHD.

Wender and colleagues (37–38) were among the first to suggest that ADHD symptoms were caused by dysfunction of the frontal-subcortical systems, and Mattes (39) specifically asserted that ADHD is the result of frontal lobe dysfunction. This theory was based on research with humans and experimental animals who had sustained frontal lobe damage, and subsequent to the damage exhibited symptoms analogous to ADHD: hyperactivity, distractibility, and problems with self-regulation and goal-directed behavior (40–42). From this body of literature, it was deduced that the frontal lobes, in particular the prefrontal regions, play a primary role in executive functioning processes. More recent studies using Functional magnetic resonance imaging (fMRI) with normal subjects have revealed that the prefrontal cortex increases in activation during higher-order cognitive processing such as working memory, and the anterior cingulate cortex increases during neuropsychological task performance (Continuous Performance Test [CPT]) (43,44). With regard to ADHD, neuroimaging research has found both structural and functional differences in individuals with ADHD relative to controls, such as