The Neuropsychology of Attention Deficit Hyperactivity Disorder

Validity of the Executive Function Hypothesis

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1. INTRODUCTION

A literature search at the end of 2003 revealed more than 200 published studies that compared groups with and without attention deficit hyperactivity disorder (ADHD) on neuropsychological measures. This rapid accumulation of new knowledge illustrates the potential utility of neuropsychological methods as a tool to refine our understanding of the pathophysiology of ADHD. Yet these studies also underscore the complexity of the neuropsychology of ADHD, and clearly demonstrate how much remains to be learned.

The overarching objective of this chapter is to evaluate the executive function (EF) hypothesis, one of the most prominent neuropsychological models of ADHD (1,2). In the first section of the chapter we provide a brief overview of the syndrome of ADHD and summarize current knowledge regarding the genetic and environmental influences that are associated with ADHD. We then describe the construct of EF and summarize four key criteria that must be met if the EF theory of ADHD is correct. We then present a meta-analytic review of studies of selected EF tasks that have been administered most frequently in previous studies of ADHD, and describe the implications of these results for the EF theory. Finally, we compare the support for the EF model vs other neuropsychological theories of ADHD, and suggest several directions for future research that are needed to develop a comprehensive model of the neuropsychology of ADHD.

2. THE NATURE OF ADHD

Approximately 5% of children meet the diagnostic criteria for ADHD described in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (3), making it one of the most common disorders of childhood (4,5). Few disorders have undergone as many changes in name and diagnostic criteria as ADHD, perhaps because few disorders have been the subject of as much taxonomic study. Based on factor analytic studies (6,7) and results of the DSM-IV clinical field trials for the disruptive behavior disorders (8), the diagnostic criteria for DSM-IV ADHD incorporate two symptom dimensions. The first includes symptoms that describe maladaptive levels of inattention and disorganization, and the second consists of
symptoms of hyperactivity and impulsivity. DSM-IV distinguishes among individuals who exhibit maladaptive levels of both inattention and hyperactivity-impulsivity (combined type), maladaptive levels of inattention only (predominantly inattentive type), and maladaptive levels of hyperactivity-impulsivity alone (predominantly hyperactive-impulsive type).

In this chapter we describe key results from the Colorado Learning Disabilities Research Center (CLDRC) \(^{(9)}\), our ongoing study of the etiology of learning difficulties and DSM-IV ADHD. We also emphasize studies of DSM-IV ADHD in the meta-analysis when sufficient data are available. However, because relatively few studies of DSM-IV ADHD have incorporated EF measures, we also review studies that used previous or alternative definitions of ADHD to provide the most complete account of current knowledge regarding the relation between ADHD and EF.

### 2.1. Etiology of ADHD

Recent etiologically informative studies provided important information regarding the genetic and environmental influences that increase susceptibility to ADHD. These methods and results are described in detail in other reviews \(^{(10,11)}\). For the purposes of this chapter we provide a streamlined summary of these findings and focus on the implications of these results for neuropsychological theories of ADHD.

#### 2.1.1. Family and Twin Studies

Family studies clearly demonstrate that ADHD is familial \(^{(12,13)}\), and twin studies suggest that this familiarity is the result of genetic influences. Specifically, studies of more than 10,000 twin pairs have found that individual differences in ADHD symptoms are largely attributable to genetic influences, with an average heritability of approx 75% \(^{(e.g., 14,15, reviewed in ref. 11)}\). These same studies indicate that the remaining phenotypic variance in ADHD symptoms is attributable to nonshared environmental influences; estimates of shared environmental influences were not significant in any previous study.

#### 2.1.2. Linkage and Candidate Gene Studies

Once a trait such as ADHD has been shown to be significantly heritable, two main methods can be used to localize the genes that increase risk for ADHD. Family-based linkage analysis can be used to screen the entire genome to identify chromosomal regions that may contain a gene or genes that increase risk for ADHD. In contrast, the candidate gene approach examines specific genes that are targeted because they play a role in a biological system that is associated with the disorder \(\text{(see refs. 16,17 for a more detailed description of candidate gene and linkage studies)}\).

More than 80 published studies have tested for an association between ADHD and 27 different candidate genes \(^{(11)}\), and a series of studies by one group has examined more than 20 additional candidate genes in a sample of individuals with ADHD and Tourette’s syndrome \(^{(18)}\). Most of these studies have focused on genes that influence dopamine (DA), norepinephrine, and serotonin, owing to evidence that these neurotransmitters may play a role in the pathophysiology of ADHD and other psychopathology \(^{(19)}\). For 14 of the 27 candidate genes a significant association with ADHD has been reported in at least one study; however, many of these results have been replicated inconsistently or await independent replication. Moreover, each of these genes appears to account for a relatively small proportion of the variance in ADHD symptoms \(^{(10,20)}\), suggesting that none is likely to be necessary or sufficient to cause ADHD.

Because the known candidate genes are not sufficient to fully explain the genetic etiology of ADHD, two recent studies used linkage analysis to screen the entire genome for additional