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Cognitive Processes of Inattention in

Attention Deficit Hyperactivity Disorder Subtypes

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Cognitive Processes of Inattention in Attention Deficit Hyperactivity Disorder Subtypes

by

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Dedication

To my parents, Jake and Winifred Booth

Cognitive Processes of Inattention in

Attention Deficit Hyperactivity Disorder Subtypes

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The primary objective of this study was to compare and evaluate attention in children with attention deficit hyperactivity disorder, predominantly inattentive (ADHD/IA) and combined (ADHD/C) types and comparison controls on the Attention Networks Test (ANT), a computer task designed to assess cognitive processes of alerting, orienting, and conflict, associated with three anatomically distinct networks of attention. A secondary aim was to examine the utility of sluggish cognitive tempo (SCT) as a classification variable for identifying a more cognitively homogeneous subgroup of children with ADHD/IA. Performance results on the ANT demonstrated an attentional distinction between the subtypes, a greater alerting effect ADHD/IA relative to ADHD/C groups. This finding suggests that the cognitive functioning of ADHD subtypes can be distinguished by the efficiency of the alerting network of attention. Groups did not differ on measures of orienting or conflict. Findings for the utility of SCT as a classification variable in this sample were mixed. Several items presumed to measure this construct did not distinguish between the ADHD subtypes. High SCT in ADHD/IA, as determined by scores on a two-item composite, was associated with slower task performance and a greater alerting effect, though these effects were nonsignificant and small. Results provide support for the neurocognitive distinction of ADHD/IA and ADHD/C subtypes and suggest further consideration of SCT symptoms in subtype classification.

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Chapter 1: Overview of Current Study

Introduction

Attention deficit hyperactivity disorder (ADHD) is a heterogeneous disorder defined by clinical history and behavioral report of impairment. As a result of observable differences in the behavioral presentation of children with ADHD, three subtypes have been identified in the Diagnostic and Statistical Manual (DSM)-IV according to their constituent symptom profiles of inattention and hyperactivity/impulsivity (American Psychiatric Association, 1994). Research, which has focused primarily on the combined subtype (ADHD/C) with impairment in both symptom domains, has suggested associated deficits with executive functions, e.g. planning, organization, interference control, distractibility, and behavioral inhibition, skills presumed to be subserved by the frontal lobes. The inattentive subtype (ADHD/IA) with impairment in the inattention domain without clinically significant hyperactivy/impulsivity, however, has been far less studied and appears to have a distinct profile of associated deficits. This group does not show the same behavioral problems with hyperactivity and impulsivity, by definition, and may not share the same executive function deficit as its counterpart. Argument has been raised that the observed symptoms of inattention in the absence of hyperactivity/impulsivity represent the expression of unique cognitive deficits (Barkley, 1997; Schaughency & Hynd, 1989). Support for this position comes from differences in social functioning, age of onset, comorbidity of externalizing disorders, academic deficits and learning styles, and factor analyses of symptom ratings between the subtypes of ADHD. Although evidence suggests that the subtypes also have different cognitive deficits, extant research does not allow for definitive conclusions. Overcoming issues with diagnostic classification and the specificity of neuropsychological tests may present the greatest challenge for differentiating the neurocognitive profiles of these two subtypes.

Although ADHD has long been viewed as a neurological condition, the relationship between the observable features of the disorder and the underlying neurocognitive impairment is not clear. Many studies have demonstrated similarity

between symptoms of ADHD and impairment associated with the dysfunction of particular brain regions. Hyperactivity and the executive control of behavior in ADHD has been predominantly linked to frontal lobe (anterior) functioning, whereas inattention in ADHD has been linked to the frontal lobes as well as to right parietal (posterior) and midline subcortical regions involved in the regulation of attention and arousal (Swanson, Posner, Cantwell, et al., 1998b), but these relationships have not been established in the subtypes. Attempts to identify a core deficit in ADHD are complicated by the existence of multiple neural networks of attention associated with various cognitive processes and clinical manifestations. A neurocognitive explanation of the impairment in this disorder must take into account the heterogeneity of symptoms encompassed both within and between subtype diagnoses.

Attentional networks within the brain can be broadly categorized into anterior, posterior, and alerting systems, each with different yet interrelated function (Posner & Raichle, 1994). The anterior system involves regions of the pre-frontal cortex and basal ganglia and is responsible for the executive control of attention, an aspect of self-regulation that appears to be deficient in the ADHD/C subtype. This system has been the target for investigation of neuropsychological impairment in ADHD and has yielded substantial findings for populations with hyperactivity (Castellanos, 1999). Descriptors used to describe the inattention of the ADHD/IA subtype (i.e., sluggish cognitive tempo, slow processing, spacey, and lethargic), however, are not typical features of executive function deficit and have not been clearly identified on neuropsychological tests of frontal lobe functions (Lahey, Applegate, McBurnett, et al., 1994; Milich, Balentine & Lynam, 2001). Alternatively, the posterior system has anatomical foci in the parietal lobes, parts of the midbrain and thalamus, and is responsible for visual orienting and shifting attention. In contrast to the executive mechanisms described above, this system is presumed to facilitate automatic processes associated with visual-spatial processing and the disengaging and reengaging of attention (Posner & Raichele, 1994). The third system of attention proposed by Posner and Raichele (1994), the alerting system, involves the locus coeruleus nucleus of the midbrain and its connections to the frontal and parietal

lobes of the right hemisphere and is believed to be involved in the regulation of vigilance and arousal. Cognitive processes associated with the posterior and alerting systems of attention may have relevance for the dysfunction in ADHD/IA, and for negotiating the differences that mark the subtypes.

Current Study

The principle aim of this study was to investigate the possibility of different neurocognitive deficits in children with ADHD/C and ADHD/IA by examining the performance of these children and a control group on a computer task measuring cognitive processes associated with three different neural systems of attention. A secondary aim was to investigate the role of a Sluggish Cognitive Factor (SCT) of attention in a subgroup of children with ADHD/IA.

This research was part of a larger grant project at the University of Texas at Austin designed to examine neurocognitive and perceptual-motor functioning in ADHD subtypes. To explore three cognitive processes of attention; alerting, orienting, and conflict in ADHD, 16 ADHD/C, 27 ADHD/IA, and 24 non-diagnosed comparison controls completed the Attention Networks Test (ANT). The testing session lasted approximately three hours and involved the administration of the ANT along with several additional experimental measures designed for research with ADHD groups. Children in the control group were also administered select intellectual and achievement measures from the standard neuropsychological battery that the clinic-referred children had received in full.

The Attention Network Test (ANT), developed by Jin Fan at the Sackler Institute (2000), is an adaptation of Posner's cuing paradigm for spatial orientation (Posner, 1980) and the Eriksen flanker task (Eriksen & Eriksen, 1974). The task is a computer-based, reaction time test developed to measure three distinct cognitive processes associated with attention. Visual stimuli are presented on the screen under three conditions, requiring: interference control of competing responses, spatial orienting to cued stimuli, and maintenance of the alert state for target detection. Participants are required to respond

quickly to stimuli by pressing the appropriate button on a mouse controller. Measures of reaction time and accuracy were recorded. Administration of a practice and three test blocks of trials took approximately 25 minutes.

Outline of this Document

Chapter 2 presents a review of the history of ADHD its symptom domains including SCT. Also discussed are the methodological limitations of neuropsychological measures for the assessment of ADHD subtypes. Chapter 3 provides an overview of the cognitive and neural correlates of attention and ADHD pathology. Chapter 4 presents a neurocognitive comparison and theoretical perspective of ADHD/IA and ADHD/C. Chapter 5 is a statement of the rationale and hypotheses for the current study. Chapter 6 describes the study participants, methodology, and measures. Results for group performance on dependent variables of the ANT and classification of SCT are presented in Chapter 7. Discussion of the findings, limitations, and future directions are addressed in Chapter 8.

Chapter 2: Advances in Research: ADHD and Associated Features.

Symptom Domains of ADHD

Attempts to clarify the etiology of ADHD represent a multidisciplinary effort that has generated considerable interest in recent years. Diagnostic emphasis on ADHD has reflected shifts in conceptualization of the disorder and its core deficits throughout its history. Despite controversy over the classification of primary symptom domains, recognition that the heterogeneous clinical appearance of ADHD is paralleled in its biological origin has increased. Study of the behavioral symptoms has led to speculation about the causes and neurological mechanisms involved. Advances in the field of neuropsychology have further brought momentum to the investigation of ADHD and its core deficits.

The determined classification structure of the disorder has evolved over the years to reflect changing perspectives and evidence concerning its etiology. Early descriptions of hyperactive children, dated to the latter part of the nineteenth century, emphasized the concept of a neurological etiology (see Barkley, 1990). These accounts reflected the belief that brain damage incurred in early childhood or prenatal development could result in the observed behavioral symptoms of the hyperactive syndrome (for review see Barkley, 1990). Clouston (1899) described the disorder as a failure of higher centers of the brain to inhibit activity, close to today's conceptualization of the neurological deficits underlying ADHD (in Barkley, 1990). Before the emergence of the disorder in the Second Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-II) (APA, 1968), both the frontal lobes and subcortical regions had been implicated in its causality based on report of similar behavior in individuals with known brain damage (Walters & Barrett, 1993). The constellation of symptoms seen in these hyperactive children had become known as Minimal Brain Damage, which reflected a presumed yet not clearly identified organic basis.

Hyperactivity has remained one of the primary symptoms of ADHD, though its role has changed throughout this century. With the growing acceptance of

psychodynamic and social theories, DSM-II (APA, 1968) introduced the disorder Hyperkinetic Reaction of Childhood Disorder. This term represented a shift away from the organic focus to allow room for prevailing environmental explanations. The idea of mild brain damage or dysfunction was still popular in the research, although the absence of marked neurological impairments made specific predictions about neurological damage in these children untenable (Clement & Peters, 1962, in Barkley, 1990). At the same time, the presence of significant attention problems in children in absence of hyperactivity had not yet gained recognition in the conceptualization of the disorder.

Interest in the cognitive correlates of the disorder was inspired by Douglas and colleagues (Douglas, 1972) who emphasized sustained attention deficit as a core feature. In 1980, DSM-III (APA) applied the diagnostic label Attention Deficit Disorder with or without hyperactivity (ADD+H or ADD-H) reflecting a focus on attention problems in the symptom presentation, and in doing so, consigning hyperactivity to the periphery. Sufficient empirical support for the two-dimensional symptom structure, however, was not established at this time and the scientific community was not at ease with the marginal status of hyperactivity. In 1987, hyperactivity regained importance as DSM-III-R (APA) consolidated the symptom domains making ADHD a unidimensional construct. The idea of distinct subtypes was thus eliminated and the composite of children identified under the new system made for a quite heterogeneous group.

Empirical evidence from DSM-IV field trials restored the subtypes distinction absent from DSM-III-R. This specification was largely based on factor analytic studies that separated symptoms of ADHD into two domains: inattention and hyperactivity/impulsivity (Lahey et al, 1994; Lahey, Carlson, & Frick, 1997). Accordingly, DSM-IV outlined three subtypes that represent the presence or absence of clinically significant levels of symptom impairment: the predominantly inattentive (ADHD/IA), predominantly hyperactive/impulsive (ADHD/HI) and, combined (ADHD/C) types (see Appendix A). The ADHD/C and ADHD/IA subtypes share considerable overlap with the previous DSM-III subtypes, although symptom overlap is not exact, and thus, have an accompanying history of theoretical debate and consideration

in the research literature. The ADHD/HI subtype, on the other hand, was newly introduced in DSM-IV and does not carry with it the same history of scientific validation.* Research presently supports the concept of ADHD as a neurodevelopmental disorder with primarily biological etiologies that are somewhat elusive, with frontal lobes and subcortical regions implicated (Barkley, 1997, Cantwell, 1996) – not unlike the descriptions that marked its early history.

Issues in Assessment of the Subtypes

Developments in the classification of ADHD continue to have implications for clinicians and researchers alike. Some children who were identified under previous criteria may change diagnostic status under the current system. Others, who would not have been identified previously, may now reach diagnostic threshold. Although consistency of receiving a diagnosis is high across the revisions, classification of individuals into particular subtypes shows more variability. Consequently, research using previous diagnostic criteria often does not generalize to current DSM-IV groups (Lahey et al, 1994, Paternite, Loney, & Roberts, 1996). As it stands, research to date has focused on those children with ADHD/C or on composite ADHD groups of unspecified subtypes. The adoption of a diagnostic system and its inherent structure gives rise to such issues that have implications for the present investigation of neurocognitive functioning in the ADHD/C and ADHD/IA subtypes.

As stated, controversy over the deficits associated with ADHD has been reflected in the changing classification schemas emphasizing different primary symptoms and subtypes of the disorder. Debate has persisted over the validity of the inattentive subtype and more recently, whether these children possess qualitatively unique deficits that would be more accurately classified as a distinct disorder (Milich, et al., 2001). The current delineation of ADHD subtypes suggests that three distinct variants of a common parent disorder occur. This clarity, however, is not necessarily reflected in the symptom structure. With the stipulation that any 6 (or more) of 9 symptoms of inattention and any

* Due to the lack of empirical support for the ADHD-HI subtype, and belief that it may represent a developmentally early manifestation of ADHD/C, this group is not included in the present study.

6 (or more) of 9 symptoms of hyperactivity/impulsivity be present for diagnostic threshold, the diagnosed cases of ADHD may represent heterogeneous symptom profiles. This renders heterogeneity of symptom profiles within as well as among the three subtypes, which presents particular concern for the generalizability of research with the ADHD/IA subtype. To illustrate, a child with a diagnosis of ADHD/IA who demonstrates subthreshold features of hyperactivity/impulsivity (3-5 symptoms) may have a different clinical appearance than the inattentive child who does not show problems with hyperactivity/impulsivity. Accordingly, it has been suggested that this diagnostic group may encompass subclinical cases of the combined type in addition to the "pure inattentives" (Carlson & Mann, 2000; Milich et. al, 2001). The picture is clouded further when one considers that item analyses for DSM-IV determined that a cut-off of 4 to 5 rather than 6 HI symptoms best distinguished between cases of the ADHD/IA and ADHD/C (Gomez, Harvey, Quick, et al., 1999; Lahey et. al. 1994). The cut-off was set at 6 in the final version to maintain consistency with the cut-off for attention items and to reduce the potentially larger number of ADHD/C diagnoses (Lahey et al. 1994). Thus, from a research perspective, diagnostic criteria are not ideal for identifying distinct ADHD/IA and ADHD/C samples.

Another issue that has implications for research with ADHD subtypes is whether the nature of the attention deficit is inherently different when found alone, as with ADHD/IA, or versus when paired with the presence of hyperactivity/impulsivity, as with ADHD/C. The diagnostic labels imply that one can have a problem with attention only or, a problem with attention in addition to a separate problem with hyperactivity/impulsivity. No indications are made about potential effects that impairment in the latter domain may have on the expression of an attention deficit. Because of the large scope of attention at the cognitive level, this caveat must be considered before developing a neurocognitive theory of the ADHD subtypes. Predictions about the role of specific cognitive processes of inattention in the subtypes, both those that are primary to attention and those that may act more indirectly to regulate attention, depend on the relationship of symptoms across and within the two domains.

For example, disruption of neural pathways associated with the various symptoms of hyperactivity and impulsivity can result in problems with the control of attentional resources. This facet of attention can be distinguished functionally from among others (e.g., sensory or automatic processes of attention and arousal). In consideration of hyperactive behavior, a child could have difficulty attending to an academic task due to a problem inhibiting pre-potent motor responses to fidget excessively, rather than a unique problem with inattention. Even though inattention usually accompanies hyperactivity, it has not been empirically confirmed that the associated attention problems are themselves etiologically distinct and not a result of the behavioral disruption caused by hyperactivity and/or impulsivity symptoms, such as the inability to inhibit behaviors that disrupt the maintenance of attention on a task or activity. If such an overlap exists between symptoms of attention and hyperactivity in ADHD/C, then the origin of the attention deficit is in this group is likely different from that of the inattentive subtype. A neurocognitive theory might consider ADHD/C in terms of a single domain of symptoms that stem from common underlying neurological dysfunction that is different from the neurological dysfunction in ADHD/IA. Consistent with these parameters, Barkley's (1997) model of deficient inhibition in the ADHD/C subtype provides a well-substantiated unifying explanation for the range of symptoms displayed in this particular group (Barkley, 1997). He proposes that the attentional components of the two subtypes are different in cognitive function and neurological origin (Barkley, 1997). It has been argued that if the attention deficits of the inattentive and combined subtypes are different in nature, then the groups are not variants of the same disorder but are essentially distinct disorders altogether (Milich et al, 2001).

A further consideration for examining the attention deficit in ADHD is that diagnosis is based on adult symptom ratings, i.e., observations of behavior that presumably reflect cognitive deficits of "inattention". The behavioral diagnosis of an attention deficit, a presumed cognitive function, is essentially misleading because the behavioral construct of attention is not synonymous with the cognitive construct of attention (Barkley, DuPaul, & McMurray, 1990; Shaywitz, Fletcher, Pugh, et al., 1999).

Many children who meet behavioral cut-offs for an attention problem do not show problems with attention on neuropsychological tests designed to measure attention at the cognitive level. Others, who show problems with inattention on cognitive tests, do not show the behavioral symptoms necessary for a diagnosis of ADHD (Barkley, 1991). Performance deficits on neuropsychological tests have been documented in a wide range of conditions outside of ADHD that are also associated with attention problems, including Alzheimer's, Turner's syndrome, Autism, Schizophrenia, Hypothyroidism, Learning Disabilities, and Depression, not just ADHD. Clearly then, measurement of cognitive attention cannot simply serve as an indicator of the presence or degree ADHD, although the use of appropriate cognitive measures could increase the reliability of diagnosis. Behavior rating scales, the definitive tool for diagnosis, are limited by their subjectivity and susceptibility to informant bias. (Marks, Himelstein, Newcorn, & Halperin, 1999; Weiler, Bellinger, Marmor, Rancier, & Waber, 1999). They offer poor correspondence between parent and teacher report of symptomology and hence diagnosis (Marks et al., 1999). A more complete and tailored assessment procedure may enhance the theoretical understanding of different symptom presentations and assist in providing a differential diagnosis between ADHD/C and ADHD/IA.

A Second Factor of Attention

Compelling, though preliminary, evidence for distinct attention deficits in the DSM-IV subtypes comes from research with previous diagnostic subtypes and factor analytic studies of the symptom items of ADHD. As previously described, DSM-III was the first classification system to include a distinct group of children who showed significant problems with attention in the absence of hyperactivity. This group of children who received a diagnosis of Attention Deficit Disorder/Without Hyperactivity (ADD-H) represents a similar, though not identical group to the current ADHD/IA group of DSM-IV. Studies examining the DSM-III subtypes found that the cognitive performance of children with ADD-H appeared to be characterized by features of slow information processing, drowsiness, sluggishness, low levels of alertness, and mild problems with memory/orientation (Barkley, et al., 1990; Lahey, Schaughency, Frame, & Strauss, 1984;

McBurnett, Lahey, & Pfiffner, 1993), whereas the performance of children with Attention Deficit Disorder/With Hyperactivity (ADD+H) was characterized by distractibility, difficulty concentrating, sloppiness, and disorganization, (Lahey, Carlson, & Frick., 1997, Carlson & Mann, 2000).

Accordingly, a second factor of attention composed of three items: Forgets, Daydreams, and Sluggish/Drowsy, extracted from factor analyses of the symptom list, was found to be associated with the inattentive subtype. Although the Sluggish Cognitive Tempo (SCT) factor was evaluated in the DSM-IV field trials, the Daydreams and Sluggish/Drowsy items were not included in the final symptom list, in part because of their poor negative predictive power for the inattention symptom group (Frick, Lahey, Applegate et al., 1994). Since the absence of SCT did not predict absence of inattention, these symptoms were considered poor representatives of a single domain of attention, which was favored in the diagnostic conceptualization at the time. This omission may have been misguided, however, for several reasons. First and foremost, the heterogeneity of the inattentive subtype with regard to number of hyperactivity/impulsivity symptoms (with some members perhaps representing subthreshold combined types, noted above) would have precluded the specificity of the second factor of attention for this subtype. A reexamination of the item pool for inclusion in DSM-IV demonstrated that the utility of the SCT symptoms for predicting inattention is quite good when cases with combined hyperactivity-impulsivity are excluded (McBurnett, Pfiffner, & Frick, 2001). Perhaps the subset of children characterized by SCT represents an effectively homogenous group, differing more from the remaining children with ADHD/IA than those children differ from their ADHD/C peers. Additionally, support for the recognition of multiple components of attention in the diagnosis of ADHD is corroborated by research, particularly within the cognitive sciences, that has demonstrated independence among various cognitive processes and functions of attention. The behavioral assessment of attention may, correspondingly, require the distinction of independence among component factors. Renewed consideration of SCT and its role in ADHD/IA is strongly

indicated in the attempt to align the clinical correlates of inattention with the underlying cognitive mechanisms that may be involved.

Demographics and Associated Features

The results of factor analytic studies of symptom structure support the distinction of children exhibiting problems with inattention and hyperactivity/impulsivity from those exhibiting predominantly inattention. To explore the extent of differentiation between the subtypes, it is necessary to examine the associated features and correlates of an ADHD/C or ADHD/IA diagnosis. Substantial evidence from studies of demographics and epidemiology, comorbidity, social functioning, and treatment response, indicates that the subtypes differ in ways other than hyperactivity. This section gives an overview of the distinguishing characteristics of the subtypes. Included in the synopsis are findings obtained both from studies that have used DSM-III diagnostic criteria as well as those more recent studies that have investigated DSM-IV defined groups.

Different demographics and associated features have been identified between the inattentive and combined types of ADHD. Studies using both epidemiological and clinic-referred samples as well as DSM-III and DSM-IV subtype distinctions provide generally consistent evidence. Compared to the combined type, children of the inattentive type tend to have a later age of onset, later age of clinic referral, and are typically older than their combined type associates in research study groups. The DSM-IV field trials found that only 57% of the ADHD/IA group met the symptom criteria before age seven while 82% of the ADHD/C group met symptom criteria at the specified age of onset criterion for diagnosis (Lahey et al., 1994; Mililch et al., 2000). The age of the ADHD/IA group was older, 9.8, than the ADHD/C group, 8.5 (Lahey et al., 1994). Gender ratios are generally found to represent a higher proportion of females in the inattentive type than in the combined type. The DSM-IV field trials reported ratios of M:F 2.7:1 for the ADHD/IA group and M:F 7.4:1 for the ADHD/C group. Different rates of prevalence have been found between the groups although the direction of this difference depends on the type of sample studied. The inattentive type is more prevalent than the combined type in

community samples whereas prevalence favors the combined type in clinical samples (Baumgaertel, Wolraich, & Dietrich, 1995; Carlson & Mann, 2000). Apparently, the nature of the subtypes is such that children with ADHD/C are referred much more frequently than children with ADHD/IA, probably due to the discrepancy in prevalence of co-occurring externalizing problems.

Estimates that 68 % of children with a DSM-IV diagnosis of ADHD receive one or more additional diagnoses yield high rates of comorbidity within the subtypes (Jensen, Martin, & Cantwell, 1997). Both parent and teacher report indicate that children with ADHD/C have more externalizing problems including delinquent and aggressive behavior than children with ADHD/IA (Paternite, et al., 1996). This group has also received more co-morbid CD and ODD diagnoses than the ADHD/IA group (Eiraldi, Power, & Nezu, 1997; Morgan, Hynd, Riccio, & Hall, 1996; Wolraich, Hannah, Pinnock, et al., 1996). It is well established that school failure and academic underachievement are common in ADHD (Faraone, Biederman, & Lehman, 1993). Studies that have examined the rates of academic problems in the subtypes have not consistently found differences in prevalence of comorbid learning disabilities. However, when a difference exists, children with ADHD/IA fare worse (Baumgaertal et al., 1995; Brito, Pereira, & Santos-Morales, 1999). A cluster of these studies, specifically, have found the inattentive type to score lower on math tests (Carlson, Lahey, & Neeper, 1986; Hynd, Lorys, Semrud-Clikeman, et al., 1991a; Marshall, Hynd, Handwerk, & Hall, 1997). Marshall et al. (1997) hypothesized that the attention deficit in ADHD/IA interferes with the processing of abstract symbol systems during the acquisition of basic arithmetic skills. It has also been documented that the children with ADHD/IA receive more school remedial help for their academic performance than those with ADHD/C (Barkley et al., 1990; Marshall et al., 1997). This finding reflects the notion that others perceive the deficits of the subtypes to be different. Both groups show poor academic performance but the pattern of intervention differs for the two subtypes.

Different patterns of social problems have been documented between the inattentive and combined subtypes (Milich et al., 2001; Maedgen & Carlson, 2000).

Studies focusing on peer relationships have demonstrated that children with ADHD, both with and without hyperactivity are less popular with their peers (King & Young, 1982, Lahey et al., 1994). Some studies have also found differences between the subtypes, particularly that ADD+H children were more likely to receive peer nominations of frequent fighters and least liked than ADD-H children (Lahey et al., 1984, Carlson, Lahey, Frame, et al., 1987). ADHD/C children were also rated by teachers as having higher levels of social problems than ADHD/IA children (Gaub & Carlson, 1997). Hynd, Lorys, et al. (1991a) found that ADD+H children were rated by adults as having more inappropriate social skills than ADHD-H children. In an experimental design, Maedgen and Carlson (2000) examined social knowledge and performance variables contributing to interpersonal styles in the ADHD subtypes. The ADHD/C children were found to be more aggressive in their solutions to social problems whereas the ADHD/IA children were found to be more passive. Overall, the different patterns of social deficits highlight the divergence of subtype specific symptoms on outcome.

With the consideration of ADHD as a neurodevelopmental disorder, it is not surprising that the most common and effective form of treatment is medication. Although not many studies have compared the responsiveness of the subtypes to stimulant medication, those that have suggest differential outcomes. In a study using DSM-III criteria, children ADD+H were less likely to be nonresponders than children with ADD-H: 24% compared to 5% (Barkley, Dupaul, & McMurray, 1991). In addition, optimal treatment response was found to occur more often at moderate to high doses for children with ADD+H, 71%, than for children with ADD-H, 41%. The symptoms associated with the combined type appear to be better suited to treatment with stimulant medication than symptoms associated with the inattentive type.

Investigation of Neurocognitive Functioning in ADHD

The purpose of integrating cognitive theory with research on ADHD in this review is twofold: 1) to identify appropriate methodology for investigating neurocognitive deficits in ADHD/IA and ADHD/C children, and 2) to determine how

these deficits may relate to behavioral impairment in the symptom domains. Although it has been well established that the symptoms of ADHD are associated with neurological dysfunction, many studies have failed to find neurological differences between the subtypes. Rather than disregard the pursuit of this relationship, a modified approach to the project, developed in accordance with a theory of cognitive functioning in ADHD, should be taken.

Developing Methodology

The lack of correspondence between success of research at differentiating ADHD symptoms on a behavioral level and on a neurocognitive level necessitates the use of methodology sensitive to the population under study. In a recent review of the efficacy of laboratory-based measures for diagnosing and monitoring treatment effects in ADHD, Rapoport, Chung, Shore, Denny, & Isaacs (2000) evaluate task parameters associated with the reliability of assessment instruments. The authors identified several defining features of reliable tests, but concluded that, as a whole, neuropsychological tests are significantly limited for assessment with ADHD. Parameters associated with increased measurement reliability included: presenting the response stimulus (e.g., the correct answer) of a visual choice task for only a portion rather than the duration of trials, establishing some degree of experimenter pacing so that stimulus-response tasks are not entirely self-paced, and using recognition and recall paradigms that tax subvocal working memory components. In spite of their merits, however, laboratory tests have offered little of value to clinical diagnosis, a result, according to the authors, of their not having been designed for the purposes of assessing deficits specific to ADHD. In consideration of factors both compromising and contributing to test reliability, the authors offer guidelines for a theoretical approach to task construction that is in accord with predictions about group performance.

From a neurocognitive perspective, testing instruments must be developed on the basis of a conceptually driven paradigm that delineates the presumed core and peripheral deficits of ADHD in order to orient assessment towards sensible targets of the hypothesized dysfunction. Such measures should allow for the manipulation of discrete

independent variables that presumably serve as indicators of the mechanisms they have been designed to assess (Rapoport et al., 2000). A task designed to measure cognitive processes of attention, for example, should place demands on the suspected neural systems by which attention is impaired. From an individual's performance on selected task parameters, conclusions can then be made about the cognitive deficits assessed and their neurological sources. These conclusions can serve as empirical validation for tenets of the framing model of ADHD. Rapoport et al. (2000) suggest that the application of scientific rigor to the development of clinic and laboratory measures will render their psychometric properties much more sensitive to individual differences within the disorder, as well as to between group differences. In terms of the present research, this psychometric feature is highly desirable as it offers much of relevance for the assessment of ADHD subtypes, and for the discrimination of individual symptom profiles from within the inattention and hyperactivity/impulsivity domains.

Due to changes in the classification structure and theory behind ADHD, the conceptual basis for determining which variables should be addressed by a neuropsychological evaluation of specific subtype deficits lacks substantiation in a history of research. To illustrate, recent studies comparing the subtypes have typically assessed executive functioning deficits, the target of research with ADHD/C. In this case, the experimental paradigm informs whether the subtypes share a common deficit (very valuable information), but cannot purposefully identify the specific deficits in ADHD/IA as predicted by a conceptual understanding of dysfunction in this subtype. As a result, assumptions underlying the experimental paradigms of past research may have limited applicability to current research with the DSM-IV subtypes.

An interesting methodological issue regarding the generalizability of research using DSM-III-R defined groups, is the lumping of ADHD children with and without hyperactive features into a conglomerate group. Combining the subtypes of ADHD into a single group simplifies the experimental design and increases the power of the study, but at the cost of introducing greater heterogeneity into the subject pool and increasing error variance. True performance trends in any cohesive subgroup of children may be masked

by performance of the outside group, reducing the probability that unique information will be revealed about the specific cognitive mechanisms to be tested by the paradigm. Additionally, unequal proportions of subtype membership in a single group could skew results in the direction of one subgroup, effecting an inaccurate conclusion about ADHD as a whole. Probably the most obvious obstacle to amalgamating a research foundation from which predictions can be made about neurocognitive differences between the ADHD/C and ADHD/IA subtypes is that the vast majority of studies have not included a group of children with inattention in the absence of hyperactivity. The foundation, from which our understanding of ADHD has been attained, may not hold lucrative for the prospects of ADHD/IA. Hence, research including this inattentive group of children resides, still, in its formative stages and is agreeably amenable to methodological reconstruction.

If ADHD/IA represents a neurologically distinct syndrome, its identification as such will only be as successful as the measurements are appropriate for assessment of the associated deficits. Of the few studies that have investigated neurocognitive functioning in the subtypes, most have used standard neuropsyhological tests that have poor sensitivity to the unique impairments associated with various childhood disorders (Pennington, Bennetto, McAleer, et al., 1996). A general neuropsychological evaluation for ADHD consists of normed and standardized tests that effectively detect the presence of neurological deficit, but often not the specific mechanisms of impairment. The tests have been designed primarily with the goals of: assessing the broad range of normal functioning, and/or discriminating between healthy versus brain damaged populations (Malloy & Richardson, 1994). They usually do not, however, provide enough information to identify the diagnosis of the presenting disorder, or to differentiate between clinic-based populations, although these populations can be distinguished quite reliably on diagnostic and behavioral grounds.

A related issue is that most neuropsychological tests are not designed to detect the contribution of individual cognitive processes to overall performance. Since multiple elementary cognitive processes are involved in a single task, e.g., in a simple choice RT

task four processes are involved; stimulus perception, stimulus discrimination, response choice, motor response (Neubauer & Knorr, 1997), slowed or inaccurate performance could be due to contribution from any one of these components. Methodology incorporating systematic manipulations of task components and subtraction analyses is needed to isolate the individual cognitive processes. The finding that both subtypes perform more poorly on a particular task than controls, does not alone support an argument for common underlying neurological dysfunction. Applying methodology from the cognitive sciences to research with ADHD should increase the specificity of testing and the precision with which hypotheses and conclusions can be made about the cognitive deficits of these groups.

Few neuropsychological tests have been developed specifically for use with ADHD populations and none have been developed with a particular focus on the cognitive profile of the purely inattentive children. Thus, the subset of tests, those measuring executive functions, that have been the most useful at detecting cognitive deficit in ADHD/C may not be as relevant for assessment with ADHD/IA. Performance deficits on these tests have been clearly associated with hyperactivity and impulsivity while, in absence of these features, the relationship between behavioral inattention and performance is less clear. Two studies have, in fact, demonstrated the limited effectiveness of using neuropsychological tests for the classification of individual cases of ADHD: Barkley & Grodinsky, 1994, and more recently, Doyle, Biederman, Seidman, Weber, and Faraone, 2000. Although abnormal scores on the test adequately predicted ADHD, normal scores on the tests did not indicate absence of the disorder. Consideration of impairments on multiple tests rather than on any single test does improve predictive power for diagnosis but still, discriminative utility of the neuropsychological assessment remains short of adequate. Doyle et al. (2000) pointed out that these results suggest that children with ADHD show variable deficits on the standard tests of attention and executive functioning, further supporting cognitive heterogeneity within groups of children diagnosed with ADHD. These studies did not examine subtypes of the disorder, which would likely render even greater uncertainty as to the effectiveness of these

measurements as diagnostic tools. Without sufficient scientific rationale for use of standard neuropsychological tests to assess cognitive functioning ADHD/IA, it is unlikely that they will have the specificity to distinguish between the subtypes.

Linking Neurocognitive and Bevioral Deficits in ADHD

The relationship between behavior and brain has long been paralleled in general theories of child development. Looking to converging evidence from the different areas of research outside as well as within the field of ADHD can help inform predictions about relationships among neurological mechanisms and observable characteristics of the disorder. Given what is currently known about the manifestation of neural dysfunction and its impact on behavior, "ground-up" inferences can be made about the neurocognitive correlates of behavior in ADHD. Broader perspectives of functioning in ADHD (e.g., behavioral, social, epidemiological) can, likewise, guide the "top-down" search for specific deficits in the subtypes. From the existing literature and previous research on ADHD, it is clear that the two subtypes differ in several major domains. What is not so apparent is how these differences map on to neurological activity.

Much of the evidence for distinct core deficits in the subtypes comes not from the direct investigation of neurocognitive functioning, but from study of the associated features of ADHD subtypes, from which inferences can be drawn about the neurological correlates of impairment. Accordingly, the case for neurocognitive distinction of the subtypes rests heavily on differences in the observable features of the disorder, e.g., comorbidity of behavioral and learning disorders, presence of SCT symptom ratings, and social deficits. Studies outside the field of ADHD, such as those that have investigated impairment in brain damaged patients, behavioral response to neural stimulation in animals, as well as cognitive performance in healthy adults also inform about the nature of the deficits in ADHD. As the pattern of findings continues to highlight observable differences between ADHD/C and ADHD/IA, the assumption that they also exist at the neurological level is strengthened. The consideration of whether the nature of the attention deficit is fundamentally different when diagnosed in conjunction with

hyperactivity/impulsivity will provide structure in this review for the development of hypotheses about the performance of the subtypes on different measures of attention.

Evidence for the neurological origin of behavior in ADHD validates the attempt to delineate a neurocognitive profile of the symptom domains, and ultimately to differentiate cohesive subtypes of children who receive the diagnosis. For the most part, studies that have investigated brain functioning in ADHD have successfully demonstrated that the neurological impairment exists but have been largely disappointing at identifying the specific correlates for the diversity of behaviors that must be explained. There remains uncertainty as to whether multiple neural mechanisms are, in fact, responsible for the heterogeneity of symptom profiles within ADHD, and if so, how this relationship between brain and behavior is borne out.

Over recent years, significant progress has been made in tracing the relationship between behavior and the brain, which has greatly advanced our knowledge of the neuroanatomy and function underlying the dysfunction in ADHD. The synthesis of literature in the next chapter attempts to outline the parallels between ADHD behavior and neurological dysfunction. Accumulative research offers substantial empirical support for the involvement of numerous brain structures and functions in ADHD, generating nearly as much confusion as clarity about the etiological nature and specificity of the disorder. Such discrepancies are often reflected in the theories that accompany the findings, making conclusions about associated deficits quite tentative. However, if some explanations serve a particular subset of symptoms better than another, or than the entirety of impairment, then the different models offered for ADHD may actually share validity when the possibility of divergent symptom outcomes is considered. Various theories will be considered in terms of their relevance for the ADHD/C and ADHD/IA subtypes, with consideration given to the group of "inattentives" who display SCT symptoms.

Chapter 3: The Brain and ADHD Symptomology

Relating ADHD Symptoms to the Brain

Over the past decade, many different neuroanatomical regions have been implicated in the origins of ADHD. Empirical evidence from studies comparing children with ADHD to controls provides support for each of the various models of the disorder, making the attempt to pinpoint the neurological bases a complicated one. That these accounts are often discrepant speaks to the symptom heterogeneity ostensibly present in the clinical profile of ADHD (Swanson, Castellanos, Murias, & Kennedy, 1998a). The theories may well offer valid explanations for certain cognitive deficits but do not provide a unifying account of the entirety of cognitive and behavioral deficits associated with ADHD (Barkley, 1997). As Swanson et al. (1998a) have suggested, the seemingly contradictory neurocognitive models of ADHD may have been proposed to account for different constellations of symptoms from within the ADHD profile. An investigation of symptoms of hyperactivity and impulsivity versus those of attention, or discernable subcomponents of attention, will likely generate different syntheses of experimental findings to account for the dysfunction. Further, since attention is a broad concept that encompasses a wide range of cognitive processes, multiple components of attention have been isolated and ascribed to their particular neural systems. This distinction comes to the forefront when considering research involving the ADHD subtypes or composite ADHD groups of mixed type. If deficits in attention found in absence of hyperactivity/impulsivity, as in ADHD/IA, are dissociable from the inattention of ADHD/C, discrepant accounts, each valid in their own right, may be put forth to explain the neurocognitive origins of the disorder.

Theories of the ADHD/C subtype must account for the robust findings of executive dysfunction in this group. The symptom similarity of the hyperactive/impulsive domain to patients with acquired lesions to frontal and associated brain regions has been identified throughout the history of the disorder (Mattes, 1980). Many studies in recent

years, each inspired by a specific focus, have demonstrated executive function deficits and the role of the prefrontal cortex and associated structures in ADHD. Prevailing neurochemical, neuropsychological, and neuroanatomical theories of ADHD typically explain the same dysfunction, but from a different perspective (Riccio, Hynd, Cohen, et al., 1993). There is general agreement over the manifestation of impairment in ADHD, although the underlying core or primary deficit has generated some debate. Disagreements are heightened, and may be partially explained, by the varied and often inconsistent terminology, pervasive in the literature, that is applied to processes of executive function and attention.

The terminology used to describe executive function and attention and its component processes has not achieved general consensus. This discordance complicates the attempt to empirically test the components of these constructs and subsequently, to delineate the specific deficits associated with ADHD. For example, terms such as behavioral inhibition, self-regulation, and executive control of attention are often used interchangeably to refer to the same deficit but may be embedded in the architecture of different theories (e.g., Douglas, 1972; Barkley, 1997; Swanson et al., 1998a). There is, clearly, overlap in the terminology that makes it difficult to independently define executive function and attention. The labels for the impairment in ADHD may differ but often the concepts are not necessarily exclusive or even inconsistent with one another. As one might expect, confusion arises when trying to replicate or assimilate findings, or generalize results from studies that have used different labels for the same cognitive function or alternatively, the same label to describe different functions. A noteworthy scenario occurs when the term used to describe the process of inattention in ADHD/C (e.g., “executive control”) is also used to describe the process by which hyperactivity/impulsivity disrupts behavior. The single label consistently denotes an executive function of the frontal lobes, but it references ADHD symptoms that are classified into the two different domains. On the other hand, the term for another subcomponent of inattention (e.g., “orienting”) describes a cognitive process that is very distinct from the previously described executive control of attention. With the current

terminology, two mechanisms of attention can be etiologically distinct, whereas a mechanism of attention and mechanism of hyperactivity/impulsivity can be identical. The overview of executive functioning and attention, presented over the next few sections, highlights the intricacy and overlap of functions of the brain.

Attention and the Brain

The neural bases of attention involve several networks of distinct yet interconnected brain systems responsible for the numerous cognitive processes that have been considered under the broad rubric of attention. Anatomical foci of the regulation of attention have been inferred through the observation of dysfunction in individuals with regional brain injury as well as through the use of technology that has advanced knowledge about the information architecture of the brain (Posner & Petersen, 1990). Neural systems of attention have been investigated in humans through use of techniques such as the recording of event-related electrical and magnetic activity in the cerebral cortex and, neuroimaging of the regional cerebral blood flow. Using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) to learn more about brain structure and function has given exposure to the patterns of neural activity that drive human cognition.

The following discussion will provide an overview of the neurological structure and function relevant to the domains of executive function and attention and ultimately, to the target population, ADHD. The frontal lobes and particularly, the pre-frontal cortex and its role in executive function have been consistently demonstrated at the neurological source of cognitive deficits in ADHD. Neuropsychological tests, neuroimaging maps, and the consistency between frontal lobe behavior and the hyperactive/impulsive deficits observed in ADHD provide such support. The neurological substrates of attention, on the other hand, have not been clearly identified in this population. This may be in part due to lack of correspondence between the behavioral and cognitive constructs of attention. Additionally, origins of certain inattentive and hyperactive/impulsive processes converge neurologically. Executive control over attention is a frontal lobe function that falls into both the categories of executive function and attention. Others types of attention

represent quite different sets of processes that are centralized in subcortical or posterior brain regions or considered, broadly, to reflect a whole brain state. Discussion of the executive functions and their overlap with attention, as well as the role of non-frontal regions in regulating attention will be put forth to address this issue.

Posner and Raichle's model (1994) of separate yet interconnected networks of attention in the brain helps illustrate the cognitive breadth of attention. Because of the anatomical and functional overlap between an anterior attention network and the pre-frontal cortex, strong support exists for an executive deficit of attention in the ADHD/C subtype. There is not the same evidence to suggest that the ADHD/IA subtype, especially those who show few or no symptoms of hyperactivity/impulsivity, have the same type of attention deficit. To limit a study of attention to the anterior system would address only a portion of the cognitive processes of attention. Posterior cortical regions of the brain are also posited to support processes of attention and may be implicated in the appearance of primary attention deficits in ADHD/IA. Additionally, midline subcortical regions involved in the homeostatic regulation of the autonomic nervous system are important for establishing an individual's state of arousal and attention, and thus create the conditions necessary for optimal cognitive performance to occur (Nolte, 1993).

The Frontal Lobes and Executive Functions

The role of the frontal lobes in controlling human behavior has long been recognized. As early as the 1800's, their importance was emphasized based on their large size and apparent expansion in human evolution (Pennington & Ozonoff, 1996). Since this time, intrigue has surrounded the status of the frontal lobes as the source of functions considered to be abstract notions of the human experience: morality and a higher conscience, the generation of humor and sarcasm and, even the tendency toward self-destructive behavior. That damage to the frontal lobes can result in complex changes in behavior while certain neurological correlates, such as components of intelligence, remain unaltered, has added to the mystique of their nature. The wide range of symptoms associated with activity of the frontal lobes has implicated their dysfunction in many conditions of human psychopathology (Fuster, 1989, Malloy & Duffy, 1994, Luria,

1966). In an attempt to understand that the pathology of varying behavioral presentations and syndromes could converge onto the frontal lobes, speculation arose as to whether the location and extent of frontal lesions actually corresponded to distinct patterns of dysfunction rather than a more diffuse "frontal syndrome". Scientists have now designated a considerable degree of specificity to the architecture of the frontal lobes and can better discriminate among the functional deficits associated with localized lesions. Over the past few decades, research has made rapid advances in uncovering the relationship between structure and function and has thus greatly increased our understanding of the role of frontal subsystems in human psychopathology.

The frontal lobes can be divided into several anatomical regions based on function. The primary motor area, premotor area, frontal eye fields, and the supplementary motor areas are involved in motor, sensorimotor, and visual functions, and in the initiation of volitional movement (Malloy and Duffy, 1994). The prefrontal cortex (PFC) lies anterior to these regions and claims a central role in human thought and cognition, and personality, as well as in the expression of mental disorder (Pennington and Ozonoff, 1996). Dysfunction of the PFC region of the frontal lobes is heavily implicated by the various terms denoting, more generally, the frontal lobes, e.g. "frontal syndrome", and "frontal dysfunction". Terminology for the two regions is often used interchangeably in the literature (Fuster, 1989). The anatomical distinction is important though, as frontal lesions outside the PFC look quite different from those within and, as localized lesions within the PFC can differ greatly in resultant impairment. The PFC regions of the frontal lobes are central to executive function and the control of attention.

The Prefrontal Cortex

Evidence of specific deficits associated with localized dysfunction throughout the PFC comes primarily from ablation studies in animals and from observation of adult patients with localized lesions (Stuss & Benson, 1984). It is important to note that the dysfunction exhibited in developmental neurological disorders in childhood is likely more diffuse and associated with a broader range of cognitive deficits than in adults with acquired lesions (Pennington & Ozonoff, 1996). Early in development, the brain has high

potential for cerebral plasticity that can influence the manifestation of cognitive/behavioral deficits in response to damage (Ridderinkhof & van der Molen, 1997; Travis, 1998). In children, the dysfunction incurred from focal lesions may not be contained to a specific site or process, as neural connections are rapidly forming new pathways and old ones are eliminated (Travis, 1998). Continuing maturation and neuronal growth of the frontal lobes throughout childhood and into early adulthood may be a contributing factor to the heterogeneous picture of ADHD and the complexity of identifying "core" deficits in ADHD/C and ADHD/IA. Establishing the relationship between performance on a neuropsychological test and localized brain damage is much more complex in children than adults. Additionally, many of the neuropsychological tests used in assessment with children were constructed for adults and cannot always be generalized to use with children (Pennington et al., 1996).

The psychological significance of the pre-frontal cortex lies in its service of the executive functions. The executive functions are broadly implicated in behavior, in the experience and expression of emotion, and in cognition. Although the executive functions disrupted from PFC lesions are quite heterogenous, it is generally agreed that they involve goal-directed behavior and an element of mental or behavioral control (Barkley 1997; Pennington et al., 1996). There is much overlap of the domain of executive functions with the domains of reasoning, problem solving and, of particular interest here, attention (Pennington et al., 1996). PFC lesions lead to disruption of executive functioning which results in problems with complex, higher order operations that include behavioral inhibition and delayed responding, planning, organization, cognitive set-shifting, working memory, integrating multimodal sensory input, and modulating emotional response (e.g., Barkley, 1997; Milich & Nietzel, 1993; Nigg, Blaskey, Huang-Pollock, & Rappley, 2002; Shaywitz et al., 1999).

The PFC receives projections from subcortical regions including the thalamus and basal ganglia, and from limbic and posterior cortical areas forming multiple functional subsystems. The mechanisms responsible for executive functions have been localized primarily to the PFC, and/or associated thalamic and subcortical striatal areas (Casey,

Castellanos, Giedd, Marsh et al., 1997; Pennington & Ozonoff, 1996). Disruption at any level of the circuitry within a given subsystem can result in deficits of executive functioning. The PFC can be divided into three regions that form functional subsystems with their associated structures: the dorsolateral pre-frontal area, orbitofrontal area, and a medial area composed of the supplementary motor area and anterior cingulate gyrus (e.g., Malloy & Richardson, 1994).

The dorso-lateral region appears to be the neural substrate for planning, working memory, and flexibility in generating cognitive responses (Barkley, 1997; Fuster, 1989; Malloy & Richardson, 1994). It has extensive connections with secondary sensory association areas in the parietal, occipital and temporal lobes, an arrangement that facilitates the role of this prefrontal area in integrating multimodal sensory information. The dorsolateral PFC forms a circuit with the caudate nucleus portion of the basal ganglia that is essentially implicated in the functions of this frontal region. Documented lesions at the cortical and subcortical levels of this circuitry have been associated with deficits of impersistence and defective response initiation and inhibition (Heilman & Valenstein, 1993). The dorsolateral cortex has been found to be active during performance of the Wisconsin Card Sort Task (WCST) and is presumed to modulate the working memory demands imposed by the task (Berman, Ostrem, Randolph, et al., 1995). Damage to either region of the system has been shown to disrupt performance on tasks of short-term spatial representational memory and tasks of rule learning, as in the WCST (Partiot, Verin, Pillon et al., 1996). Greater regional Cerebral Blood Flow (rCBF), a measure of neuronal activity, in the left dorsolateral region is associated with better performance on the Tower of London, a measure of planning ability.

The orbito-frontal region has been implicated primarily in motor inhibition and emotional and social impulsivity (Fuster 1989; Malloy & Duffy, 1994). Orbito-frontal connections with limbic structures form the circuitry responsible for integrating motivational and emotional processes (Malloy & Duffy, 1994). Lesions to this system have been documented to result in a euphoric syndrome characterized by hypomania, immature humor, sexual and eating impulsivity and, lack of moral principles (Fuster,

1989; Pennington & Ozonoff, 1996; Rolls, 1996). The orbitofrontal cortex is also centrally involved with reinforcement association learning, which is necessary for adjusting behavior in accordance with rewards and punishement (e.g., Rolls, 1996). EEG recordings show heightened activity in the orbito-frontal cortex during the go-no-go and stop tasks of behavioral inhibition which require the subject to inhibit the pre-potent motor response on "no-go" or "stop" trials. To successfully pursue the goal, the current thought or action needs to be stopped in response to a change in task demands, a process Logan (1994) has linked to executive control. Patients with lesions to this orbito-frontal area show performance deficits on these tasks (Malloy & Richardson, 1994, Rolls, 1996). The Stroop test, which requires the suppression of competing responses, places demands on the inhibitory functions of this subsystem and of the anterior cingulate frontal zones.

The medial subsystem includes the anterior cingulate gyrus of the PFC and the supplementary motor area. These two frontal regions operate reciprocally in a system understood to regulate environmental search and inhibit exploratory behavior (Malloy & Richardson, 1994). Lesions to this system are associated with a syndrome of akinetic mutism in which the initiation of speech and other spontaneous behavior is severely impaired (Pennington & Ozonoff, 1996). This system overlaps much in function with the orbito-frontal PFC, playing an important role in utilization behavior, perseverations, distractibility, and interference control: the defining characteristic of effortful attentional control (Posner, 1994). Like the orbito-frontal region, the medial PFC has been shown through rCBF studies to be active during the go-no-go and stop tasks of behavioral inhibition and the Stroop task measuring interference control. These medial frontal areas operate in an executive control network of attention that will be discussed below.

Constructs of Attention

Attention is viewed in the cognitive and neuropsychological literature as a multidimensional construct (Barkley, 1991; Mirsky, Pascualvaca, Duncan, & French, 1999). Over the years attention has been defined in various ways, from a limited capacity of memory to a filter mechanism for extracting relevant incoming information

(Broadbent, 1958; Shifrin, 1976). Multiple components of attention have been identified to describe the breadth of processes encompassed by its domain. Presumably, these components can be distinguished by their neurological location, cognitive function, and behavioral expression (Posner & Petersen, 1990). Certain dissections of the construct of attention have been given more emphasis than others in the ADHD literature. Neuropsychological perspectives of attention tend to digress somewhat from the models of attention derived from the cognitive sciences. Cognitive theories of attention are largely driven by experimental paradigms used in the laboratory that isolate specific component processes. Conversely, neuropsychological theories often identify dimensions of attention that span multiple cognitive processes. Compromised precision thus reintroduces the problem of foggy terminology and the ability to generalize across findings.

A neuropsychological model of attention that expands the work of Barkley (1996), Douglas (1980), Halperin, Wolf, Pascualvaca, et al. (1988), Mirsky et al. (1999), Shelton and Barkley (1994), and Pascualvaca, Anthony, Arnold, et al. (1997) incorporates components of attention that have been considered in the investigation of cognitive deficits in ADHD. This model has specified several dimensions of attentional functioning including: arousal or alertness, selective or focused, sustained, shift, divided, and encoding. These components have been associated with neural systems that interact dynamically within a larger network of attention, although there is not necessarily agreement as to which specific systems those are. Low priority will be given to defining each of these functions of attention since there is still inconsistency in their application to the cognitive processes of ADHD. The point is rather to illustrate the multifaceted and neurologically diverse basis of attention.

The processes of sustained and selective attention have been prominent in the research of cognitive dysfunction in ADHD (Barkley, 1997; Douglas, 1980; Riccio, Hynd, Cohen, & Gonzales, 1993). Sustained attention is generally agreed to involve the maintenance of on task behavior over an extended period of time. Descriptions of the arousal or alertness component of attention often overlap with the concept of sustained

attention or vigilance and the terms are often used interchangeably (Mirsky et al., 1999). Arousal or alertness is typically considered to be a whole brain state representing an individual's readiness to respond to sensory information (Lorys, Hynd, & Lahey, 1990; Posner, 1990). Children with ADHD/C have consistently been shown to perform poorly on Continuous Performance Tests (CPT) presumed to assess sustained attention (Barkley, 1997; Seidel & Joschko, 1990).

A review of the literature reveals that selective attention (focused attention) invites the greatest variety of definitions and applications, rendering the term rather inadequate for isolating cognitive processes in ADHD. Generally speaking, this term refers to the ability to focus cognitive resources on a meaningful event while screening out extraneous information. However, selective attention also represents an entire domain of research that subsumes multiple cognitive processes that fall within the general description (Posner, 1990). Two major processes of selective attention are: a sensory process involving the right parietal lobe, and an executive process of response inhibition involving the prefrontal cortex (Swanson, Posner, Cantwell, et al., 1988b; Posner, 1990; Carte, Nigg, & Hinshaw, 1996). A task that places demands on both the sensory and executive systems could be classified as a test of selective attention, although the cognitive variable being assessed represents a composite function rather than the process of a single system (Shaywitz et al., 1999). This complexity is often not recognized in research with ADHD. Unfortunately, conclusions drawn about performance on tasks purported to assess selective attention are often discordant, perhaps because they reflect the mechanisms of distinct neurocognitive systems. The hypotheses generated about the core deficits of the ADHD/IA and ADHD/C subtypes often lack specification because the term selective attention is used but not clarified.

Many researchers have suggested that children with ADHD/IA have a deficit in selective attention (e.g., Goodyear & Hynd, 1992; Lahey & Carlson, 1991; Shelton & Barkley, 1994; Barkley, 1997), whereas children with ADHD/C have deficits in the executive control of attention, or disinhibition, and sustained attention processes (Barkley, 1996; Berger & Posner, 2000; Castellanos, 1997; Seidman, Biederman,

Faraone, et al., 1997). Given that the construct of selective attention is too broad for the hypothesis of differential cognitive deficits in the subtypes, its use precludes the development of a conceptually driven experimental paradigm sensitive to potential between-group performance differences. Fortunately a number of researchers have detailed the nature of the hypothesized deficit in ADHD/IA, which is presumed to affect the sensory driven process of visual spatial orienting that resides centrally in the right posterior parietal lobe. This sensory/spatial "selective attention" deficit in ADHD/IA contrasts with the executive dysfunction of the ADHD/C subtype.

The Stroop task, a familiar paradigm in the cognitive and clinical psychology literature, is commonly referred to as a measure of selective attention. The paradigm places demands predominantly on interference control, an EF, (although it has been noted to be confounded by non EF components), that places demands on the dorsolateral prefrontal cortex and the anterior cingulate gyrus frontal regions (Nigg, 1999; Pennington & Ozonoff, 1996). Children with ADHD/C have consistently demonstrated deficits on the Stroop and other tasks including priming and flanker tasks that make similar performance demands (Seidman, et al., 1997; Nigg, 2000; Travis, 1998). Specific patterns of performance deficits in ADHD/IA have yet to be established for this type of paradigm. However, considering that this subtype (or a subgroup of children with ADHD/IA) might have a different attention deficit, tests that contain an executive component, alone or in conjunction with a lower level component of selective attention, would not be suited to investigate the nature of inattention in ADHD/IA. Additionally, failure to find a difference between the subtypes (ADHD/IA worse than ADHD/C) on a test popularly regarded as a measure of selective attention cannot be interpreted as counter-evidence for the hypothesized distinction of deficits in the subtypes.

The breadth of attention and its terminology within the literature is illustrated by the multiple nosological frameworks that break down the construct of attention into component parts. A second model of attention will be presented briefly as it may provide a useful terminological distinction for core deficits in the subtypes. In this model, automatic and control processes of attention are distinguished (Borcherding, Thompson,

Kruesi, et al., 1988; Nigg, 2000). An automatic process can be executed unconsciously or involuntarily and can occur simultaneously along with other tasks. Examples include encoding of spatial relationships, visual orienting, word recognition, and the activation of word meaning (Hasher & Zacks, 1979; Posner & Petersen, 1990). Automatic attention is generally identified with subcortical ascending and posterior cortical locations (Denckla, 1996; Posner & Petersen, 1990). The arousal component of attention fits relatively well into this end of the dichotomy since it has much to do with regulation of the autonomic nervous system and does not require the intervention of goal directed behavior. Effortful processing, on the other hand, requires that attention is controlled voluntarily or with effort and is susceptible to interference from concurrent tasks. Examples of effortful processing include rehearsal strategies, the free recall of words from a list, response inhibition, self-monitoring and related functions associated with the frontal lobes (Hasher & Zacks, 1979; Posner & Petersen, 1990). Although most processes fall on an automatic/effortful continuum, rather than at dichotomous ends, the distinction is useful for describing the accompanying state of attention. Sustained attention, for instance, shares both automatic and effortful elements of processing in the course to maintain goal directed behavior over an extended time.

Networks of Attention

Posner and Raichle (1994) offered a theory of attention based on the assumption that distinct neural networks support component processes of attention. The subsystems of attention outlined perform different but interrelated functions that can be specified in cognitive terms (Posner, Petersen, Fox, & Raichle, 1988). The three functions considered in their theory have been prominent in the cognitive attention literature and a significant focus of experimental research: executive control, orienting, and alerting (Posner & Petersen, 1990). The authors proposed the neuroanatomical basis and associated cognitive processes of neural networks that serve each of these three functions.

The Anterior Attentional System

The anterior system of attention is closely involved with aspects of executive functioning. This system is assigned the executive control of attentional resources and closely participates in the self-regulation of human behavior (Posner & Dehaene, 1994). The anterior cingulate gyrus is central to this network of connected brain regions that also includes the superior supplementary motor areas of the frontal lobes and portions of the basal ganglia. The medial frontal regions of the PFC (one of the three PFC divisions described above) that support behavioral inhibition among other executive functions define this network of attention. Processes of executive control are responsible for managing the effects of cognitive interference. Negotiation of conflict between competing stimuli is required in order to facilitate suppression of the pre-potent automatic response that interferes with target detection (Posner and Raichele, 1994). Put in different terms, this control network inhibits responses to irrelevant stimuli. Disruption of this inhibitory process results in the appearance of distractibility and a reduction in goal-oriented behavior.

The attention associated with the anterior system involves higher order effortful processing typical of PFC functions. This system is engaged when generating a unique response or when actively attending to a visual target as opposed to just passively viewing stimuli. Successful engagement of the relevant information draws attention away from irrelevant stimuli so that the intended activity can proceed. The high-level of attentional control exerted by this network is also necessary for planning, error detection, and responding to novel stimuli (Posner and Raichele, 1994). The supplementary motor cortex is thought to play a primary role in this network when a verbal or motor response is required in the course of task performance.

The Posterior Attentional System

The posterior attention system is involved primarily in orienting to sensory stimuli (Posner & Raichele, 1994). What is known about this network and its functions comes from work within the visual-spatial information-processing domain. Its function is quite different from that of the anterior system. The posterior system does not take part in

the high level control of attention, but rather, in the more basic sensory processing level of attention. The neural network for orienting is situated in the posterior parietal lobes and connected brain regions: the superior colliculus of the midbrain and the thalamus (Berger & Posner, 2000). Studies of patients with regional brain injury indicate that each of these anatomical areas carries out a different process of the attention shift. The parietal lobe disengages attention from the initial focus, then the midbrain orchestrates the move of attention to the target area, and finally, the pulvinar of the thalamus acts to reengage attention at the new location (Posner & Peterson, 1990). This entire sequence can take place covertly, that is without accompanying movements of the eye or head. Cognitive resources must be reallocated internally to support the attention shift that is usually associated with overt physical movements, when occurring in the visual domain. Selective attention has been illustrated as a function of enhanced processing at the "selected" location and attenuated processing at ignored locations. The attention subserved by the posterior system can be considered under the scope of automatic processing since it requires little or no voluntary control.

The Alerting Network of Attention

Posner has described an alerting component of attention that serves to establish and maintain a vigilant state. The neural network of alerting is a noradrenergic system that originates in the locus coeruleus nucleus of the midbrain and projects to right frontal and right parietal cortical regions. The noradrenergic cells originating in the locus coeruleus project diffusely to the cortex and broadly influence brain activation levels via the neurotransmitter norepinephrine (Fernandez-Duque, Baird, & Posner, 2000). Alertness requires that a general state of readiness be sustained so that important information can be processed as it occurs. Ongoing or irrelevant neural activity is presumably suppressed in order to establish readiness to act. With this condition imposed, the individual is prepared to respond to anticipated environmental events or, as in the case of an experimental paradigm, to target stimuli (Posner and Raichele, 1994). Rate of responding to stimuli is increased when alertness is high, but at the expense of a higher error rate (Posner and Raichele, 1994).

Evidence suggests that the ability to establish and maintain an alert state is heavily lateralized to the right cerebral hemisphere. The connection between vigilance and the right hemisphere has been demonstrated through studies of blood flow and metabolic activity, measurement of physiological responses in humans and monkeys as well as the performance of patients with right versus left hemispheric lesions on vigilance tasks (Posner & Petersen, 1990). The norepinephrine (NE) system arising in the locus coeruleus is thought to be involved in regulating the alert state (Posner & Petersen, 1990).

Maturation of Anterior and Posterior Regions

Support for the dissociation of cognitive processes associated with the anterior and posterior attention systems comes from studies showing developmentally related changes in performance on cognitive tasks (Ridderinkhof, & van der Molen, 1997). Kramer Humphrey, Larish, et al., (1994) for example, found different patterns of inhibitory control between old and young adults on tasks assessing executive functions of the frontal lobes versus those assessing visual-spatial functions mediated by posterior parietal pathways. The older adults were relatively slower at inhibiting a manual response once it had been initiated on a stop task paradigm and they perseverated longer in irrelevant categorization rules on the WCST. In contrast, old and young adults showed equal inhibitory control on the negative priming and spatial cueing tasks. These findings are consistent with the idea that the differential effects of maturation and aging on brain structures are mirrored by measurable changes in the cognitive functions associated with these regions (Kramer, Hahn, & Gopher, 1999; Rubia, Overmeyer, Taylor, et al., 2000; Travis, 1998). Posterior brain regions reach maturation in early and middle childhood years, whereas the frontal lobes continue to mature into the mid-twenties or later (Rubia et al., 2000).

It has been noted that the continued myelination and synaptic pruning of the pre-frontal circuitry into adulthood is consistent with the improved prognosis for adults with ADHD (Castellanos, 1997). Hyperactivity is most salient in childhood and shows remission over the developmental course. Certain components of inattention, on the other hand, show little improvement with time and may even become more impairing as

academic demands increase in school. Divergent developmental trajectories suggest that these symptoms correspond to different underlying neurological deficits. If the attentional impairment in ADHD/IA is not primarily a function of the frontal lobes, the developmental course of the disorder would be expected to be relatively stable and show less improvement over time.

Dissociating Cognitive Processes of Attention

A paradigm that is sensitive to variation in an attention deficit must be able to isolate different processes of attention, by which task performance can thus be interpreted. The following study illustrates the class of methodology involved in this endeavor. Stuss, Toth, Franchi, et al., (1998) explored the dissociation of attentional processes in patients with brain lesions via a well-controlled design that enabled them to assess the contribution of presumed anterior and posterior processes on task performance. The experimental groups included 36 patients with anterior or posterior lesions, specific site of region varied, to the right, left or spanning both hemispheres. They used a spatial selection task in which subjects were required to identify targets, presented either with or without distractors. Their task was designed to measure 3 distinguishable cognitive processes: interference, negative priming, and response inhibition under 3 levels of complexity. For the purposes of brevity and relevance, only interference and negative priming will be discussed here. Interference occurs when a target stimulus must be identified and selected in the presence of "distracting" non-target stimuli. The effects of interference on task performance are expected to increase as a function of task complexity, as was demonstrated in the control group. Negative priming measures a shift in selecting target location, when the new location to be selected was previously occupied by a distractor. The negative priming task condition involved a prime display that presented both a target and a distractor, and a probe display that presented a target in the location previously occupied by the distractor. Negative priming was not affected by increasing task complexity in controls.

The results of the study demonstrate a dissociation of interference and negative priming processes on a cognitive test of attention. Patients with right frontal and medial

frontal damage were impaired on the most complex interference condition, i.e. demonstrated significantly greater cognitive interference than controls, whereas patients with posterior lesions showed no impairment of interference functions. A specific role of frontal regions in the executive control over cognitive interference is indicative of Posner's anterior network of attention. Stuss et al. (1998) did note the discrepancy of their findings from PET studies that have indicated a non-lateralized effect of the medial frontal regions in interference control. Right hemisphere damage (right frontal and right posterior) obliterated negative priming effects, numbers did not differ significantly from zero, in all levels of complexity. Left frontal patient showed a different pattern of performance for this measure. They demonstrated normal negative priming for the easier two conditions, but then lost negative priming in the most complex condition. Patients with left posterior lesions did not differ from controls. In this paradigm, negative priming involves inhibiting selection of a spatial location, and appears to be predominantly anchored in the right hemisphere, or posterior attention system.

This study illustrates two major points that are central to the present research. First, through sound methodology, the paradigm established measurable independence among cognitive processes on a visual test of attention. Second, the findings demonstrate a dissociation of processes linked to the anterior and posterior systems of attention in patients with focal brain lesions. Importantly, region of neurological impairment and task demand differentially affected the mechanisms of interference and negative priming (Stuss et al., 1998). Neuropsychological instruments that are sensitive to the dissociation of cognitive attentional processes are greatly needed for assessment of the dysfunction in ADHD subtypes. Additionally, the use of a noninvasive behavioral test that provides an indirect measure of the efficiency of attention networks while also demonstrating the effects of the associated cognitive mechanisms on task performance is highly appealing for use with ADHD children.

Chapter 4: Neurocognitive Profiles of ADHD and its Subtypes

Neurocognitive Comparison of the Subtypes

Most studies that have conducted a comparison of ADHD/IA and ADHD/C have had difficulty in showing different patterns of deficits between the subtypes on neuropsychological measures (for review see Carlson, Shin, & Booth, 2000, & Milich et al., 2001). Strong support for heterogeneity within and across ADHD subtypes is further corroborated by inconsistent findings between the diagnostically classified subtypes documented throughout the literature. A pattern of null findings emerged for a variety of neuropsychological measures of frontal lobe functioning including, the Trail Making Test, the CPT- omissions and commissions, the Stroop, and the WCST (Barkley et al., 1990; Barkley, Grodinsky, and DuPaul, 1992; Carlson, Lahey, & Neeper, 1986; Patternite, Loney, & Roberts, 1996). Not only was subtype differentiation a problem, these measures also frequently failed to distinguish ADHD groups from LD or control groups. Mixed findings were reported for the Matching Familiar Figure Test (MFFT), a test designed to assess impulse control. One study found the ADD-H group to be more impaired than the ADD+H group on this task (Conte, Kinsbourne, Swanson, et al., 1986), while others failed to find group differences between the subtypes (Carlson et al., 1986; Barkley et al., 1990). Barkley et al. (1990) found a relative performance deficit for the ADD-H compared to the ADD+H group on the Weschler Coding scale. This finding, however, is not robust as it lacks substantiation through replication. A recent study found no differences between ADHD/IA and ADHD/C groups on a task of paired-associate learning that requires the encoding and subsequent recall of word pairs (Chang, Klorman, Shaywitz, et al., 1999). The complexity of this task it is likely to implicate both executive and non-executive cognitive processes, which could potentially mask between-group differences.

In a 1994 report, Barkley & Grodzinsky examined the usefulness of tests of frontal lobe functioning for diagnosing ADHD subtypes, relying primarily on studies using DSM-III criteria for ADD with versus without hyperactivity (ADD-H vs. ADD+H).

They addressed the issue of different cognitive deficits in the subtypes by reviewing the pattern of sensitivities found for some of the tests. Although these patterns were only partially corroborated by statistical significance, they were suggestive that certain deficits were more indicative of one subtype or the other. Sensitivities for CPT commissions and WCST set failures were somewhat higher for the ADD+H group than the ADD-H group suggesting some specificity for a deficit in response inhibition in ADD+H. Higher sensitivities for ADD-H were found on tests considered to weight less heavily on frontal lobe functions including, CPT omissions, Trail Making, Stroop words, and verbal fluency, indicating that certain aspects of inattention and speed of perceptual-motor processing are more impaired in this group.

Some of the early studies attempted to examine mechanisms of automatic and effortful processing in the subtypes. Performance on tasks presumed to assess automatic processing, including, naming and temporal sensitivity, speed of writing O's, and rapid addition and subtraction did not differentiate the subtypes (Ackerman, Anhalt, Dykman, & Holcomb 1986a). Nor were differences found on tasks presumed to assess effortful processing, including, semantic and acoustic encoding, list learning of high and low-imagery words, memory for two words, and rapid addition and subtraction, (Ackerman, Anhalt, Dykman, & Holcomb, 1986b). Overlap in the functional assessment of the selected measures may have limited the chance of finding group differences. Hynd, Lorys, Semrud-Clikeman, et al. (1991a), on the other hand, did find differences between the groups in their investigation of automatic processing speed. They followed a naming paradigm, using rapid alternating naming (RAN) and rapid alternating stimulus (RAS) naming measures believed to challenge the mechanisms of automatic processing. The ADD-H group was slower than the ADD+H group on these tasks suggesting an automatic processing deficit. Although no other studies have evaluated performance of the inattentive subtype within this paradigm, Borcherding et al. (1988) did find in their study that effortful processing tasks differentiated between hyperactive children and nondisordered controls, whereas automatic processing tasks did not. Overall, the emergent pattern of findings indicates that neurocognitive differences exist between the

ADHD subtypes, but does not lend to definitive conclusions about what those differences are.

Schaughency and Hynd. (1989) first proposed and investigated the anterior/posterior model of neurocognitive deficit in the ADHD subtypes. They tested the hypothesis that the sluggish cognitive tempo exhibited in ADD-H children stems from primary deficiencies in a posterior arousal system of attention whereas, the problems with behavioral inhibition and impulsivity in ADD+H are subserved by an anterior motor-readiness system of attentional control. The researchers administered a neuropsychological battery of tests assessing various mechanisms of memory, visual-attention, executive function, motor regulation and other cognitive variables to ADD-H, ADD+H, and clinic control groups. With IQ covaried, performance indexes failed to distinguish among the three groups. Although the ADHD subtypes were not differentiated from each other, neither was the clinical control group differentiated from ADHD. This underscores the methodological issue concerning the limited utility of neuropsychological tests for distinguishing among disordered populations, despite their ability to detect the presence of impairment. Lorys, Hynd, and Lahey (1990) further examined the anterior-posterior hypothesis of attention deficit in the subtypes. Using measures of perceptual/sensory attention that are thought to assess posterior processes and motor regulation and inhibition tasks requiring anterior executive control the authors failed to differentiate ADD-H from ADD+H. What has been concluded is that neuropsychological research of ADHD dysfunction sorely needs alternative assessment measures that are sensitive to discrete neurocognitive processes (Goodyear & Hynd, 1992; Riccio, et al., 1993).

Recent studies have achieved increased success at differentiating the subtypes on neurocognitive measures, although mixed findings overall still confuse the interpretation of differences. A recent study used a powerful design to examine EF deficit in 201 children with ADHD/C and 102 children with ADHD/IA, in addition to Reading Disordered groups (Klorman, Hazel-Fernandez, Shaywitz, et al., 1999). Their major finding was that EF deficits, as measured by the Tower of Hanoi (TOH) and WCST,

characterized only ADHD children with hyperactivity/impulsivity. The ADHD/C group exhibited deficient performance on the TOH compared to the ADHD/IA and non-ADHD groups. The TOH is an indicator of the ability to manipulate visual information in working memory, or planning. This task has been shown to place demands on the frontal lobes as evidenced by fCBF studies and performance in patients with prefrontal lesions (Goel & Grafman, 1995). The investigators found the same pattern of performance, ADHD/C worse than ADHD/IA on WCST nonperseverative errors, but not for perseverative errors, for which there were no group differences. This task is presumed to measure flexibility in problem solving. Klorman and colleague's findings (1999) are especially impressive considering the ADHD/IA group outperformed the ADHD/C group on these measures of executive function even though they had significantly lower IQ scores.

Another valuable study conducted by Nigg, Blaskey, Huang, & Rappley (2002) investigated several components of executive function in the ADHD subtypes. The ADHD/C group had slower stop reaction time on a stop-signal task than ADHD/IA who did not differ from controls, indicating a distinct deficit in behavioral inhibition. On the Stroop color-word interference condition, no deficits were found for either subtype with IQ controlled. Interestingly, though, the ADHD/IA group demonstrated slower overall naming speed, a non-executive function related to reading ability, on this task. The inattentive group demonstrated significantly slowed performance on the Trailmaking test of set-shifting, with stronger effects for Trails B, that was not independent of reading ability or IQ. The Trailmaking paper and pencil test requires the subject to draw a path connecting consecutive numbers or alternating numbers and letters and is traditionally considered a test of perceptual-motor processing (Barkley & Grodinsky, 1994) although here, it is used for its executive components. A speed of processing deficit that is related to reading ability but does not fall into the domain of EF is perhaps being expressed on the above timed test components, naming speed on the Stroop and perceptual-motor/set-shifting speed on the Trails test. On the Tower of London test of planning, no group-deficits were found that were independent of IQ. The last domain of executive

functioning, visual working memory, was measured by a delayed response alternation task for which no group deficits were found. This work validates earlier findings of a deficit in inhibitory control functions in children with hyperactivity, but perhaps more importantly, it demonstrates that behavioral inhibition is not a deficit shared by children with inattention only.

Conclusions and Limitations of Existing Literature

A number of conclusions can be drawn from the above reviewed studies. One of those is that methodological limitations (see chapter 2) make it difficult to test the theoretical predictions involved in differentiating the subtypes. The majority of studies used tests of frontal lobe functioning that, for the most part, lacked sensitivity to the specific deficit in ADHD/IA and/or failed to yield definitive conclusions about subtype similarities or differences. Data are needed on a wider variety of cognitive and attentional measures that extend beyond the domain of executive function. Goodyear and Hynd (1992) recognized that measurement issues failed the sophistication of the paradigm to investigate an anterior-posterior gradient of cognitive deficit in ADHD subtypes. They recommended the use of measures that tap discrete processes of non-frontal functions, e.g. visual-perceptual sensitivity, orientation, recognition, and association that may be more sensitive to the parameters of the investigation. This endeavor has been largely neglected though, and the anterior-posterior model of attention deficits in ADHD subtypes remains unfounded.

Another limitation of the existing research is the reliance on neuropsychological tests that assess multiple EF's. This has been cited as a methodological limitation for paradigms intended to discern core deficits in clinical populations (Pennington, et al., 1996). Because executive functioning is such a broad domain, measurement instruments are needed that isolate narrower, or single, component processes. Such instruments would be useful for specifying the pattern of EF deficits in ADHD/C and how that might vary within individuals. Increased measurement sensitivity is also needed to determine whether and which EF deficits extend to children with ADHD/IA. No doubt there is

overlapping dysfunction between members of the subtypes, since the two diagnoses represent a continuum of symptoms in the hyperactive/impulsivity domain.

Although many inconsistent findings have been presented about the core deficit of ADHD/IA, certain inferences can made about what that deficit might be. The converging evidence points to visual-spatial attention and cognitive processing speed. Studies that have found differences between the subtypes suggest that the more automatic posterior mechanisms are impaired in the inattentive group. Slower naming speed on the Stroop, RAS and RAN tasks, Trailmaking, and Coding, are consistent with the behavioral evidence of sluggish cognitive tempo in this group. Cognitive processing speed appears represent a lower-level, automatic component of attention that is not subject to executive control. This deficit, neuroanatomically, has been linked primarily to posterior brain regions, especially in the right hemisphere, and lower brain stem regions that regulate attention and arousal. Visual-perceptual processing, which is predominantly subserved by the posterior cortical regions and their extensive connections with lower subcortical regions, is a primary function of the posterior attentional system.

Alternatively, evidence indicates that the core deficit in ADHD/C is one of behavior inhibition or, to use attentional terms, the executive control of attention. This deficit appears to be of much smaller scope than the entire domain of executive functioning. However, because tests of frontal lobe functioning typically assess multiple EF's, its presence can disrupt performance on tests that do not purport to measure behavioral inhibition. Interestingly, a review of the studies comparing ADHD/C to controls on tests of EF revealed that the purer measures of inhibition, e.g., the Go No-Go and Stop tasks, most consistently demonstrated group differences and thus, were most sensitive to the deficit in this clinical group (Pennington & Ozonoff, 1996). Fronto-striatal with a focus on the orbito-frontal and ACG prefrontal regions have been identified as the substrate of the executive control of attention and linked to the dysfunction in ADHD/C (e.g., Swanson et al., 1998a).

Neurobiological Mechanisms of ADHD

Numerous theories have offered their conceptualization of the mechanisms underlying the brain-behavior relationship of ADHD symptoms, with an emphasis on ADHD/C or previously classified groups with hyperactivity. Although many of the hypotheses differ in focus, they may be characterized more by that which is common. Typically, these theories have implicated the prefrontal cortex and its role in executive function. Those that dissent have, for the most part, proposed subcortical involvement in the regulation of sustained attention and arousal functions. In relation to Posner's model of attention, the overall picture points to the anterior network of executive control and the alerting network of arousal as the source of impairment in ADHD.

Models of Prefrontal Dysfunction in ADHD/C

There is an abundance of evidence suggesting prefrontal cortex dysfunction in ADHD. Theories of prefrontal involvement in ADHD are similarly supported by the evidence that lesions to prefrontal regions can produce hyperactivity, distractibility, and impulsivity, in addition to empirical findings that children with ADHD display performance deficits on tests of executive function. The difference lies in their relative emphasis on the neural versus cognitive mechanisms of impairment and on the level at which the prefrontal cortex is involved in the neural circuitry of dysfunction. These theories do not include ADHD/IA in their framework.

Cognitive Dysfunction

Barkley's model of ADHD (1997) provides a perspective of the cognitive pathology associated with ADHD/C. He introduces the role of neural systems only to establish that the associated deficits reflect dysfunction of the frontal lobes. Based on prior neuropsychological theories of prefrontal function, Barkley has proposed that behavioral inhibition is the core deficit of ADHD and that this deficit interferes with the execution of other executive functions. Failures in behavioral inhibition prevent the necessary delay in action required for self-control and goal directed behavior. The reduction in control of intentional behavior imposed by the totality of impairment results

in a secondary problem with sustained attention. The concept of a primary intention deficit that stems from the prefrontal cortex and mimics the appearance of inattention has also been advanced by other prominent researchers (e.g., Denckla, 1996; Van der Meere & Sergeant, 1988). Problems with inhibition and the capacity to delay responding result in inappropriate or no action in response to instruction or direction. Unlike inattention, "in-intention", according to Denckla (1996), would be the failure of received instructions to elicit desired actions rather than direct failure to receive instructions.

While some models of cognitive functioning in ADHD consider the attention deficit to be an extension of behavioral inhibition, others purport that disruption of attention mechanisms extends the problems associated with disinhibition and impulsiveness (Shaywitz, et al., 1999; Swanson, et al., 1998a). Swanson et al. (1998a) characterized the core deficit of ADHD as a primary dysfunction of both the executive control and alerting components of attention, wherein behavioral inhibition would be considered an attention deficit. Swanson et al. (1998a) have suggested that since these cognitive explanations of ADHD were developed to account for the same findings of executive function deficits, their differences may lie primarily in semantics. By implicating the alerting component of attention in ADHD symptomology, the neurobiological mechanisms of ADHD must correspondingly involve the activity of subcortical brain stem regions in addition to the prefrontal cortex.

Basal Ganglia in Executive Dysfunction

Lesions in non-frontal, as well as frontal, areas of the brain can produce the symptoms manifested in ADHD. Likewise, deficient executive functioning could result from damage to brain structures connected with the prefrontal cortex, and to the prefrontal cortex itself. Converging lines of evidence support a neuroanatomical model of circuitry involving prefrontal and subcortical regions in ADHD. A particular region that networks closely with the PFC and has been implicated in ADHD is the basal ganglia. A circuit through the PFC, basal ganglia relay stations, thalamic nuclei and back to the cortex communicates with other cortical regions and is believed to be the anatomic substrate for many of the executive functions (Castellanos, 1997; Partiot et al., 1996).

Studies examining regional cerebral blood flow during cognitive task performance suggest that the right prefrontal cortex, in particular, acts to inhibit responses to salient but irrelevant events in the course of goal directed behavior that are executed by the striatum (caudate nucleus and putamen) of the basal ganglia (Casey et al. 1997; Partiot et al. 1996). Structures of the basal ganglia are implicated in the automatization of behavioral programs. Lesions to the striatum result in difficulty re-engaging attention and maintaining information on line during delayed response tasks (Partiot et al., 1996). Much additional evidence highlights the integral role of the basal ganglia and of the caudate nucleus in cognitive functioning (Berger & Posner 2000; Lou, Hendrikson, & Bruhn, 1984). Together, the frontal lobes and basal ganglia participate in frontal networks that control attention and motor intentional behavior (Seidman, et al., 1997).

Support for Dysfunction in Fronto-Striatal Networks

Frontostriatal networks appear to be the primary source of dysfunction in children who display problems with hyperactivity and attention. Recent neuroimaging studies provide support for the involvement of fronto-striatal structures in ADHD/C (Zametkin, Nordahl, King, et al, 1990; Castellanos Giedd, Eckburg, et al., 1994, Semrud-Clikeman, Filipek, Biederman et al., 1994; for review see Castellanos, 1997). The right greater than left asymmetry typical of healthy brains has been found to be decreased in the frontal areas; primarily due to smaller measurements within the right hemisphere (Castellanos, Geidd, Marsh et. al., 1996; Filipeck Semrud-Clikeman, Steingard et al., 1997; Hynd et al., 1991b). Findings of smaller volumetric measurements and asymmetry also indicate abnormalities of the basal ganglia. Both the caudate nucleus (Castellanos et al., 1996; Filipeck et al., 1997; Hynd et al., 1993; Mataro, Garcia-Sanchez, Junque, Estevez-Gonzalez, & Puhol, 1997) and the globus pallidus structures of the basal ganglia have been found to be significantly smaller in ADHD (Aylward, Reiss, Reader et al., 1996; Castellanos et al., 1996), although the studies have differed as to whether the decrease was measured on the left or the right side. Regional brain differences have also been documented in the corpus callosum of ADHD groups compared to controls. A number of studies have reported the anterior region to be smaller (Baumgardner, Singer, Denkla et

al., 1996; Giedd, Castellanos, Casey et al., 1994; Hynd et al., 1991b) and one study reported smaller measurements of the posterior region.

An fMRI study examined fronto-striatal activation in ADHD children and controls during performance on a response inhibition task with and without methylphenidate (MPH) (Vaidya, Austin, Kirkorian et al., 1998). The investigators found that without medication, striatal activation was lower in the ADHD group. Interestingly, the stimulant medication increased striatal activation in the ADHD group but decreased it in the control group. MPH increased frontal activation in both groups. These data are consistent with PET measurements of decreased frontal cerebral metabolism in prefrontal and premotor areas in children and adults with ADHD (Lou et al., 1984; Zametkin et al., 1990). The convergence of findings from fMRI studies supports the hypothesized substrate of prefrontal-basal ganglia circuitry in the executive function deficits of ADHD.

Theories of ADHD that have Implications for ADHD/IA

The most accepted and substantiated model of ADHD points to abnormalities of frontostriatal networks that result in cognitive deficits of attention, motor regulation and EF. The conceptual framework of this model, however, does not provide a suitable account for the cognitive deficits and neurobiological mechanisms of the ADHD/IA subtype. ADHD/IA symptomology is inconsistent with isolated pathology of the frontal lobes and basal ganglia and, cognitively, may not represent specific EF impairment. Although the same theory may not apply to the ADHD/C and ADHD/IA subtypes, a subset of hypotheses that have gained adequate support with regard to certain features of ADHD, have relevance for the inattentive profile of ADHD/IA. Functions of the right hemisphere, especially the parietal lobe, and the reticular formation of the brain stem offer possible substrates for the cognitive dysfunction of this often overlooked group.

Right-Hemisphere Model of Attentional Dysfunction

Another approach to characterizing the neurobiology of ADHD emphasizes the role of the right-hemisphere. Its impetus came from the similarities observed between lateralized deficits in adults with unilateral brain lesions, particularly those with

accompanying neglect, and certain deficits in children with ADHD. Failure of patients with neglect to detect, recognize, and orient to stimuli in the contralateral field has been attributed to dysfunction of attention and arousal systems (Heilman, Voeller, & Nadeau, 1991). The neglect syndrome is found more commonly with right hemisphere lesions, suggesting dominance of this hemisphere in the regulation of attention, arousal, and motor activation (Heilman et al., 1991). A right-hemisphere model of ADHD emphasizes the role of the right frontal lobe and fronto-striatal system, and the midbrain reticular formation in the pathology of the disorder. Support for right greater than left (but not exclusively right) hemisphere dysfunction in ADHD comes from structural MRI findings, also discussed above, of smaller right prefrontal cortex and regions of the basal ganglia in children with ADHD (Casey et al., 1997; Castellanos et al., 1996).

There is some evidence to suggest that reduced right hemisphere activity may characterize children with attention problems in absence of hyperactivity. Visual spatial paradigms that are thought to be sensitive to right hemisphere and especially right parietal lobe functioning are often used to assess attention. Voeller and Heliman (1988) found that ADHD children performed similarly to patients with right-hemisphere lesions, making more frequent cancellation failures on the left side of a paper and pencil administrated visual-spatial cancellation task. Interestingly, in a later report, Voeller (1991) attributed this finding to the specific constituency of the ADHD group, which contained a majority of children with attention deficit disorder without hyperactivity. Other studies that have reported similar findings of lateralized performance in ADHD using visual spatial reaction time paradigms (Carter, Krener, Chaderjian, et al., 1995; Novak, Solanto, & Abikoff, 1995; Nigg, Swanson, & Hinshaw, 1997) may have investigated only a narrow component of inattention that is represented within the symptom spread of the disorder, but perhaps more characteristic of those children with ADHD/IA. For example, Swanson, Posner, Potkin, et al. (1991) found atypical slowing in reaction time to targets in the right visual field following invalid cues and an 800ms interval, performance consistent with right parietal lobe dysfunction. They interpreted this asymmetric slowing as reflecting either an orienting deficit in response to the target

or a vigilance decrement in response to the cue (Swanson et al., 1998b). Swanson et al. (1998b) suggest that these findings may elucidate a link between certain symptoms of inattention and their neurological substrate, i.e., selective attention and the orienting network described by Posner & Raichele (1994).

Subcortical Model of Attentional Dysfunction

Theories of ADHD that emphasize the role of arousal in the regulation of attention contend that the central deficit lies in subcortical brain-stem regions. Recent support of an arousal model of ADHD comes from Mirsky and colleagues (1999) who posit that midline subcortical brain damage or dysfunction, rather than cortical damage, is responsible for problems with sustained attention. Specifically, this disturbance is thought to lie at the level of the brainstem reticular formation, which has the major responsibility for the maintenance of arousal, wakefulness, consciousness, and attention. This disturbance thus affects the activity of the corticoreticular system, disrupting the communication between the reticular and cortical regions of the brain. The reticular formation includes the locus ceruleus structure of the alerting network proposed by Posner. Although Mirsky et al. (1999) does not address subtypes of ADHD, their model may have more relevance for the inattentive subtype.

Symptoms such as daydreaming, loss of attention to detail, and failure to attend to all but novel stimuli have been ascribed to deficits in vigilance (Weinberg & Harper, 1993). These components of attention have relevance for the clinical presentation of ADHD/IA, especially the sluggish cognitive tempo exhibited by at least a subset of these children. It has been previously suggested that the cognitive deficits of children with inattention in absence of hyperactivity may stem from dysfunction of an arousal or vigilance network (Weinberg & Harper, 1993; Shaughency & Hynd, 1989). The underlying theory presumes involvement of different neurotransmitters in the subtypes, with dopamine (DA) dominance in ADHD/C and norepinephrine (NE) in the selective attention processing of ADHD/IA. There is substantial evidence that DA is related to anterior and motor processing, whereas, NE is involved to a greater extent in posterior or sensory processing. Along with arousal deficits of the brainstem, the differential attention

hypothesis assumes that dysregulation of the NE system affects posterior (parietal and temporal) cortical regions in ADHD/IA, in contrast to the DA/anterior action in ADHD/C (Lorys et al., 1990). The right parietal is also thought to have regulatory involvement with arousal functions via reciprocal connections with the reticular activating system (Weinberg & Harper, 1993). Using Posner's paradigm, a related hypothesis would predict that ADHD/IA is an attentional disorder of the alerting and orienting networks that are centrally anchored in the locus coeruleus of the reticular formation and the right parietal lobe. In contrast, the deficits of ADHD/C would reside primarily in the executive control network of the frontal lobes and basal ganglia.

Future Directions

In order to advance a neurocognitive model of ADHD in the subtypes, the scope of clinical and etiological heterogeneity must be considered at the forefront of any investigation. The repeated use of the two diagnostically classified subtypes to explore all areas of interest is clearly insufficient for generating testable hypothesis about the discrete deficits that may characterize certain subroups. Inconclusive findings reported across the neuropsychological literature are widely being recognized as support for heterogeneity that eludes subtype classification rather than lack of true differences between inattentive only and combined inattentive and hyperactive/impulsive children with ADHD (Seidman, et al., 1997). Following suit, Swanson et al. (1998b) offer predictions about the alignment of clinical symptoms of ADHD with cognitive processes and neural networks of attention (see Appendix C). They suggest that multiple biological bases of ADHD are reflected in various clusters of DSM-IV inattention and hyperactivity/impulsivity symptoms. By applying Posner's model of attention to the heterogeneous disorder, specific predictions can be made about the underlying etiology. This novel approach to ADHD research has the potential to address existing discrepancies about the nature of the disorder and its subtypes. While awaiting the exciting results from the various brain imaging, fMRI, and EEG techniques recruited for Swanson et al.'s investigation, the current study will apply Posner's model to its plight. Predictions about the performance of subgroups of children with ADHD on a cognitive

task of attention are hoped to expand the scope of research on the relatively unattended ADHD/IA subtype, and introduce the almost forgotten SCT variable into consideration of associated neurocognitive impairment.

Chapter 5: Rationale and Hypotheses

Statement of the Problem

For the impressive history of research on children with ADHD, very little is known about the cognitive deficits associated with the heterogeneous symptom domains. Certain subgroups have clustered from within the behavioral profile of the disorder, resulting in the diagnostic separation of ADHD/C and ADHD/IA subtypes. Many researchers have suggested, however, that the distinction between these subtypes lies not only in the degree or absence of hyperactivity, but in the nature of the attention deficit.

If a second factor of attention can be identified from within the behavioral profiles of ADHD, it is perhaps the children who represent this subgroup that have a distinct pattern of cognitive deficit. The current diagnostic nosology for ADHD, which recognizes only a single domain of attention, may not specify the criteria that would allow for subtype differentiation on neurocognitive tests, particularly those purported to measure attention. Since an SCT factor of attention has emerged from symptom item analyses when hyperactivity/impulsivity items are excluded, its presence may be the better indicator of a truly distinct inattentive group of children than inattention items alone (McBurnett, Pfiffner, & Frick, 2001).

Another consideration for the proposed study is that methodological issues in neuropsychological testing may have contaminated previously reached conclusions about the validity of the subtypes. Recent efforts to identify the neurocognitive correlates of the subtypes have relied almost exclusively on tests of frontal lobe functions that have been generally successful at detecting EF deficit in ADHD/C. Emerging evidence suggests that the ADHD/IA subtype does not share this same EF deficit. With the limited scope and specificity of available testing instruments, however little has been revealed about the specific attention process deficits that distinguish this group. A conceptually driven paradigm is needed that extends assessment beyond the realm of EF and offers predictions about the mechanisms of attention deficit in ADHD/IA.

The current study is intended to investigate the cognitive mechanisms underlying inattention in ADHD subgroups. The anterior, posterior, and alerting networks of attention proposed by Posner provide the basis for a multidimensional model of attention in ADHD. Given the heterogeneous nature of impairment, and the apparent differences between the ADHD/IA and ADHD/C subtypes, predictions can be made about differential group performance on a task that isolates cognitive processes associated with three distinct neural networks of attention. Evidence from factor analytic studies that attention is not a single construct in ADHD suggests that the presence of SCT in children with attentional impairment may denote a homogenous subgroup of inattentive children who show a different dysfunction than those with inattention and hyperactivity/impulsivity. From a theoretical standpoint, this profile may represent the most appropriate group for comparison, or contrast, with the ADHD/C subtype on neurocognitive measures. Thus, a secondary aim of this study is to delineate experimental groups based on the coherence of inattention, SCT, and hyperactivity/impulsivity symptoms, rather than using DSM-IV ADHD/IA and ADHD/C groups that are specified by a six item cut point on the continuous hyperactivity/impulsivity dimension.

Hypotheses

The driving prediction of this study was that the attention deficit in subgroups of children with ADHD could be differentiated by a test designed to isolate specific cognitive processes associated with three anatomically distinct networks of attention. This basis for this hypothesis was the idea that ADHD/C and ADHD/IA children do not share the same problem with inattention. Hypotheses for group performance on the three attention networks of the Attention Networks Test (ANT) were as follows:

1. ADHD subgroups were predicted to show different patterns of performance on the ANT as measured by alerting, conflict, and orienting effects.

2. It was hypothesized that the ADHD/IA group, particularly ADHD/IA with SCT, would show a greater Alerting effect than ADHD/C and Control groups.
3. The ADHD/C group was expected to show a greater Conflict effect than other groups.
4. Although it was unclear whether orienting would distinguish attention deficits of the ADHD groups, a prediction was made that inattentive subgroup(s) of ADHD would perform more poorly on this measure than the ADHD/C and Control groups.

We proposed that a subgroup of ADHD/IA children with a specific "sluggish cognitive tempo" style of inattention could be identified by behavioral ratings. Hypotheses about the behavioral measures and their relevance for classifying ADHD subgroups were as follows:

1. Non-experimental SCT items and experimental SCT items would distinguish between ADHD/IA and ADHD/C groups. A subgroup of ADHD/IA children characterized by SCT was expected to emerge from the behavioral ratings.
2. It was predicted that a subgroup of children with ADHD/IA plus SCT would present the greatest contrast to the ADHD/C group on the ANT, due to a unique deficit of attention characterized by SCT.

Chapter 6: Methods

Participants

Participants were 67 children between the ages of 7 and 13, including 16 who met criteria for ADHD/ Combined Type (ADHD/C), 27 who met criteria for ADHD/ Predominantly Inattentive Type (ADHD/IA), and 24 non-diagnosed comparison controls. The participants in this study were part of a larger investigation of neurocognitive functioning in the ADHD/C and ADHD/IA subtypes supported by a grant from the Hogg Foundation. Children were excluded from participation in the study if they had sustained a head injury, showed evidence of other neurological disorder such as epilepsy, had history of psychosis or current psychiatric disturbance, or had an estimated full-scale IQ of less than 80. Children taking psychoactive medications, other than stimulants prescribed to treat ADHD symptoms, were also excluded from participation in the study.

These children were recruited from patients who had been evaluated for attention, academic, and behavioral problems at the Austin Neurological Clinic. Children were invited to participate in the study if the available parent and teacher data were consistent with a diagnosis of ADHD. Parent and teacher ratings on the DSM-IV diagnostic checklist were used to classify participants. Thirty-six of these children with ADHD (10 ADHD/C and 24 ADHD/IA) met DSM-IV criteria based on both parent and teacher ratings. In order to maximize subtype differentiation, children classified as IA were required to have 4 or fewer HI symptoms with one exception[*]. This cut-off is supported by analyses from (Lahey et al., 1994) showing that 5 HI symptoms best discriminate classification of impaired versus non-impaired cases in this domain and maximizes agreement with clinician judgment. An additional 9 ADHD children (6 C and 3 IA) were included who met criteria by one rater and missed criteria by the other rater by 1 symptom. Thus, all ADHD children would have met criteria by the less stringent algorithm used in the MTA (MTA Cooperative Group, 1999), in which a symptom was counted as "present" if it were endorsed by either the parent or teacher.

[*] One child in the ADHD/IA group had 5 HI symptoms on teacher ratings.

Participants for the control group who did not meet diagnostic criteria for ADHD or a Learning Disability were recruited primarily from responses to a solicitation letter for the larger study given to and distributed by parents of the clinic-referred children. These children were required to have been rated by both parent and teacher, (or parent only in the case of 4 children whose teacher forms were not returned), as having fewer than 4 symptoms of IA and HI. Nineteen children met these criteria and were included in the control group. Six additional control children were recruited from participants of another research study at the University of Texas to complete the current study. These children could not have been diagnosed with ADHD or a Learning Disability and were required to have fewer than 4 symptoms of either IA or HI based on parent ratings. Teacher ratings are not available for these children.

Comorbidity

Participants were experimentally classified as having a learning disability (LD) if they displayed below average achievement (standardized score of ≤ 85) and a discrepancy of greater than one standard deviation, i.e., > 15 points, between estimated Full Scale IQ on the Wechsler Intelligence Scale for Children – III (WISC-III; 1991) and the Wide Range Achievement Test – III (WRAT-III; 1993) Reading or Arithmetic subtests. LD was identified in 1 of the ADHD/C participants (i.e., 1 Reading LD) and 1 of the ADHD/IA participants (i.e., 1 Math LD). To consider the effects of Learning Disabilities on task performance, analyses were rerun without these children. Excluding these children resulted in the same pattern of findings on all dependent variables, thus they were included in final analyses.

Symptom ratings on the DSM-IV rating scale were also used to establish comorbid ODD (4 or more symptoms endorsed by either parent or teacher). Nine (56%) of the ADHD/C, 5 (19%) of the ADHD/IA, and 1 (4%) of the Control children met ODD diagnostic criteria. Thus, as found in previous research on the ADHD subtypes (see Carlson & Mann, 2000) the ADHD/C group had significantly higher rates of ODD. The rates of ODD found for the ADHD/C group are consistent with other studies, which

report comorbid ODD/CD rates between 42.7% and 93% (Jensen, Martin, & Cantwell, 1997).

Demographic characteristics

Demographic and descriptive characteristics of the sample are summarized in Table 1. ANOVA's and Chi square analyses were used to compare groups on demographic and descriptive variables. Groups did not differ on age [$F(2, 64) = .081$, $p = 0.92$]. Groups showed a trend to differ on sex [$X^2 = 5.81$, $p = .055$]. Pairwise comparisons revealed that the ADHD/C group had significantly more boys than the Control group [$X^2 = 4.86$, $p = .027$] and showed a trend to have more boys than the ADHD/IA group [$X^2 = 2.94$, $p = .087$]. Groups showed a trend to differ on ethnicity [$X^2 = 4.64$, $p = .098$]. Pairwise comparisons revealed a trend for the Control group to differ in ethnic composition from the ADHD/C group [$X^2 = 3.32$, $p = .069$]. The other group comparisons for ethnicity were not significant. The groups also showed a trend to differ on IQ [$F(2, 58) = 3.06$, $p = .054$]. Post hoc Tukey comparisons revealed that the Control group showed a trend to have higher IQ than the ADHD/IA group ($p = .051$). Group differences were also found for achievement variables. Groups showed a trend to differ on WRAT math [$F(2, 56) = 3.01$, $p = .057$]. Post hoc comparisons showed a trend for higher math achievement in the Control group than the ADHD/IA group ($p = .056$). Groups differed significantly on WRAT reading [$F(2, 56) = 8.19$, $p = .001$)]. Post hoc comparisons revealed that the two ADHD groups had significantly lower reading scores than controls ($p < .01$) but that the ADHD groups did not differ from each other.

Procedure

Testing sessions took place at the Austin Neurological Clinic and lasted approximately three hours. Eighty-eight percent of ADHD/C (14/16) and 56% of ADHD/IA (15/27) children were being treated with stimulant medication. All participants taking stimulant medication followed an 18-hour or greater washout period prior to participation. At the beginning of the session, parents signed consent forms and children

signed assent forms. Parents then filled out the diagnostic, descriptive, and experimental forms included in the study.

Participants completed several experimental neuropsychological measures developed for research with ADHD groups, including the Attention Networks Task (ANT), during the study session. The examiner stayed in the room while the child performed the ANT. To help reduce the effects of mental fatigue, the practice and test blocks of the ANT were separated by short, predominantly motor tasks that were included in the larger study, such as: throwing a ball or bean bag, cutting or tracing designs, balancing on boards, and scanning images of the child's hands. Towards the end of the session, children in the control group and ADHD children who had been evaluated at Austin Neurological Clinic more than a year prior to the study were administered select intellectual, achievement, attention, and memory measures from the standard neuropsychological battery that clinic-referred children had received in full as part of the evaluation through the Austin Neurological Clinic. At the end of the testing session, a research assistant gave the parent a packet of diagnostic and experimental forms to be delivered to and completed by the child's teacher. Families received $40 for their participation in the study. Teachers who participated returned the forms by mail and received payment of $10.

Measures

Descriptive Measures

Three subtests of the Weschler Intelligence Scale for Children- Third Edition (WISC-III; Wechsler, 1991) were administered. Block Design and Vocabulary were used to obtain an estimate of intellectual functioning (Sattler, 1992). Rather than use the FSIQ for ADHD children who had received the WISC-III in full during their clinic evaluation, IQ's for all children were prorated from these two subtests. Data for Digit Span were also collected but not included as a variable in this study.

The Wide Range Achievement Test-Revision 3 (WRAT-3; Jastak & Wilkinson, 1993) reading and arithmetic subtests were administered to assess achievement levels.

These measures require reading single words out loud and completing a timed set of arithmetic problems.

The DSM-IV diagnostic checklist assesses symptoms of inattention, hyperactivity, and oppositional behavior based on DSM-IV criteria for ADHD and Oppositional Defiant Disorder, ODD, diagnoses. Level of impairment for each symptom is rated on a 4-point scale: 0 = not at all, 1 = just a little, 2 = pretty much, and 3 = very much. A symptom was considered "present" if rated as "pretty much" or "very much."

Experimental Measures

The Rating of Behavioral Style

The Rating of Behavioral Style (see appendix C) developed for the larger study to be rated by parent and teacher informants, was used to assess frequency of failures in perception, attention, memory, sleep, and motor functions. This questionnaire consists of items adapted from Broadbent's Cognitive Failures Questionnaire (1982) and new items thought to assess the relevant domains, including sluggish cognitive tempo (SCT). Three "SCT" items ("does the child daydream or get lost in his/her thoughts?", "is the child apathetic or unmotivated?", and "is the child underactive, slow moving, or lacks energy?") were added to the Rating of Behavioral Style but only after the start of data collection when 24 participants had already completed the study. These items are from the original Achenbach teacher and parent rating forms, the Teacher Report Form and the Child Behavior Checklist (Achenbach, 1991). Although the teacher Achenbach form contains all three of these items, the parent version only contains two; daydreams and underactive. For participants who received the earlier version of the questionnaire, or had missing teacher data due to non-return of the teacher questionnaire, who had completed parent and/or teacher Achenbach forms as part of their clinical evaluation at the Austin Neurological Clinic, data for these items were obtained from the original Achenbach forms. Items obtained from the Achenbach Teacher Report Form and Child Behavior Checklist were converted from their original three point scale (0, 1, and 2) to matching descriptors of the five point scale (1, 3, and 5) on the Rating of Behavioral Style. The

final parent and teacher version of the Rating of Behavioral Style consists of 34 items rated on a 5-point scale. Two of these items, assessing quality of sleep, are marked "Parent Only." All but two items are rated as: 1 = not at all, 2 = just a little, 3 = somewhat, 4 = quite a bit, 5 = very much. The two items that read: "Relative to his/her same-aged peers, the child's handwriting/penmanship is," and "Relative to his/her same-aged peers, the child's sports/athletic skills are," are rated as: 1 = much poorer, 2 = a little poorer, 3 = about the same, 4 = a little better, 5 = much better.

Attention Networks Test

The Attention Network Test (ANT), developed by Jin Fan at the Sackler Institute (2000), is an adaptation of Posner's cuing paradigm for spatial orientation (Posner, 1980) and the Eriksen flanker task (Eriksen & Eriksen, 1974). The task measures alerting, orienting and executive attention, the cognitive processes associated with Posner's three networks of attention. The task is a computer-based reaction time task that requires subjects to respond to the target-stimulus, a fish, on a screen. Children are instructed to focus on the central fixation point and respond quickly to the target fish that appears in the center of the screen. A practice of 24 trials followed by three 5 minute test sessions of 48 trials each was administered to each participant.

The task presented a target fish, facing either to the right or left, in the vertical center of the screen. Consistent with the direction of the fish, the child was to respond by pressing the right or left button of a mouse controller with the corresponding thumb. The target fish appeared either alone, or with four additional fish, two flanking each side, so that five fish stimuli were presented in a horizontal row. In congruent trials, the flanking fish all pointed in the same direction as the target. In incongruent trials, the flanking fish pointed in the opposite direction as the target. The child was to ignore the flanking fish, and respond only to the target fish in the center.

Trial intervals consisted of a fixation period, cue or no cue, fixation period, target (i.e., a fish, either alone or flanked) and a final fixation period to finish out the 4500ms total trial duration. The fixation stimulus was a plus sign that remains at the center of the screen throughout the block of trials. The first fixation period was variable in duration,

from 400-1600ms, preceding the presentation of a spatial cue, and fixed at 200ms preceding the target in no cue trials. For the cued trials, either one or two asterisks were presented for 200ms. In the single condition, the cue appeared at the center fixation point, above this point, or below the fixation point. When two asterisks appeared simultaneously, they appeared above and below the center fixation point. A 400ms fixation period marked the cue-target SOA. Target fish and flankers were presented in one of the two vertically centered locations above or below the fixation point until a response was made or for a maximum 2000ms time out period. Following the fish disappearance, a variable post-target fixation period (3900ms minus the first fixation time and subject response time) rode out the end of the trial. After the total 4500ms trial duration, the interval for the next trial began.

Alerting. The presence of cues is presumed to alert the subject to the upcoming target. For the no-cue trials, only a 200ms fixation period preceded the target, providing no warning for the upcoming event. The double cue trials presented two warning cues corresponding to the two possible target positions, up or down, providing warning of upcoming target appearance. The alerting effect was calculated by subtracting the mean RT of double cue trials from the mean RT of no cue trials. Neither of these conditions provided information about whether the target stimulus would appear above or below the fixation point.

Orienting. This task component is established by presenting stimuli at a location outside the fixation point. Although center and spatial cues both serve as a form of alerting cue, only the spatial cue provided predictive information that allowed subjects to shift attention in space. The spatial cue (above or below the fixation) was always valid and thus facilitated orienting to the appropriate location. Under all other cue/no cue conditions, target location was uncertain. To calculate the orienting effect, mean RT of the single spatial cue trials was subtracted from the mean RT of the center cue, or control, trials.

Conflict. Conflict is a measure of the response conflict introduced by incongruent trials. Congruent, incongruent, and no-flanked neutral trials occurred with a one third

probability. The interference effect was calculated by subtracting the mean RT of congruent trials from the mean RT of incongruent trials.

Chapter 7: Results

SCT and Behavioral Style Questionnaire

Missing data

Data were missing for several reasons for items on the Rating of Behavioral Style questionnaire. Reasons for missing data include the non-return of teacher forms and the return of incomplete teacher forms, i.e., select items left unrated, presumably because the behaviors had not been observed in the classroom. As discussed in Methods, data were also missing for the three original SCT items, daydreams, apathetic, and underactive, that were added to the Rating of Behavioral Style after the start of data collection. In some cases, data for these items could be obtained for ADHD children from the original Achenbach parent and teacher rating forms that were available as part of their clinical evaluation at the Austin Neurological Clinic. This was not possible for the apathetic item for parents because that item was not included on the original Achenbach parent form. Lastly, teacher data were not collected for the six controls who did not participate in the larger study. Corrected group N's and mean scores for candidate SCT items are included in table 2.

Determination of SCT Composite

Because SCT has previously been researched as a teacher rated variable and has a stronger presence in the teacher ratings in this sample, we used teacher data to calculate a final SCT scale. However, both parent and teacher data were considered in the analyses and are discussed in this section. The construct was examined with four items that were chosen based on previous literature suggesting that these descriptors characterized the attentional style of children with ADHD; daydreams, apathetic, underactive, and the one item retained in DSM-IV, forgetful (Achenbach, 1991). As with the three Achenbach items, the DSM-IV item was recoded from its original scale to matching descriptors of the five point scale (1, 2, 4, and 5) of the Rating of Behavioral Style. Using the method described in Carlson and Mann (2002), mean scores for the ADHD/IA and ADHD/C groups for each of these items were compared separately for parent and teacher ratings to

determine which items differentiated the groups. Group means differed significantly ($p = .003$) only on the underactive item rated by teachers. For parent ratings on this item, group means were in the same direction, although not significantly different ($p = .132$). The next most discriminating teacher item (again not significant, $p = .332$) was the apathetic item. For all other parent and teacher SCT items on which ADHD/IA scored higher than ADHD/C, P values for the group comparisons were greater than .387. Unexpectedly, group means were higher for ADHD/C than ADHD/IA, for the teacher and parent rated forgetful item, and for the teacher rated daydreams item, although these differences were not significant.

The two teacher rated items that best differentiated the groups (underactive, and apathetic) were combined to form an SCT score (0 – 10); these two-items showed a correlation of .720 ($p<.001$) in the entire sample. Because of missing data, the SCT score was computed for 12 ADHD/C, 26 ADHD/IA and 10 Control children. These items correlated more strongly with each other than with total inattentive diagnostic symptoms ($r = .587$, $p = .000$). The SCT score did not correlate significantly with total hyperactive diagnostic symptoms ($r = -.178$, $p = .227$). High scores on the SCT scale (8, 9, or 10) were considered to indicate the presence of SCT. Using this cutoff, SCT was identified in 11 of the 26 ADHD/IA children who had data for this variable; these children were classified as high SCT and the other 15 as low SCT. There were no high scorers in the other groups, although, as noted above, SCT data were missing for many ADHD/C and Control participants.

Behavioral Style Questionnaire

The 29 experimental items on the teacher Rating of Behavioral Style were examined in relation to the SCT. As a preliminary analysis, means for each of the items were compared for the ADHD/IA and ADHD/C groups. Only one item significantly differentiated the groups and four items showed trends to differentiate the groups, all with higher scores for ADHD/C suggesting that the descriptors characterize some aspect of the behavioral style of this group. These items were, “does the child get unduly irritable about minor matters?” ($p < .003$), and “does the child say something and realize

afterward that it was inappropriate?", "does the child have trouble making up his/her mind", "does the child forget people's names?", and "is the child generally messy" (p's < .10). No items were significantly more prominent in the ADHD/IA relative to the ADHD/C group. Results from this exploratory analysis suggested that items on the Rating of Behavioral Style do not appear to be helpful in characterizing the attentional style of ADHD/IA.

As a next step in assessing the potential utility of the scale in characterizing SCT, items from the teacher ratings were correlated with three other teacher variables for the entire sample: The two-item SCT scale, total inattentive symptoms, and total hyperactive/impulsive diagnostic symptoms. Items that correlated with total inattentive symptoms and with the two-item SCT score, but more strongly with the SCT score, and that did not correlate positively with total hyperactive/impulsive symptoms were selected for further analysis. The only two items that met this criteria: Item 5. "does the child forget whether he/she has turned off a light or locked the door", and Item 34. "Relative to his/her same-aged peers how are the child's sports/athletic skills?" did not distinguish between the diagnostic groups either in simple logistic regression (p's $\geq$ .214) or entered jointly into multiple logistic regression (p = .292) analyses. Item and symptom domain correlations are presented in Table 3.

Based on the above results, only the original SCT distinction from previously researched items was considered for group classification. Analyses for the ANT dependent variables were calculated for both the original three groups: ADHD/C, ADHD/IA, and Controls, and again for four groups: ADHD/C, ADHD/IA no SCT (n = 15), ADHD/IA with SCT (n = 11), and Controls. Analyses were also replicated for a boys' only sample for each of the three and four group solutions.

Attention Networks Test

Missing data and outliers for the ANT

Not all participants who qualified for the larger investigation of neurocognitive functioning in ADHD subtypes completed the Attention Networks Task. Reasons for

missing data include: availability of the task at the time of subject participation, technical failure, and incomplete data in the case that a participant did not complete the task, thus, excluding 9 children; 1 ADHD/C, 2 ADHD/IA, and 6 Controls who participated in the larger study.

Two additional participants, 1 ADHD/C and 1 Control, completed the task but had very low accuracy, < 80%. When overall accuracy is low, the probability of chance responding for any given trial is high. Correct responses for cases with low mean accuracy are less likely to reflect the cognitive processes involved in accurate responding. Thus, these participants were not included in the task or demographic/descriptive variable analyses.

Outlier analyses were conducted for each of the network scores. Histogram plots of the distribution of data for orienting, alerting, and conflict scores were examined. Extreme values, infrequent and delineated by a break in the distribution of data were considered to be outliers. Three outlier values were identified for the network scores, one for alerting (1 ADHD/C) and two for orienting (1 ADHD/C and 1 ADHD/IA); these 3 data points were excluded from analyses. The alerting outlier was 2.56 standard deviations and the orienting outliers were 3.10 and 2.59 standard deviations away from their respective group means. No outliers for control cases were identified. Corrected N's are reported in tables for the performance variables.

Independence of attention networks

Correlations were computed to examine the independence of the attention networks. Tables 4, 5, 6, and 7 show the relationships found among the attention networks for the total sample and for each of the three groups. For the total, Control and ADHD/IA groups, no significant correlations were found among the performance indexes of network efficiency: alerting, orienting, and conflict. For the ADHD/C group, alerting and conflict correlated significantly, $r = .584$ ($p = .022$).

Calculation of attention scores

Alerting, Orienting, and Conflict network scores were the dependent variables of interest. These values were calculated from the reaction time data of correct trials. Only

correct trials were examined in the interest of investigating those processes involved in making an accurate response. Medians were obtained for each of the 12 test conditions: (4 cue levels by 3 congruency levels, i.e., central, no, double, and spatial by neutral, congruent, and incongruent) to help avoid the influence of within-subject outliers. The alerting effect was calculated by subtracting the mean RT of the double cue trials from the mean RT of the no cue trials. An ANOVA for cue condition: (double cue and no cue) showed a main effect of cue [$F(1, 66) = 111.14$, $p = .000$] indicating overall faster response time in the presence of a cue. The alerting effect had a mean of 77.66 msec with a standard deviation of 58.61 msec. The orienting effect was calculated by subtracting the mean RT of the spatial cue trials from the mean RT of the center cue trials. An ANOVA for spatial cue condition: (spatial and center) showed a main effect of cue [$F(1, 66) = 35.11$, $p = .000$]. The mean of the orienting effect was 44.98 msec with a standard deviation of 45.86 msec. Overall response time is faster in the spatial cue condition, which provides information about the location of the upcoming target, than in the center cue condition. The conflict effect was calculated by subtracting the mean RT of the incongruent trials from the mean RT of the congruent trials. Congruent and incongruent conditions were examined with an ANOVA. As expected, there was a main effect of condition [$F(1, 66) = 135.65$, $p = .000$] indicating that performance is faster in congruent than in incongruent conditions. The conflict effect had a mean of 63.15 msec with a standard deviation of 44.38 msec. Thus, Alerting = no cue – double cue, Orienting = center cue – spatial cue, and Conflict = incongruent – congruent.

Dependent variables also included global measures of task performance. The first of these, task reaction time, was obtained by taking the mean of the median reaction times for each of the 12 test conditions, computed for only correct trials. The second, accuracy rate, was calculated as the percent of correct trials. Correlations among inattention, hyperactive/impulsive, and SCT symptom scores and the five ANT dependent variables are reported for the total sample, Control, ADHD/C, and ADHD/IA groups in tables 4, 5, 6, and 7 respectively. Not surprisingly, significant negative correlations were found between mean RT and accuracy for all group comparisons.

Different patterns of relationships were found among several of the variables between the different groups. For the total sample and for ADHD/IA, alerting was significantly negatively correlated with the HI symptom domain and showed no relationship to IA symptoms. The reverse pattern was found for ADHD/C and Control groups with alerting showing stronger, although not significant, correlations with IA symptoms and much weaker correlations with HI symptoms. For the ANT task variables, SCT showed a significant correlation only with conflict in the Control group. Other correlation values are included in the tables.

Consideration of covariates and moderators

To consider the effects of gender and IQ, which differentiated the groups, these variables were correlated with the 5 task DV's; orienting, alerting, conflict, accuracy, and overall reaction time. IQ did not correlate with any of the DV's and thus was not entered as a covariate in the task analyses. Gender showed a trend to correlate with conflict ($p = .068$). Evaluating possible gender effects is important because of the uncertainty of the similarity of deficits in boys and girls with ADHD. Because of the low n of ADHD/C girls, precluding the separate analysis of girls only, we sought to assess the extent by which the findings characterized ADHD boys. Thus, analyses were conducted for the complete sample of boys and girls, and again for the sample of boys only.

ADHD/C, ADHD/IA, and Control group performance on the ANT

Group performance on the dependent measures was examined with a 3 (group: ADHD/C, ADHD/IA, Control) x 3 (cognitive process: orienting, alerting, conflict) repeated measures multivariate analysis of variance (MANOVA). Effect sizes were calculated between groups for all ANT dependent measures to help assess the clinical significance of results. D values are reported as indexes of effect size. Effects of .2 or greater, .5 or greater, and .8 or greater were considered small, medium, and large, respectively (Cohen, 1992). Performance scores for ADHD/C, ADHD/IA, and Control groups for the entire sample and for boys only are reported in table 8, and effect sizes for the group comparisons are reported in Table 9.

Repeated measures MANOVA results revealed a main effect for cognitive process [F (2) = 3.54, p = .032] and an interaction between cognitive process and group [F (4) = 2.73, p = .032], with the groups showing different patterns of performance in response to demands placed by the three attention networks.

Univariate ANOVAs comparing the three groups were conducted separately for each of the attention networks. The main effects for orienting and conflict were both nonsignificant. In contrast, a main effect was found for alerting [F (2, 63) = 5.03, p = .009]. Post hoc Tukey comparisons revealed that the ADHD/IA group showed a large and significantly greater alerting effect than the ADHD/C group (p = .009) indicating that the ADHD/IA group benefited more from cuing than did the ADHD/C group. The other between group comparisons were not significant.

An ANOVA for accuracy revealed a main effect for group [F (2, 64) = 9.53, p = .000]. Post hoc Tukey comparisons showed that the Control group showed a large effect to be more accurate than the ADHD/C group (p = .000) and a medium effect to be more accurate than the ADHD/IA group (p = .039). The ADHD/IA group showed a medium effect and nonsignificant trend to be more accurate than the ADHD/C group (p = .079). Groups also differed significantly on reaction time [F (2, 64) = 8.60, p = .000]. Post hoc comparisons revealed that the control group was faster than the ADHD/C group (p = .003) and the ADHD/IA group (p = .001); both were large effects. The ADHD groups did not differ significantly from each other on reaction time.

Boys only: ANT analyses resulted in a similar pattern of findings for the boys' only sample. The repeated measures MANOVA for alerting, orienting, and conflict by group revealed a trend for process [F (2) = 2.51, p = .088]. The interaction between group and process was not significant [F (4) = 1.93, p = .114]. The ANOVAs for orienting [F (2, 38) = 0.99, p = .383] and conflict [F (2, 40) = 0.02, p = .979] did not yield significant group differences. Alerting showed a trend to differentiate the groups [F (2, 40) = 3.08, p = .057] and post hoc Tukey comparisons revealed that the ADHD/IA group again showed a large and significantly greater alerting effect than the ADHD/C group (p = .046). The other group comparisons for alerting were not significant. Groups differed

on accuracy [F (2, 40) = 5.82, p = .006]. Post hoc comparisons showed greater accuracy for the control group than the ADHD/C group (large effect; p = .004). Though nonsignificant, controls again showed a medium effect for greater accuracy than the ADHD/IA group. The boy groups showed a trend to differ on mean reaction time [F (2, 40) = 2.61, p = .086]. Post hoc comparisons showed a trend for the control group to be faster than the ADHD/C group (large effect; p = .092). The control group showed a medium (though nonsignificant) effect to be faster than the ADHD/IA group.

ADHD/C, ADHD/IA no SCT, ADHD/IA with SCT and Control performance on the ANT

Group performance on the dependent measures was examined with a 4 (group: ADHD/C, ADHD/IA no SCT, ADHD/IA with SCT, Control) x 3 (cognitive process: orienting, alerting, conflict) repeated measures MANOVA. Performance scores for the four groups for the entire sample and for boys only are reported in table 10. Selected effect sizes for the four group comparisons are reported in Table 11.

Repeated measures MANOVA results revealed a main effect for cognitive process [F (2) = 5.47, p = .005] but no significant interaction between cognitive process and group [F (6) = 1.83, p = .100].

Univariate ANOVAs for orienting [F (3, 60) = 0.80, p = .501] and conflict [F (3, 62) = 0.13, p = .941] did not yield significant group differences. Groups differed significantly on alerting [F (3, 61) = 3.37, p = .024] with post hoc Tukey comparisons revealing that the ADHD/IA with SCT group showed a large and significantly greater alerting effect than the ADHD/C group (p = .035) and the ADHD/IA no SCT group showed a trend; large effect size, to have a greater alerting effect than the ADHD/C group (p = .075). A main effect for group was found for accuracy [F (3, 62) = 6.37, p = .001]. Post hoc comparisons revealed that the control group showed a large and significant effect to be more accurate than the ADHD/C group (.001). Other pairwise comparisons for accuracy were not significant. A main effect for group was also found for mean reaction time [F (3, 62) = 6.03, p = .001] with post hoc comparisons showing that the Control group showed large effects to be faster than the ADHD/C group (p = .007) and

the ADHD/IA with SCT group (p = .005), and showed a trend; also large effect size, to be faster than the ADHD/IA no SCT group (p = .057).

Boys only: The boys only analyses for the SCT groups are included although group n's are small (ADHD/C = 14, ADHD/IA no SCT = 8, ADHD/IA with SCT = 7, Control = 12). The 4 x 3 repeated measures ANOVA revealed a main effect for process [F (2, 35) = 3.19, p = .047] but no interaction between group and process [F (6, 32) = 1.59, p = .161]. ANOVA's for orienting [F (3, 36) = 2.17, p = .109], conflict [F (3, 38) = 0.23, p = .994], and alerting [F (3, 38) = 1.96, p = .137], comparing group performance were not significant. Planned post hoc comparisons did not show significant group differences. However, both ADHD/IA groups still demonstrated large effects for greater alerting than the ADHD/C group. The ANOVA for accuracy showed a main effect for group [F (3, 38) = 3.80, p = .018]. Post hoc Tukey comparisons showed that the Control group was significantly more accurate than the ADHD/C group; large effect size (p = .010). Groups did not differ significantly on mean reaction time [F (3, 38) = 2.00, p = .131] although a large effect was demonstrated for the Control versus ADHD/IA with SCT comparison.

Chapter 8: Discussion

Overview of the Results

The purpose of this study was to examine the performance of ADHD subtypes and comparison controls on a cognitive task that assesses the efficiency of three neuroanatomically distinct attention networks. It was hypothesized that the ADHD subtypes would show different patterns of performance on the Attention Networks Task (ANT) reflecting unique underlying attention deficits characteristic of this diagnostic distinction. Results showing a specific performance effect of alerting sensitive to ADHD/C and ADHD/IA group differences supported this hypothesis. This finding is among the first to demonstrate a cognitive/attentional distinction between the subtypes on a neurocognitive measure.

The following sections are organized to present the findings, address specific hypotheses, and to discuss study limitations and directions for future research. First, overall results for the ANT and the three attention networks are discussed. The next sections provide a synthesis of the pattern of findings for the three primary groups; DSM-IV ADHD/C and ADHD/IA and Controls and the four secondary groups; ADHD/C, ADHD/IA with SCT, ADHD/IA no SCT, and Controls on the ANT. The use of Sluggish cognitive tempo (SCT) as a classification variable and its presence in this sample is considered. Additional sections address limitations and caveats of the study.

ANT

Since overlap among cognitive measures is often expected, particularly with neuropsychological measures that place shared demands on various cognitive and executive abilities, e.g., information processing speed, and working memory, we sought to examine the independence of attention networks on the ANT. Our findings of different relationships among the network scores for the different groups suggest that disorder status and developmental factors influence the degree of independence and interaction among networks. Data suggest that networks function relatively

independently (no significant correlations among these scores) in Control and ADHD/IA children; this was also true for the total sample. However, in ADHD/C, alerting correlated significantly with conflict, the measure of executive functioning. The ANT placed different demands on the attention networks in ADHD/C children than in our other groups. As discussed by Fan and colleagues, preliminary research into the interaction of attention networks on the ANT in adults has not generalized to child populations (Fan, McCandliss, Sommer, Raz, & Posner, 2002). Conflict, orienting, and alerting measures appear to place demands on distinct cognitive processes of attention in comparison controls, who represent a population of children with normal neurological development. Children with neurological disorders may (ADHD/IA) or may not (ADHD/C) show this same pattern.

The efficiency of each of the attention networks was assessed by the mean reaction times on the two task conditions that when subtracted provide an index of the associated cognitive process. Results show that alerting, orienting, and conflict effects were successfully produced by the changing cognitive demands of the task and were robust across the entire sample. As demonstrated in previous studies, response time was faster in the double cue than in the no cue conditions, the alerting effect. The orienting effect was demonstrated by faster response time in the spatial cue versus the center cue conditions. And, faster response time in the congruent versus the incongruent flanker conditions produced the conflict effect.

ADHD/C, ADHD/IA and Control group performance on the ANT

Children in the study did not show differential efficiency of the orienting or conflict attention networks as a function of ADHD group status. The performance indexes indicated essentially equal performance gains in the spatial cue over the no cue conditions for orienting, and in the congruent over the incongruent flanker conditions for conflict for all groups. The effects were demonstrated across the sample but these results did not provide information about the attentional style of ADHD or its subtypes.

In contrast, the alerting effect was sensitive to group membership. The ADHD/IA group showed a greater alerting effect than the ADHD/C group as indicated by a greater

difference in response latency between the double cue and no cue conditions. When the cue appears on the computer screen to warn of the upcoming target, ADHD/IA children speed their performance to a greater degree than do the ADHD/C children relative to their respective baseline performance when no cue or warning signal is provided. Although ADHD group showed a large effect to differ from each other on this variable, they did not differ significantly from the control group, with the control group performance falling between that of the ADHD groups. Effect sizes for group comparisons on alerting revealed a medium effect for ADHD/IA to benefit more from cues than controls and a small effect for ADHD/C to benefit less from the warning cues than controls.

Groups differed on overall task reaction time and accuracy on the ANT. As found in previous research, ADHD groups were less accurate and slower than controls. Effect sizes for accuracy were large and medium in magnitude for the ADHD/C and ADHD/IA groups, respectively, to make more errors than Controls. In addition, the trend for the ADHD/C group to make more errors than the ADHD/IA group was medium in effect size. Effect sizes for reaction time were large for both ADHD groups to be slower than controls. The question of differential deficits in processing speed distinguishing the subtypes, with slower processing in ADHD/IA, has been raised (Barkley et al., 1990, Hynd et al., 1991, Sergeant and Scholten, 1985) but the only consistent finding across studies has shown both ADHD groups to be slower than comparison controls on reaction time tasks. More recent research posits that the dimension of inattention symptoms (rather than the diagnostic presence or absence of HI) is associated with a deficit in processing speed, predicting that both ADHD subtypes would demonstrate slower performance than controls (Chhabildas, Pennington, & Willcut, 2001). Our findings showing no significant difference between ADHD groups in reaction time is consistent with this position.

For analyses conducted with boys only, a similar pattern of findings emerged. The orienting and conflict effects did not discriminate among groups whereas there was a large and significant effect showing greater alerting for the ADHD/IA group than the ADHD/C group. Group means and effect sizes for accuracy were consistent with results

for the entire sample, although significance levels changed (only comparison controls were significantly more accurate than the ADHD/C group). For reaction time analyses, again there was a large effect for the ADHD/C group to be slower than comparison controls (trend), but a reduced, medium as opposed to large, effect for the ADHD/IA group to be slower than controls (nonsignificant).

The consistency of findings for the efficiency of attention networks in the boys' sample suggests that the alerting effect characterizes at least some aspect of the difference in cognitive functioning for ADHD/C and IA boys. While low n's precluded group analyses for a girls only sample (there were only 2 girls in the ADHD/C group), in the ADHD/IA group, girls (n = 10) performed much like boys on the attention network variables, with a mean of 113.07 msec for alerting; boys demonstrated a mean of 94.12 msec for the alerting effect. (Appendix D reports mean scores for ADHD/IA girls and boys on d.v.'s of the ANT). This finding suggests that performance on the ANT reflects a common pattern of neurocognitive functioning in ADHD/IA boys and girls. For reaction time analyses, a review of the results for the ADHD/IA group showed slower mean reaction times for girls (849.92) than boys (807.56), thus accounting for the diminished effect for the ADHD/IA versus control comparison in the boys' only compared to the entire sample. Further research and adequate statistical power are indicated to examine these potential sex differences in alerting and reaction time in the ADHD/IA subtype.

Conclusions cannot be drawn about sex differences in ADHD/C on performance variables of the ANT. The girls in this group did not look like their male cohorts on the performance variables, although an n of two does not allow for generalizations about the cognitive style of ADHD/C girls. Further, the one alerting outlier removed from analyses was demonstrated by an ADHD/C girl, thus the alerting score was obtained for only one ADHD/C girl. A recent study that examined subtype performance on various cognitive measures in a sample of girls found the performance of ADHD/C girls to be more discrepant than ADHD/IA girls from comparison controls on several executive, motor, and linguistic measures as indicated by larger effect sizes (Hinshaw, Carte, Sami,

Treuting, & Zupan, 2002). However, the pattern of performance was similar for the subtypes, suggesting that the ADHD/C girls were more impaired but not qualitatively different from ADHD/IA girls. In our study, for ADHD/IA, both girls and boys showed the same pattern of benefiting from cues, so overall, results hold for IA girls and boys relative to ADHD/C boys on the alerting effect. We cannot, with our data, generalize to ADHD/C girls.

Unique Neurocognitive Profiles in ADHD subtypes

Performance of the ADHD/C and ADHD/IA groups on the ANT differed significantly in response to demands placed on the alerting network of attention. The finding of a divergent pattern of performance between the subtypes on a cognitive task is relatively unique in the literature. Studies that report subtype differences on neurocognitive measures have typically found one subtype to differ from controls but have not found ADHD subtypes to differ significantly from each other. Performance means for ADHD groups usually fall in same direction, with the most extreme ADHD group showing a greater effect to differ from comparison controls. Probably the most striking finding of significant subtype differences on neurocognitive measures has been demonstrated by studies showing that the combined type performed worse than the inattentive type on measures of inhibition (Nigg et. al, 2002, Willcut, Lahey, Pennington, Carlson, Nigg, & McBurnett, under review). However, these such findings do not provide evidence that the subtypes differ qualitatively on some cognitive deficit, but rather that they differ in degree of impairment.

Relative to each other, the ADHD/IA group showed a greater alerting effect and the ADHD/C group showed a smaller alerting effect, with the mean of the control group falling in between. If the subtypes truly have a distinct neurocognitive profile, then the positive finding in our study appears to be due to largely the sensitivity of the measurement tool. The design of the ANT makes it possible to determine whether networks of attention are functionally independent and provides indexes of the efficiency of each. This task provides the mechanism by which attention deficits could be

dissociated in populations with abnormal attentional functioning (Fan et al., 2002). Neuropsychological measures used in most studies examining the performance of ADHD subtypes have not been as sensitive to the various cognitive processes involved in attention, thus making it difficult to draw conclusions about the etiology of the attention deficit. Moreover, studies that have examined the neurocognitive correlates of subtypes have focused primarily on executive functions. Fewer studies have examined non-executive cognitive domains that may be more relevant to the inattentive subtype.

Alerting

Alerting is defined as achieving and maintaining an alert state (Posner and Petersen, 1990). The alerting system has been associated with frontal and parietal regions of the right hemisphere and the mechanisms of the alerting effect are presumed to lie in the subcortical noradrenergic system arising in the locus coeruleus (Posner and Petersen, 1990). The effects of this system are diffuse, due to the broad distribution of axons innervating large areas of the cerebral cortex. The breadth of modulation of this system may have some bearing on our findings of group differences in the efficiency of this attention network. The integrity of the alerting system plays a critical role in arousal and vigilance and maintaining readiness to react and may be particularly sensitive to attentional differences in disordered populations.

We hypothesized that the ADHD/IA group would show a greater alerting effect than both ADHD/C and control groups. For the ADHD/IA subtype to show a greater alerting effect due to impaired performance in the no cue baseline condition is consistent with research suggesting that this subtype has a unique attention deficit of arousal systems. The large alerting effect demonstrated by this group would reflect the improvement of performance with the assistance of a cue. Previous research has been demonstrated that task modifications such as reward or response cost can "normalize" or improve ADHD children's performance.

Given the dissociation of findings for ADHD/IA and ADHD/C, it must also be considered that the performance of children with ADHD/C on the ANT reflects a unique attentional correlate of a diminished alerting effect. Studies have shown that disrupting

activity of the noradrenergic systems involved in arousal can reduce the effectiveness of alerting produced by a warning signal (Fan et al., 2002). In any case, research providing evidence for individual differences in the correlates of alerting should be considered in the interpretation of the ADHD group differences.

Conflict and Orienting

In contrast to alerting, the effects of orienting and conflict are supported by neural pathways that are densely innervated to more localized regions of the cortex. Our hypotheses for group differences in conflict and orienting were not supported. Failure to find group differences is the most surprising for conflict, which is a measure of executive functioning. Strong evidence points to a deficit of executive functions in ADHD/C. However, within the executive domain some measures are sensitive to ADHD dysfunction whereas others are not. Thus, executive functions represent a broad domain and different tasks of executive functions tap various and overlapping abilities. The most consistent findings have been reported for tests of motor inhibition such as continuous performance tests and the Stop Task (Chhabildas et al., 2001). Even the narrow spectrum of conflict tasks produce different patterns of brain activation although they are considered to assess the same cognitive construct. Studies have shown that the flanker task activates an area of the anterior cingulate which is distinct from but which overlaps activation produced by other conflict tasks (Fan et al., 2002). Perhaps conflict as measured by the ANT, which is a flanker task, is not as sensitive to the impairment in ADHD as other tasks of executive functioning.

It is noted by Posner and colleagues that there is little empirical support for the involvement of the orienting network in ADHD pathology. Although this has not been directly tested by many studies, there is question as to whether the neural pathways involved in orienting contribute to the impairment of attention observed in this population (Berger and Posner, 2000). Our study does test the efficiency of the orienting network in ADHD and provides no additional evidence to suggest that the attention deficit in either ADHD subtype is due to or can be detected by impaired orienting to visual spatial cues.

SCT classification and group performance on the ANT

The purpose of the four group comparisons was to consider the performance of a potentially "purer" inattentive group of ADHD children characterized by sluggish cognitive tempo. As with the three group comparisons, the groups did not differ on the efficiency of orienting or conflict attention networks. Both ADHD/IA with and without SCT groups showed large and greater alerting effects than the ADHD/C group, although this comparison was stronger for the ADHD/IA with SCT group; significant, than for the ADHD/IA no SCT group (trend). The ADHD/IA with SCT showed a stronger alerting effect than the ADHD/IA no SCT group, though the effect size of this comparison just missed magnitude for the "small" level. Also, the SCT symptom score showed a slightly stronger correlation with alerting (.184) than did the IA symptom score (.004). For reaction time, although not significant, the ADHD/IA with SCT group showed a small effect to be slower than the ADHD/IA no SCT group. A finding of slower reaction time in the SCT group is consistent with results from Hinshaw et al. (2002) showing, in a sample of ADHD girls, that the one neuropsychological characteristic to distinguish this group from the rest of the inattentive type was markedly slow performance. SCT classification did not provide additional information about accuracy over the use of DSM-IV subtype distinctions. The pattern of results for the two ADHD/IA groups provides some, albeit fairly weak, support for the utility of SCT in identifying a more homogeneous subgroup of children with ADHD/IA.

An obvious limitation to the interpretation of SCT in this sample is an issue of measurement. Items that have been shown in previous research to characterize the attentional style of a subset of children with ADHD/IA did not have a strong presence in our sample. In fact, only the teacher rated underactive item differentiated ADHD/IA from ADHD/C, and the SCT symptom cluster we used for classification consisted of only two items; underactive, and the next most discriminating teacher item, apathetic. It is notable that while "underactive" may appear at face value to be a measure of hyperactivity/impulsivity, the symptom domain that determines the distinction between ADHD/IA and ADHD/C, this item correlated strongly with the attention symptom domain and only weakly (in the expected negative direction) with

hyperactivity/impulsivity. This is important in the attempt to measure SCT, a second factor of attention with relevance for an inattentive group of children with ADHD. Since not all studies that have identified SCT in ADHD have used the same symptom items or measurement criteria, it is difficult to make direct comparisons about the clinical correlations of this symptom domain. Our designation of a cutoff score to classify high versus low SCT in children with ADHD/IA was somewhat arbitrary, although consistent with methods to classify SCT in previous studies (Carlson & Mann, 2002). In any case, the potential utility of SCT items has been established by factor analytic studies showing that these items emerge as a second factor of inattention for ADHD/IA children.

Given that many of the original SCT items selected from the Teacher Report Form and Child Behavior Checklist did not differentiate the ADHD subtypes, it was difficult to anchor experimental items on the Rating of Behavioral Style to an SCT construct. Moreover, the only items that discriminated between ADHD subtypes on our experimental questionnaire showed higher means for the ADHD/C group. It is possible that items on this measure were difficult to rate, perhaps reflecting low frequency or difficult to observe behaviors. This explanation is especially plausible in the classroom given that teachers often returned incomplete forms, leaving several items blank. Further, we have no reliability data for the questionnaire and our sample size does not lend itself to scale development. Thus, we limited our classification of SCT to the two-item scale derived from Achenbach teacher rated items. The Rating of Behavioral Style may have potential as a measure of cognitive failures in ADHD, however, further research is needed to address the validity, reliability, and factor structure of this questionnaire.

A potentially important sample characteristic that likely influenced the structure of SCT in our sample is the very low mean number of hyperactivity/impulsivity symptoms in the ADHD/IA group (mean HI symptoms = 1.07 for teacher and 1.44 for parent). This is a relatively unique sample in that the ADHD/IA group is a truly “no hyperactive group”. The ADHD/IA group is already quite homogeneous in terms of HI symptoms without the addition of SCT to further subclassify a group of “pure inattentives”. Nor is our ADHD/IA group representative of the DSM-IV diagnostic

continuum of ADHD with 5 HI symptoms as the cutoff for subtype classification due to the low variance of HI symptoms in this group. SCT, presumed to emerge as a second factor of attention within ADHD/IA, may not have the same presence in a sample that is so homogeneous on lack of the second symptom domain.

The pattern of group means and effect sizes for the four boy groups was consistent with the pattern of means for the entire sample. However, sample sizes for the boys' only analyses were small and the findings for alerting and reaction time that emerged in previous comparisons were not significant. Only the finding that the control group was more accurate than the ADHD/C group, previously discussed for the three group analyses, was significant. As with the three group comparisons, removing girls from the analyses resulted in slightly smaller means for both ADHD/IA groups for the alerting effect and shorter reaction time latencies, again, suggesting that the greater alerting effect and slower response time may be more characteristic of ADHD/IA girls than boys.

Caveats and Limitations

In interpreting the findings, several caveats must be noted along with a consideration of study limitations. As noted previously, sex differences could not be examined due to the small number of girls in our sample. Results suggest that, at least for the ADHD/IA subtype, girls show the same pattern to benefit from cues as do boys, thus sharing the distinction of a greater alerting effect than ADHD/C boys. Our data do not, however, allow for the generalization of findings to girls in the ADHD/C group. Another caveat is the low HI symptom scores for our ADHD/IA group making our sample different from many others. The low HI symptoms of this group may have contributed to the significant findings differentiating ADHD/IA from ADHD/C on the cognitive/attentional process of alerting. The composition of our groups may also have implications for DSM-IV classification, since our results demonstrate attentional differences in at least one network, alerting, when a "nonhyper" inattentive group is examined.

Another consideration for cognitive testing with children, particularly of disordered populations, is the variability introduced to the data due to factors such as poor motivation or off-task behaviors that influence task performance. Whereas with normal adult populations, one can measure more precisely the variables of interest, with children, added noise can be expected to dilute the strength of results in a general way. This is clearly reflected by the large variances of our dependent variables. Studies measuring similar cognitive/ reaction time task variables, including studies using the ANT, find much smaller variability in adult performance.

As mentioned previously, developmental factors such as neural maturation and cognitive development would influence the efficiency of attention networks. Thus, findings for children on cognitive tasks may not reflect the same underlying abilities as for adults. Further, these developmental trajectories influencing brain growth and function have been shown to differentiate disordered from normal populations. It is thus important to consider population specific factors and individual differences when interpreting results.

Given the negative findings for conflict and orienting measures to differentiate groups, methodological considerations must also be raised. Future research might explore alternative tasks or procedures for assessing these domains, such as by varying inter-stimulus intervals, using degraded stimuli, etc…

Finally, the low statistical power limits the strength of conclusions that can be drawn from these data. The sample size allowed sufficient statistical power to detect at least large effects, supporting our hypothesis that the ADHD/IA subtype would show a significantly greater alerting effect than the ADHD/C subtype on the ANT. However, small and medium effect sizes showing ADHD/C and ADHD/IA to have smaller and greater alerting effects, respectively, than controls raise this possibility that a larger sample would have provided the power to detect statistically significant differences allowing for more definitive conclusions about impairment. The issue of sample size is even more problematic for the four group analyses and analyses conducted with boys only for which fewer significant differences were found. However effect sizes for these

comparisons were similar to those of the entire sample, medium and large for many of the comparisons, encouraging that the strength of conclusions may hold up to future study.

Tables

Table 1
Participant demographic and descriptive characteristics

	ADHD/C Mean (SD) n = 16	ADHD/IA Mean (SD) n = 27	Control Mean (SD) n = 24
Age in months	114.44 (21.94)	116.59 (22.12)	114.50 (19.35)
Sex ratio male	88%	64%	50%
Ethnicity			
Caucasian	94%	89%	71%
Hispanic	0%	7%	17%
Asian	6%	4%	12%
Parent DSM-IV			
Inattention	8.00 (1.26)	7.15 (1.13)	0.13 (0.45)
Hyperactivity/Impulsivity	6.94 (1.53)	1.44 (1.42)	0.21 (0.66)
ODD	3.31 (2.18)	1.26 (1.91)	0.46 (1.32)
Teacher DSM-IV			*n = 14*
Inattention	7.81 (1.17)	7.37 (1.15)	0.29 (0.61)
Hyperactivity/Impulsivity	7.00 (1.41)	1.07 (1.30)	0.29 (0.73)
ODD	3.06 (2.38)	0.44 (1.48)	0.07 (0.27)
			n = 18
WISC IQ (pro-rated)	110.94 (17.16)	109.30 (13.73)	119.50 (10.84)
WRAT3	*n = 15*	*n = 26*	*n = 18*
Arithmetic	102.80(14.56)	101.62 (12.20)	110.89 (12.20)
Reading	98.47(11.72)	102.85 (10.41)	113.06 (10.75)
Learning Disability*			
Math	0	1	0
Reading	1	0	0
Oppositional Defiant Disorder	56%	19%	4%

*Note: LD classification was based on study criteria (below average achievement and discrepancy between IQ and achievement). See text for details.
Corrected *N's* are reported for several variables. Complete data were not collected for the six controls who did not participate in the larger study. WRAT Math and Reading scores were unavailable for 2 participants.

Table 2
Group means and ADHD group comparisons on SCT candidate items

	ADHD/C Mean (sd) n = 16	ADHD/IA Mean (sd) n = 27	Control Mean (sd) n = 24	t score, df, p ADHD/IA & C
Teacher				
			n = 14	
Forgetful	4.13 (0.96)	3.78 (1.05)	1.36 (0.84)	-1.08, 41, p=.286
	n = 12	*n = 26*	*n = 9*	
Daydreams	3.33 (1.56)	3.31 (1.29)	1.00 (0.00)	-0.05, 36, p=.958
	n = 12	*n = 26*	*n = 10*	
Apathetic/ Unmotivated	3.25 (0.97)	3.69 (1.41)	1.50 (0.97)	0.98, 36, p=.332
	n = 12	*n = 26*	*n = 10*	
Underactive	1.50 (0.80)	2.92 (1.44)	1.10 (0.32)	3.19, 36, p=.003*
Parent				
			n = 18	
Forgetful	3.56 (1.32)	3.48 (1.31)	1.39 (0.50)	-0.20, 41, p=.846
	n = 15	*n = 26*	*n = 10*	
Daydreams	2.53 (1.55)	2.96 (1.48)	1.00 (0.00)	0.88, 39, p=.387
	n = 9	*n = 18*	*n = 10*	
Apathetic/ Unmotivated	3.22 (1.39)	3.56 (1.42)	1.40 (0.52)	0.58, 25, p=.569
	n = 14	*n = 26*	*n = 10*	
Underactive	1.43 (0.94)	2.04 (1.31)	1.00 (0.00)	1.54, 38, p=.132

*p < .05 based on t-tests

Table 3
Teacher SCT item and symptom domain correlations

Rating of Behavioral Style	Underactive	Apathetic/ unmotivated	2-item SCT	DSM-IV IA	DSM-IV HI
Underactive	1.00	0.72***		0.46***	-0.33*
Apathetic/unmotivated	0.72***	1.00		0.62***	-0.10
Item 5. Forgets			0.49**	0.43**	0.86
Item 34. Athletic skills			0.57***	0.44**	0.28

*** correlation is significant at the .001 level (2-tailed)
** correlation is significant at the .01 level (2-tailed)
* correlation is significant at the .05 level (2-tailed)

Table 4
Correlations of teacher symptom scores and ANT dependent variables for entire sample

	DSM-IV IA	DSM-IV HI	Orienting	Alerting	Conflict	Mean RT	Accuracy
SCT	.587***	-.178	.085	.184	.089	.221	-.056
TSNAP IA		.450***	.021	-.004	-.014	.397**	-.301*
TSNAP HI			.109	-.385**	.043	.209	-.404**
Orienting				-.160	-.056	.126	-.151
Alerting					.033	.259*	.042
Conflict						.084	.048
Mean RT							-.570***

*** correlation is significant at the .001 level (2-tailed)
** correlation is significant at the .01 level (2-tailed)
* correlation is significant at the .05 level (2-tailed)

Table 5
Correlations of teacher symptom scores and ANT dependent variables for Controls

	DSM-IV IA	DSM-IV HI	Orienting	Alerting	Conflict	Mean RT	Accuracy
SCT	.583	-.250	-.357	-.244	.674*	-.162	.375
DSM-IV IA		.149	-.184	-.525	.441	.189	.012
DSM-IV HI			.065	-.049	-.528	-.016	-.283
Orienting				-.016	-.313	.162	-.267
Alerting					-.338	.088	.334
Conflict						.104	.264
Mean RT							-.406*

*** correlation is significant at the .001 level (2-tailed)
** correlation is significant at the .01 level (2-tailed)
* correlation is significant at the .05 level (2-tailed)

Table 6
Correlations of teacher symptom scores and ANT dependent variables for ADHD/C

	DSM-IV IA	DSM-IV HI	Orienting	Alerting	Conflict	Mean RT	Accuracy
SCT	-.014	-.306	.314	.004	.117	-.018	.051
DSM-IV IA		-.121	-.220	-.426	-.212	-.114	.236
DSM-IV HI			.069	-.217	.161	.343	-.364
Orienting				-.052	.161	.146	-.004
Alerting					.584*	.287	-.059
Conflict						.138	-.011
Mean RT							-.676**

*** correlation is significant at the .001 level (2-tailed)
** correlation is significant at the .01 level (2-tailed)
* correlation is significant at the .05 level (2-tailed)

Table 7
Correlations of teacher symptom scores and ANT dependent variables for ADHD/IA

	DSM-IV IA	DSM-IV HI	Orienting	Alerting	Conflict	Mean RT	Accuracy
SCT	.543**	-.389*	.157	.168	-.005	.097	-.084
DSM-IV IA		.084	-.068	.077	.110	.003	.119
DSM-IV HI			-.090	-.400*	.216	-.126	.047
Orienting				-.228	-.026	.131	-.127
Alerting					-.150	.352	-.214
Conflict						.054	.006
Mean RT							-.421*

*** correlation is significant at the .001 level (2-tailed)
** correlation is significant at the .01 level (2-tailed)
* correlation is significant at the .05 level (2-tailed)

Table 8
ADHD/C, ADHD/IA, and Control group performance on the ANT

	ADHD/C Mean (SD)	ADHD/IA Mean (SD)	Control Mean (SD)
Boys and Girls	**n = 16**	**n = 27**	**n = 24**
	n = 15	*n = 26*	
Orienting	52.90 (35.45)	39.84 (52.33)	45.60 (45.18)
	n = 15		
Alerting	46.32 (60.14)	101.14 (56.64)	70.85 (50.43)
Conflict	63.98 (61.88)	63.07 (41.90)	62.70 (34.22)
Mean RT msec	830.34 (110.70)	823.25 (128.49)	709.29 (85.51)
Accuracy %	91.02 (4.41)	93.83 (4.27)	96.67 (3.52)
Boys only	**n = 14**	**n = 17**	**n = 12**
	n = 13	*n = 16*	
Orienting	61.69 (28.70)	41.23 (50.72)	41.21 (46.06)
Alerting	42.95 (60.93)	94.12 (49.81)	67.79 (62.79)
Conflict	68.59 (64.24)	70.71 (43.61)	72.59 (35.93)
Mean RT msec	825.21 (115.85)	807.56 (138.49)	727.53 (68.33)
Accuracy %	91.27 (4.33)	93.83 (4.76)	97.05 (3.52)

Table 9
Effect sizes for ADHD/C, ADHD/IA, and Control group comparisons on the ANT

Effect size Cohen's d	ADHD/C & Control d	ADHD/C & ADHD/IA d	ADHD/IA & Control d
Boys and Girls			
Orienting	0.16	0.29[S]	0.12
Alerting	0.44[S]	0.94[L]	0.56[M]
Conflict	0.03	0.02	0.01
Mean RT	1.22[L]	0.06	1.04[L]
Accuracy	1.42[L]	0.63[M]	0.73[M]
Boys only			
Orienting	0.53[M]	0.50[M]	0.00
Alerting	0.40[S]	0.92[L]	0.46[S]
Conflict	0.08	0.04	0.05
Mean RT	1.03 [L]	0.14	0.73[M]
Accuracy	1.46[L]	0.56[M]	0.77[M]

[S] = small; [M] = medium; [L] = Large

Table 10
ADHD/C, ADHD/IA no SCT, ADHD/IA with SCT, and Control group performance on the ANT

	ADHD/C Mean (SD)	ADHD/IA no SCT Mean (SD)	ADHD/IA with SCT Mean (SD)	Control Mean (SD)
Boys and Girls	**n = 16**	**n = 15**	**n = 11**	**n = 24**
Orienting	*n = 15* 52.90 (35.45)	30.24 (51.48)	*n = 10* 54.68 (55.53)	45.60 (45.18)
Alerting	*n = 15* 46.32 (60.14)	96.88 (57.20)	108.33 (60.44)	70.85 (50.43)
Conflict	63.98 (61.88)	59.93 (43.22)	70.94 (41.34)	62.70 (34.22)
Mean RT msec	830.34 (110.70)	804.05 (116.47)	850.93 (150.04)	709.29 (85.51)
Accuracy %	91.02 (4.41)	94.35 (2.73)	93.18 (6.01)	96.67 (3.52)
Boys only	**n = 14**	**n = 8**	**n = 8**	**n = 12**
Orienting	*n = 13* 61.69 (28.70)	20.13 (57.79)	*n = 7* 66.19 (34.76)	41.21 (46.06)
Alerting	42.95 (60.93)	90.83 (51.42)	98.44 (54.63)	67.79 (62.79)
Conflict	68.59 (64.24)	73.28 (47.33)	74.03 (42.04)	72.59 (35.93)
Mean RT msec	825.21 (115.85)	779.30 (104.91)	835.93 (176.07)	727.53 (68.33)
Accuracy %	91.27 (4.33)	94.44 (2.65)	93.32 (6.63)	97.05 (3.52)

Table 11
Effect sizes for ADHD/C, ADHD/IA no SCT, ADHD/IA with SCT, and Control group comparisons on the ANT

Effect size Cohen's d	ADHD/IA sct & Control	ADHD/IA sct & ADHD/C	ADHD/IA sct & IA no sct	ADHD/IA no sct & Control	ADHD/IA no sct & ADHD/C
Boys and Girls					
Orienting	0.16	0.04	0.46 [S]	0.32 [S]	0.51 [M]
Alerting	0.67 [M]	1.03 [L]	0.19	0.48 [S]	0.86 [L]
Conflict	0.22 [S]	0.13	0.26 [S]	0.07	0.08
Mean RT	1.16 [L]	0.16	0.35 [S]	0.93 [L]	0.23 [S]
Accuracy	0.71 [M]	0.41 [S]	0.25 [S]	0.74 [M]	0.91 [L]
Boys only					
Orienting	0.61 [M]	0.14	0.97 [L]	0.40 [S]	0.91 [L]
Alerting	0.52 [M]	0.95 [L]	0.14	0.40 [S]	0.85 [L]
Conflict	0.04	0.10	0.02	0.02	0.08
Mean RT	0.81 [L]	0.07	0.39 [S]	0.58 [M]	0.42 [S]
Accuracy	0.70 [M]	0.37 [S]	0.22 [S]	0.84 [L]	0.88 [L]

[S] = small; [M] = medium; [L] = large

APPENDIX A

DSM-IV Diagnostic Criteria for ADHD

A. Either (1) or (2):

(1) Six (or more) of the following symptoms of inattention have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

Inattention

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

(2) Six (or more) of the following symptoms of hyperactivity-impulsivity have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

Hyperactivity

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

Impulsivity

g. Often blurts out answers to questions before the questions have been completed.
h. Often has difficulty waiting turn.
i. Often interrupts or intrudes on others (e.g., butts into others' conversations or games).

APPENDIX A (cont')

B. Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before age 7 years.

C. Some impairment from the symptoms is present in two or more settings (e.g., at school (or work) and at home).

D. There must be clear evidence of clinically significant impairment of social, academic, or occupational functioning.

E. The symptoms do not occur exclusively during the course of a Pervasive Developmental Disorder, Schizophrenia, or other Psychotic Disorder and are not better accounted for by another mental disorder (e.g., Mood Disorder, Anxiety Disorder, Dissociative Disorder, or a Personality Disorder).

Code based on type:

314.01 Attention Deficit Hyperactivity Disorder, Combined Type: If both Criteria A1 and A2 are met for the past 6 months.
314.00 Attention Deficit Hyperactivity Disorder, Predominantly Inattentive Type: If Criterion A1 is met but Criterion A2 is not met for the past 6 months.
314. Attention Deficit Hyperactivity Disorder, Predominantly Hyperactive-Impulsive Type: If Criterion A2 is met but Criterion A1 is not met for the past 6 months.

APPENDIX B

Alignment of Symptom Domains, Cognitive Processes, and Neural Networks

Swanson, Posner, Cantwell, Wigal, Crinella, Filipek, Emerson, Tucker, and Nalcioglu (1998) propose a tentative alignment of DSM-IV symptoms, cognitive processes, and neural networks in ADHD based on Posner and Raichle's model of attention (1994). Cognitive processes considered are those tested by Continuous Performance Test (CPT), visuospatial orienting test (VOT), and conflict resolution test (CRT) paradigms.

Symptom Domains	Cognitive Processes	Neural Networks
Inattentive - A	*Alerting/Sustained attention*	*Right frontal/parietal and Locus coeruleus*
Has difficulty sustaining attention in tasks or play activities	CPT fast presentation, (vigilance level)	Right frontal
Does not follow through instructions and fails to finish work	CPT slow presentation, (vigilant decrement)	Right parietal
Avoids tasks that require sustained mental effort	CPT high load, (attention capacity)	Locus coeruleus
Inattentive – O	*Orienting/Selective attention*	*Posterior parietal and thalamus*
Easily distracted by extraneous stimuli	VOT cue effects, (rapid, short response)	Bilateral parietal
Does not seem to listen when spoken to directly	VOT validity effect (difficulty engaging)	Superior colliculus
Fails to give close attention to	VOT visual search,	Thalamus

details or makes careless mistakes	(neglect)	
Hyperactive/Impulsive	*Executive control*	*Anterior Cingulate and Basal Ganglia*
Blurts out answers to questions before they have been completed	CRT Stroop (too automatic in response)	Anterior Cingulate
Interrupts or intrudes on others (e.g., butting into conversations)	CRT stop tasks (difficulty stopping)	Left lateral frontal
Has difficulty waiting in lines or for turn in games or group situations	CRT start tasks (difficulty inhibiting)	Basal ganglia

APPENDIX C

Parent/Teacher Rating of Behavioral Style

This form is for the child in our study. If applicable, please rate behavior off medication.

Instructions: For each of the following items, please rate the extent to which the described behavior occurs or is problematic using the 1-5 scale. For all items, a score of "5" indicates highest severity or frequency and a score of "1" indicates lowest severity or frequency.

1	2	3	4	5
Never or not at all	Very Rarely or just a little	Occasionally or somewhat	Quite Often or quite a bit	Very Often or very much

1. Does the child have to reread something (instructions or a school assignment) because he/she wasn't concentrating the first time?	1.	1	2	3	4	5
2. Does the child forget the reason he/she went from one part of the house or school environment to another?	2.	1	2	3	4	5
3. Is the child unaware of his/her surroundings, for example, not noticing a wet paint sign?	3.	1	2	3	4	5
4. Does the child confuse right and left when following directions?						
5. Does the child forget whether he/she has turned off a light or locked the door?	4.	1	2	3	4	5
6. Does the child fail to listen to people's names when meeting them?	5.	1	2	3	4	5
7. Does the child say something and realize afterwards that it might be inappropriate (taken the wrong way, offensive)?	6.	1	2	3	4	5
8. Does the child fail to hear people speaking to him/her when he/she is doing something else?	7.	1	2	3	4	5
9. Does the child lose his/her temper and regret it?	8.	1	2	3	4	5
10. Does the child leave important school documents (e.g., permission slips) unattended for days?	9.	1	2	3	4	5
11. Does the child fail to see what he/she wants in the cabinet, refrigerator, pantry (although it's there)?	10.	1	2	3	4	5
12. Does the child have trouble making up his/her mind?	11.	1	2	3	4	5
13. Does the child forget scheduled events or activities?						
14. Does the child forget where he/she put something like a toy or shoes?	12.	1	2	3	4	5
	13.	1	2	3	4	5
15. Does the child daydream when he/she ought to be listening to something?	14.	1	2	3	4	5
16. Does the child forget people's names?	15.	1	2	3	4	5
17. Does the child start doing one thing and get distracted into doing						

something else (unintentionally)?	16. 1 2 3 4 5
18. Does the child have trouble remembering something although it seems to be 'on the tip of the tongue'?	17. 1 2 3 4 5
19. Does the child appear to "draw a blank" (e.g., can't think of anything to say)?	18. 1 2 3 4 5
20. Does the child appear absent-minded (e.g., making mistakes because he/she is thinking of something else)?	19. 1 2 3 4 5
21. Does the child find it difficult to concentrate because his/her attention tends to wander from one thing to another?	20. 1 2 3 4 5
22. Does the child appear preoccupied with his/her own thoughts and so doesn't notice what is going on around him/her?	21. 1 2 3 4 5
23. Is the child clumsy (e.g., dropping things or bumping into people)?	22. 1 2 3 4 5
24. Is the child disorganized (e.g, displays lack of planning)?	
25. Does the child get unduly irritable about minor matters?	23. 1 2 3 4 5
26. Is the child generally messy (e.g., messy backpack, desk, room, locker)?	24. 1 2 3 4 5
27. Does the child run out of time when completing school assignments or other tasks?	25. 1 2 3 4 5 26. 1 2 3 4 5
28. (**Parent only**) Does the child have difficulty falling asleep?	
29. (**Parent only**) Is it difficult to wake the child (even after a full night's sleep)?	27. 1 2 3 4 5
30. Is the child apathetic or unmotivated?	28. 1 2 3 4 5
31. Does the child daydream or get lost in his/her thoughts?	29. 1 2 3 4 5
32. Is the child underactive, slow moving, or lacks energy?	30. 1 2 3 4 5 31. 1 2 3 4 5 32. 1 2 3 4 5

Use the following 5 point scale for the next two items. Circle your answer.

33. Relative to his/her same-aged peers, the child's handwriting/penmanship is:

5	4	3	2	1
much poorer	a little poorer	about the same	a little better	much better

34. Relative to his/her same-aged peers, the child's sports/athletic skills are:

5	4	3	2	1
much poorer	a little poorer	about the same	a little better	much better

APPENDIX D

Mean Scores for ADHD/IA Girls and Boys on the ANT

	ADHD/IA girls Mean (SD)	ADHD/IA boys Mean (SD)
ANT	**n = 10**	**n = 17**
		n = 16
Orienting	37.62 (57.53)	41.23 (50.72)
Alerting	113.07 (67.86)	94.12 (49.81)
Conflict	50.09 (37.32)	70.71 (43.61)
Mean RT msec	849.92 (111.11)	807.56 (138.49)
Accuracy %	93.82 (3.52)	93.83 (4.76)

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