ANATOMICAL CORRELATES OF EXECUTIVE FUNCTIONING IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND DEVELOPMENTAL DYSLEXIA

by

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The purpose of this study was to explore the brain-behavior relationship of the frontostriatal circuit to executive functioning (EF) in children with Attention-Deficit/Hyperactivity Disorder (ADHD) and developmental dyslexia. It was expected that the volume and asymmetry of the caudate nucleus head and body would be related to ADHD; the relationship between caudate volume and asymmetry and dyslexia was exploratory. It also was expected that children with ADHD and children with dyslexia would be impaired on measures of EF compared to those without each disorder. Lastly, it was predicted that verbal and spatial working memory would mediate the relationship between the volumes of the left and right caudate nuclei, respectively, and performance on other EF measures. One hundred five children from the Southern Illinois region who successfully completed a full-day neuropsychological test battery and an 8-minute structural magnetic resonance imaging (MRI) scan were included in this study.

Results indicated that children with ADHD had greater rightward asymmetry for the caudate head as hypothesized, but not leftward asymmetry for the caudate body, when compared to those without it; however, there were no differences in caudate asymmetry for those with dyslexia. An exploratory factor analysis of the data revealed three EF factors: EF abilities in the home, problem solving/perseveration, and working memory/fluency. The ADHD and the dyslexia groups were more impaired than those without each disorder on EF abilities in the home

and working memory/fluency. Further analysis revealed that working memory was a significant covariate in the relationship between diagnosis and performance on EF measures for these groups and greatly reduced EF differences between groups when looking at dyslexia. Children with ADHD-Combined Type were not more impaired on a measure of inhibition when compared to those with ADHD-Predominantly Inattentive Type, but low power may have affected the ability to find a significant effect. The two subtypes were similar on all other EF measures. The diagnostic groups did not differ on a complex non-EF measure requiring attention (i.e., a verbal long-term memory task), which shows a dissociation between performance on complex tasks requiring attention with and without an EF component. The mediation models were not tested further since there was no significant relationship between left and right caudate volume and performance on EF measures.

These results indicate that the caudate head volume is related to the pathophysiology of ADHD, suggesting that more research is needed using segmentation. In addition, results showed that deficits in EF go beyond working memory in ADHD given that ADHD is still related to executive dysfunction after controlling for working memory. In contrast, the difference between children with and without dyslexia was no longer significant on EF measures after controlling working memory, suggesting that working memory may be the main factor driving EF impairment in dyslexia. Further work on this topic is indicated. An exploratory analysis revealed that left caudate head volume approached significance when correlated with a verbal working memory measure; therefore, further research is needed in the area of brain-behavior relationships of the frontostriatal circuit and performance on EF measures, especially working memory.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER ONE

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) and developmental dyslexia are two of the most commonly diagnosed childhood disorders and have been shown to be highly comorbid with one another (Willcutt & Pennington, 2000). Poor response inhibition is believed to be a key contributor to ADHD (Barkley, 1997), whereas phonological processing deficits are believed to be a main contributor to developmental dyslexia (Lyon, Fletcher, & Barnes, 2003; Wagner & Torgensen, 1987). Research suggests that executive dysfunction may be a potential source of the comorbidity between ADHD and developmental dyslexia (Willcutt et al., 2001). Executive functioning, which includes functions such as working memory, planning, problem-solving, emotional/behavioral regulation, and cognitive self-regulation and flexibility, has been extensively studied in children and adults and has been linked to specific brain regions such as the frontal lobes and pathways, including the frontostriatal circuit (Castellanos et al., 1994; Hynd et al., 1993; Qiu et al., 2009).

The recent explosion of data collected using neuroimaging techniques has provided a unique insight into anatomical correlates that may contribute to the pathology of brain-based disorders such as ADHD and developmental dyslexia (Cherkasova & Heckman, 2009). Data collected from neuropsychological testing provides a means to examine an individual's cognitive strengths and weaknesses, and, in conjunction with their developmental history, to provide individualized feedback and recommendations (Roth & Saykin, 2004).

The current study uses data collected from both structural magnetic resonance imaging (MRI) and neuropsychological testing from 105 children ages 8-12 with ADHD, developmental dyslexia, combined ADHD/developmental dyslexia, and controls who were recruited as part of a

larger, ongoing, university-based study. The main goal of the current study was to investigate some of the neurobiological and cognitive mechanisms that may underlie the comorbidity between ADHD and developmental dyslexia. Cognitive executive functions, a subset of the neuropsychological measures collected as part of the cognitive testing battery, were used in the current study given that executive dysfunction is a common neuropsychological deficit in ADHD, as well as in individuals with developmental dyslexia. A specific brain region, the caudate nucleus, which is believed to be part of the frontostriatal contribution to executive functioning (Valera, Faraone, Murray, & Seidman, 2007), was traced and segmented into head and body as outlined by Filipek and colleagues (1997). The volume of the right and left sides of the caudate were used to investigate the brain-behavior relationships between the caudate nucleus and performance on cognitive executive functioning in ADHD and developmental dyslexia. Given that previous research segmenting the caudate nucleus into head and body showed that volume/asymmetry was related to a diagnosis of ADHD (Tremols et al., 2008), one of the goals of the current study was to replicate this finding. Since there have been no prior studies investigating the volume/asymmetry of the caudate nucleus in developmental dyslexia following segmentation, this relationship was exploratory and will add to the current research on the neuroanatomy of developmental dyslexia. Next, differences in cognitive executive functioning based on diagnostic group membership was assessed given that prior research has shown executive dysfunction as a shared cognitive deficit in both diagnostic groups (Barkley, 1997; Willcutt et al., 2001). It also was hypothesized that diagnostic groups would be impaired on measures of executive functioning, but not on a complex non-executive functioning task that also required attention. Lastly, a mediation model outlined by Baron & Kenny (1986) was used to test whether verbal and spatial working memory mediated the relationship between the

caudate volume on the right and left sides of the brain, respectively, and performance on executive functioning measures such as the NEPSY Tower and Design Fluency subsets and the Wisconsin Card Sorting Task given previous literature implicating differences in the caudate nucleus in these measures (Beauchamp et al., 2003; Monchi et al., 2001). Working memory was chosen as a mediator given that it is believed to influence performance on other EF tasks (Barkley, 1997; Miyake et al., 2000).

Studies such as this are important because they may have implications for improving the diagnostic system and aiding with earlier diagnosis of developmental disabilities such as ADHD and developmental dyslexia than could be obtained from behavioral approaches alone (de Jong et al., 2009). Since both disorders are believed to be developmental and multifactorial in nature, it is crucial to identify and treat these disorders early and aggressively in hopes of preventing, or at least partially remediating, a lifelong disability that pervades into adulthood (Mash & Barkley, 2003).

CHAPTER TWO

REVIEW OF THE LITERATURE

Executive functioning

Definition of Executive Functioning

Executive functioning (EF) is a construct that is highly debated in terms of the best definition, but it is often described as an "umbrella term" (Anderson et al., 2001; Denckla, 1996; Eslinger, 1996; Stuss et al., 1986). There is evidence for the idea that EF is a construct of interrelated, but at least partially independent abilities, which is illustrated by the fact that executive dysfunction often presents itself as a "cluster of deficiencies," with one or two being especially striking (Lezak, 1993b). Mash & Barkley (2003) describe EF as a heterogeneous set of higher-order cognitive skills such as self-regulatory processes, including inhibitory control and goal-directed behaviors (e.g., working memory and planning), which are used to modify a later outcome. Although the construct of EF is generally accepted and supported by scientific literature, the components of this heterogeneous term are still under debate (Anderson et al., 2001). This will be illustrated in the subsequent section.

History of Executive Functioning

In 1973, Alexander Luria, a Russian psychologist, described executive functions as "the ability to maintain an appropriate set to achieve a future goal." A decade later, Baddeley (l986) defined executive functioning as a way to optimize performance in situations that require an individual to simultaneously manage several cognitive processes at once. Welsh, Pennington, & Groisser (1991) characterized executive functions as involving planning, control over impulses, organization, and flexibility of thought and behavior. Denckla (1989) described executive functions as the ability to perform complex behaviors using planning and sequencing, while

simultaneously attending to multiple stimuli. Included in this definition is the necessity to understand complexity, focus on the task at hand, avoid inappropriate responses, and maintain a behavior for a certain length of time. Lezak (1993b) states that the term 'executive function' encompasses "capacities that enable a person to engage successfully in independent, purposeful, self-serving behaviors (p. 43)." She proposed four "core" executive functions including volition, planning, purposeful behavior, and effective performance. In addition, Mirsky's model of attention (1996) is argued to be measuring 3 executive functions rather than strictly attention: cognitive flexibility, verbal working memory, and self-regulation. Moreover, as many as 33 different factors were thought to comprise executive functions when a panel of experts was surveyed to help clarify the definition and come to a consensus in the field (Eslinger, 1996). As a result of the survey, six components were agreed upon, including self-regulation, sequencing of behavior, cognitive flexibility, response inhibition, planning, and organization of behavior. Other proposed EF skills include working memory, auditory and visual sustained attention, and aspects of verbal and nonverbal fluency (Korkman et al., 2001).

In conclusion, there are numerous proposed components that comprise the umbrella term of EF. Several studies include deficits in the areas of problem solving, planning, working memory, and rapid generation of ideas/fluency, as well as difficulties with inhibition, set-shifting, and cognitive flexibility. It is likely that these deficit areas overlap with one another to various degrees given the current literature on EF. Recent research has been conducted using statistical methods to better understand the factor loading of various EF components, which will be outlined next.

Identifying Components Executive Functioning Using Statistics

Miyake, Emerson, and Friedman (2000) used statistical analyses, including structural equation modeling and latent variable analysis, to demonstrate that executive functioning is not a single construct but rather comprised of several different factors. This study assessed 137 undergraduates to determine whether a one- or three-factor model of executive functioning was the best fit. The authors found that the three-factor model, which included shifting, inhibition, and working memory, was the best fit based on apriori hypotheses. These findings were supported by other researchers who used factor analysis on data from eight neuropsychological measures and also concluded that executive functioning includes three factors: working memory, inhibition, and set shifting (Lehto, Juujarvi, Kooistra, & Pulkkinen, 2003). Using data from the Behavior Rating Inventory of Executive Functioning (BRIEF) and factor analysis, Gioia, Isquith, and Guy (2000) reported that behavioral regulatory (e.g., inhibition, shift) and metacognitive (e.g., working memory, planning) skills are included in the term executive functioning. Using a neuropsychological viewpoint, Emond et al. (2009) broke down EF into “hot” and “cool” aspects. Impairment of the affective or "hot" aspects of EF, often relating to rewards and punishments, is associated with problems with behavioral inhibition and impulsivity. These “hot” characteristics are associated with the ventral and medial regions of the prefrontal cortex and the anterior cingulate cortex. More cognitive or "cool" aspects of EF include cognitive self-regulation, working memory, sustained attention, planning, and cognitive flexibility and are associated with the dorsolateral prefrontal cortex and the frontostriatal circuit (Jurado & Rosselli, 2007; Korkman et al., 2001; Pennington, 2009).

Neuropsychological Measures Used to Investigate Executive Functioning

For the purposes of neuropsychological assessment, EF is typically operationalized to include planning, problem-solving, working memory, self-regulation, rapid generation of novel ideas/fluency, and mental flexibility (Duncan, 1986; Luria, 1973). Difficulty on tasks believed to assess these skills is often termed "executive dysfunction." The Wisconsin Card Sorting Test (WCST) is a traditional neuropsychological task that is believed to test the ability to shift mental sets based upon feedback (Heaton, 1981), although it likely measures more than that such as problem solving, working memory, and motivation (Hartman et al., 2001). The WCST has been used to assess a variety of clinical presentations, including patients with traumatic brain injuries (TBIs), neurodegenerative disorders such as dementia, and mental disorders such as schizophrenia and ADHD (Mash & Barkley, 2003). Neuroimaging studies using positron emission tomography (PET) scans have shown activation in the dorsolateral prefrontal cortex on the WCST (Berman et al., 1995; Cabeza & Nyberg, 2000). More recently, however, functional magnetic resonance imaging (fMRI) scans have implicated the ventrolateral prefrontal cortex in conjunction with the caudate nucleus as the brain regions most important for shifting mental set (Konishi et al., 1999; Monchi et al., 2001, 2006b). While there is some variability in findings, both sets of studies implicate lateral frontal regions in set shifting, which are part of the frontostriatal circuit.

The Trailmaking Test Part B (TMT-B) is a measure of set shifting that requires the participant to sequentially order letters and numbers while alternating between numbers and letters (Reitan and Wolfson, 1985). Kortte, Horner, and Windham (2002) argued that the constructs that TMT-B measures are not clear. They suggested that the task is more likely measuring cognitive flexibility than the ability to shift mental set when compared to data

collected from the WCST-64. Two studies indicated that increased blood flow to the dorsolateral prefrontal cortex was related to task performance on the TMT-B (Kubo et al., 2008; Shibuya-Tayoshi et al., 2007).

The Stop-signal Reaction Time (SSRT) task is another EF task that is commonly used in the literature (Logan et al., 1997). It is thought to assess the inhibition of a response that has already been started. A go/no-go task, which requires a participant to respond on a "go" item and inhibit a response on a "no-go" item, also is commonly used to measure response inhibition by counting commission and omission errors (Trommer et al., 1988). The SSRT is believed to be a more "pure" measure of response inhibition compared to go/no-go tasks because the respondent is inhibiting a response that they have already initiated compared to the "response selection" that is used in go/no-go tasks since the actual stimuli is the signal to inhibit the response (Rubia et al., 2001). Another task that measures the construct of response inhibition is the Continuous Performance Test, which assesses errors of commission and omission to a distracter that is not the target sequence. Such response inhibition tasks have been scrutinized due to the fact that these tasks require sustained attention, which is often impaired in ADHD, and can cause frustration, which may impair performance along with any inhibition deficits present (Li et al., 2008). fMRI studies have implicated the prefrontal cortex, including the right inferior frontal gyrus, in response inhibition and working memory tasks when comparing individuals with ADHD to controls (Aron & Poldrack, 2005; Chamberlain & Sahakian, 2007; Rubia et al., 1999; Westerberg & Klingberg, 2007; Vaidya et al., 1998).

Common measures of planning include the Tower of Hanoi/Tower of London and the Rey-Osterrieth Complex Figure Test (Borys et al., 1982; Shallice & Plaut, 1992; Waber & Holmes, 1985). The Tower of Hanoi involves moving different pieces from peg to peg while

following strict rules such as only moving one piece at a time, keeping all pieces on the pegs when not using them, placing the smaller blocks or rings on top of the larger ones, and completing the item in the requisite number of moves. Although it is thought to be a measure of planning, Tower tasks also require working memory and inhibition, making it a less specific task overall (Welsh, Satterlee-Cartmell, & Stine, 1999). Neuroimaging experiments using the Tower of London as a measure of planning have mostly reported activation in the bilateral dorsolateral prefrontal cortex (Shallice, 1992). Another commonly used neuropsychological task, the Rey-Osterrieth Complex Figure Test, requires the participant to copy a complex line drawing, and it is scored based on the way that the design was sequentially drawn, first by copying and then by memory. Although this task involves planning, especially when constructing the design from memory, it also demands a variety of other skills necessary for completion such as attention, working memory, and visuospatial skills (Hubley & Jassal, 2006). As such, it is not a specific measure of planning. The aforementioned areas measured by the Rey-Osterrieth Complex Figure Test are believed to be related to the right occipital-parietal lobe and the prefrontal cortex (Lezak, 1995).

Baddeley and Hitch (1974) introduced the idea that the "central executive" is responsible for keeping relevant information in the short-term memory, suppressing unnecessary information, and coordinating multiple cognitive processes all at once. They proposed that two "slave systems" maintain information in short-term storage briefly: the phonological loop, which stores verbal information phonologically, and the visuospatial sketchpad, which stores visual and spatial information. Nonetheless, there may be separate stores for visual and visuospatial information rather than a single visuospatial sketchpad (Smith & Jonides, 1997), and there may

be separate stores for phonetic and semantic material rather than a single phonological loop (Kibby, 2009a; Kibby & Cohen, 2008; Martin & Romani, 1994).

Verbal working memory has been assessed through the use of Digit Span Forward and Digit Span Backward from the Wechsler intelligence scales (i.e., WISC, WAIS). These tasks require the participant to recite back a series of numbers that increase in length in the forward and backward direction, respectively. Digits Forward is believed to be a measure of the phonological loop, whereas Digits Backward also taps the central executive. Much like the other tasks noted previously, these are not specific to verbal working memory and also may be tapping other areas of functioning including focused attention and general fluid intelligence (Kane et al., 2005). The prefrontal and parietal areas of the brain have been implicated in the central executive component and slave systems of working memory (Collette & Van de Linden, 2002; D'Esposito et al., 1995). In a study using PET, Landau, Lal, O'Neil, Baker and Jagust (2009) reported that the caudate dopamine density was correlated with working memory capacity in a sample of healthy controls who completed two working memory tasks: the Salthouse and Babcock Listening Span task (Salthouse et al., 1991) and the Sternberg delayed recognition task (Sternberg, 1966).

Furthermore, researchers who use the same measure may interpret the results differently, and researchers may use different measures to arrive at similar skills (Pennington & Ozonoff, 1996). For example, one research team used the Five-Point Test, which requires participants to generate as many novel designs as possible in a set amount of time (Regard, Strauss, & Knapp, 1982). They interpreted it to measure response fluency. Another group of researchers (Vik & Ruff, 1988) used the Ruff Figural Fluency Test (RFFT) to investigate "figural fluency," which is related to the construct of design fluency in the Five-Point Test. In the RFFT, the participant

is asked to produce novel figures in sequence that increase in complexity as the test progresses. Although the RFFT involves more visual-spatial and working memory demands than the Five-Point Test, it can be argued that both tests measure rapid divergent thinking in a nonverbal way in contrast to tasks involving verbal fluency where one is asked to quickly generate as many words as possible, starting with a given letter. Both the left prefrontal and right cerebellar regions of the brain were activated in a functional neuroimaging study (i.e., fMRI) of verbal fluency (Schlosser et al., 1998). The WCST has been interpreted in different ways as well, with some researchers focusing on the Categories Achieved score as the best measure of problem-solving (Chelune & Baer, 1986), whereas others have used this score as a representation of concept formation (Pennington & Ozonoff, 1996). A recent factor analysis of adults with EF showed that Perseverative Errors might be the most pertinent measure on the WCST to measure executive dysfunction given that it is more sensitive to age-related decline compared to Categories Achieved, which was demonstrated by another meta-analysis (Greve et al., 2005; Rhodes, 2004). Similarly, a meta-analysis investigating the sensitivity and specificity of the WCST in a variety of childhood disorders showed that children with ADHD had more consistently poorer performance compared to controls on Percent Correct, Total Errors, and Perseverative Errors, but not on Failure to Maintain Mental Set (Romine & Reynolds, 2005). Pennington & Ozonoff (1996) reported mixed findings on significant differences in WCST performance when comparing individuals with ADHD and controls. More specifically, only five out of ten studies showed a poorer performance by those with ADHD.

Measuring Executive Functioning in Children

Developmental research has suggested that children often improve their performance on executive functioning measures as they get older and their brain continues to mature. This brain

growth is specifically noticeable in the frontal lobes, which continue to develop past adolescence into young adulthood (Bell & Fox, 1992; Levin et al., 1991; Thatcher, 1991, 1992; Welsh & Pennington, 1988). Korkman, Kemp, and Kirk (2001) found that there are differences in neurocognitive performance depending on age. Specifically, children 5-8 years of age showed heightened developmental changes during this age range compared to children 9-12 years of age. Levin, Culhane, Hartmann, and Evankovich (1991) showed another distinct period of cognitive growth in children 13-15 years of age. This will be discussed in more detail in a subsequent section.

Since the lobes of the brain do not function in isolation, it is important to understand the functional connectivity within and among the cerebral hemispheres. Research has implicated the anterior cerebral regions in EF, specifically the prefrontal cortex (Castellanos et al., 1996; Durston et al., 2004; Filipek et al., 1997; Mostofsky et al., 2002). The dorsolateral prefrontal cortex has projections to the parietal cortex via two divisions of the superior longitudinal fasciculus and the striatum (Croxson et al., 2005; Kolb & Whishaw, 2009). The orbitofrontal cortex has projections to the posterior temporal cortex via the extreme capsule, the anterior temporal cortex via the uncinate fasciculus, the amygdala and hippocampal projections via the fornix (Amaral and Price, 1984; Porrino et al., 1981), and the hippocampal and other medial temporal connections via the cingulum bundle (Goldman-Rakic et al., 1984; Kolb & Whishaw, 2009; Morris et al., 1999). Leh, Ptito, Chakravarty, and Strafella (2007) used diffusion tractography to outline the frontostriatal connections in the human brain. They identified connections between the dorsolateral prefrontal areas and the dorsal-posterior caudate nucleus and between the ventrolateral prefrontal areas and the ventral-anterior caudate nucleus. Thus, based on the interconnectedness of the brain, proper development of other cerebral areas is

imperative for intact function of the frontal region. More specifically, the development of executive functions relies on the correct development of other building blocks of cognitive functioning such as language (Gaddes & Crockett, 1975; Halperin et al., 1989; Luria, 1973), attention (McKay, Halperin, Schwartz, & Sharma, 1994; Miller & Weiss, 1981), processing speed (Howard & Polich, 1985), and memory (Baddeley, 1986; Case, 1985; Simon, 1975).

Lastly, it is important to keep in mind that as children mature, certain skills may become more automatic and demand less cognitive effort due to the fact that they are no longer novel to the child. Specifically, novel tasks for preschoolers may not be new for older children, and, thus, would no longer be good measures of EF, given that novelty is important for good EF tasks. At that point, other cognitive skills may be engaged to complete the task such as language, memory, and processing speed, requiring less demand on the EF skill set (Denckla, 1994; Duncan, 1986; Shallice & Burgess, 1991b). For example, Diamond (2002) adapted a response inhibition task that used developmentally appropriate stimuli for preschool children. Children were presented with discordant scenes in the day-night task and asked to say "night" to a picture of the sun and to say "day" to a picture of the moon and stars. As children mature, this type of task would no longer be a valid measure of inhibition due to the fact that it is too easy and automatic for school-aged children (Diamond et al., 2002). Studies such as this are important, however, because it underscores the importance of understanding the development of EF in typically developing children and of using age-appropriate tests.

Executive Functioning from a Developmental Prospective

When studying aspects of cognitive functioning such as EF, it is important to note concurrent biological development. Several studies have shown that improved performance on executive functioning tasks parallels growth in the central nervous system. In the past, cognitive

models, including Piaget's theory of cognitive development, have supported a "hierarchical" view of development (Piaget, 1963). Theories such as this attempt to explain the qualitative and quantitative intellectual abilities that develop over time. Piaget's stages were described in a more qualitative manner, whereas most developmental psychologists believe that cognitive development is quantitative/continuous (Flavell, 1971). Piaget never specifically referenced potential neurobiological contributors, but the hierarchical view used in his stages of cognitive development supports the idea that the nervous system may be developing in spurts corresponding to different stages (Anderson et al., 2001). Numerous researchers have used Piagetian concepts to test the hypothesis that cognitive development maps onto brain maturation. For example, Diamond and Goldman-Rakic used the Piagetian concept of object permanence and a task involving object retrieval to learn more about purposeful behaviors in infants (Diamond, 1988; Diamond & Goldman-Rakic, 1989).

Given the importance of development, a few key concerns should be highlighted in the administration of EF measures, especially in children. First, it is important to use age-sensitive norms when assessing EF abilities to be sensitive to developmental factors (Korkman et al., 2001). Second, due to the fact that EF performance is related to brain maturation in "sensitive periods," (Passler, Isaac, & Hynd, 1985), it is crucial to be cognizant of the developmental progression of EF skills as a function of age. Passler, Isaac, and Hynd (1985) studied older children by using EF measures that were adapted from adult neuropsychology to study age-related improvements in frontal lobe functioning. Results showed that children as young as six years of age were able to use strategy and planning on tasks modified for children from a battery of frontal cortical tasks for adults (Luria, 1973). More specifically, children mastered tasks measuring verbal conflict and auditory sequential conflict at age 8, perseveration at age 10, and

proactive/retroactive inhibition after age 12. Verbal conflict is defined as an examinee's ability to control motor responses based on verbal instructions such as knocking one time on the table when the examiner knocks twice and knocking twice when the examiner knocks once. Auditory sequential conflict is similar except that the examinee's eyes are closed during the task, and they are asked to tap once if the examiner taps twice and vice versa. Proactive inhibition occurs when past memories inhibit an individual's ability to retain new memories, whereas retroactive inhibition affects the retrieval of information due to the acquisition of new information. According to the results from this study, most behaviors associated with frontal lobe functioning developed in stages between the ages of 6 and 12, depending on the task, with the ability to retroactively inhibit a response being the most advanced skill given that it was not fully developed by the age of 12, which is the oldest age studied. A subsequent study by Becker, Isaac, and Hynd (1987) showed similar results, which suggested that children were not able to function at the level of adults by age 12 when using the same tasks noted in Passler, Isaac, and Hynd (1985) above. Chelune and Baer (1986) used the WCST to measure the progression of EF skills. They reported notable improvements between 6-10 years of age, with adult-level skill exhibited by age 12. Interestingly, children at the age of 6 had performances similar to adults with frontal lobes lesions. Others have shown adult-like performance on the Tower of Hanoi, a planning task, emerges at various ages ranging from 6-12 years of age (Anderson et al., 2001; Korkman et al., 2001; Welsh et al., 1991). Espy (1997) reported that a computerized task that measured inhibition and shifting of mental set is useful when investigating EF in a sample of young children given that they are typically capable of these functions. In addition, Senn, Espy, and Kaufmann (2004) showed that, in a sample of children 2-6 years of age, inhibition was more likely to be influencing performance on problem solving tasks at the younger end of the age

range, whereas working memory was more important in older preschool-aged children. This suggests that various types of measures may measure different EF abilities at different ages. This is an important factor in that children may use different subskills of EF in order to complete problems rather than solving them with the same level of skill and with the same subskills as an adult. Although researchers have shown that children reach adult-like levels of EF at differing ages, depending upon the task, most attain some of these skills (i.e., inhibition and working memory) by the time they enter school at approximately age 6 (Welsh, Pennington, & Groisser, 1991).

Along with other researchers at the time, Levin and colleagues (1991) changed the way that tests were administered by implementing a "battery model," involving the consistent administration of a range of tasks that tap different dimensions of EF; this allowed for the ability to test different relationships amongst various measures and across time. They used a cross-sectional design to study 52 typically developing children and adolescents in three different age groups: 7-8 years, 9-12 years, and 13-15 years. All children were given the same EF tests measuring verbal and design fluency, memory, problem solving and concept formation, and response modulation in order to monitor the developmental progression through childhood. The researchers used principal component analysis on a small sample of children and identified three unique factors: semantic association/concept formation, impulse control/mental flexibility, and problem solving. Each of these factors showed incremental growth across time, and all three factors reached the same level as adults by 12 years of age.

A sample of typically developing children, aged 3-12 years, was evaluated using a range of different EF measures to further investigate the developmental gains associated with EF (Welsh, Pennington, & Groisser, 1991). Much like the aforementioned studies, they found that

certain executive functions emerged earlier than others in a “stage-like” fashion. They proposed three different developmental stages beginning at ages 6 (ability to focus), 10 (organized search/impulse control), and a “final spurt” around 12 years of age (verbal fluency, motor sequencing, and planning). Further analysis concluded that three separate factors existed: response speed, use of hypothesis testing/impulse control, and planning. Brocki & Bohlin (2004) further supported the idea that there are 3 discrete stages of frontal lobe maturation: early childhood (6-8 years), middle childhood (9-12 years), and the beginning of adolescence.

More recently, Jurado & Rosselli (2007) provided further evidence for the progressive development of EF skills throughout childhood and even into adulthood. The authors suggested that the first EF skill to emerge in young children is capability to inhibit inappropriate behavior at age 6, and the last EF skill to mature is verbal fluency. Set shifting was well developed by age 9, planning improved greatly by age 11, and perseverative errors were significantly diminished by age 12. They also supported the idea that advances in EF skills map onto the structural maturation of the frontal lobe, as well as its connections to supporting brain regions, given that all executive abilities improved with age from infancy to childhood with mastery of most skills assessed in early adolescence.

Neuroimaging research has demonstrated that younger children have more diffuse activation of the prefrontal cortex, which is hypothesized to be due to a lack of cognitive resources to organize, monitor, and plan actions, as well as inhibiting certain behavioral responses (Luciana & Nelson, 2002). Higher-order EF skills likely require the recruitment of widespread areas of the brain in younger children, whereas older children may be tapping into more specific areas of the prefrontal cortex, depending on the demands of the EF task (Luciana & Nelson, 2002). Skills such as working memory (Conklin et al., 2007; Huizinga, Dolan, & van

der Molen, 2006) and set shifting (Kalkut et al., 2009) continue to mature to adult-like levels into and through adolescence as the interconnections of the brain continue to strengthen.

The frontal lobe develops rapidly with age beginning in early childhood and continuing into early adulthood, although the rate at which it develops slows from adolescence into adulthood (Romine & Reynolds, 2005). Giedd and colleagues (1999) reported that several cross-sectional pediatric neuroimaging studies of individuals ages 4-20 have shown a decrease in gray matter of the cortex linearly with age with a concurrent increase in white matter. These changes to the cortical gray matter were specific to lobes of the cerebral cortex with the frontal and parietal lobes reaching maturation at approximately age 12, the temporal lobe at approximately age 16, and the occipital lobe at age 20.

Executive Functioning & Brain Pathology

According to Lezak (1993b), executive dysfunction is a characteristic of numerous pathologies resulting from brain lesions to the frontal, subcortical, and limbic regions (Goldberg & Bilder, 1987; Lezak, 1994). Difficulties with EF have been found in various psychopathologies such as antisocial personality disorder, schizophrenia, autism spectrum disorder, and attention-deficit/hyperactivity disorder (Hanes et al., 1996; Mash & Barkley, 2003; Pennington & Ozonoff, 1996). This brought about the "discriminant validity problem," which attempted to make sense of why different behavioral disorders share difficulties characteristic of EF (Pennington, Bennetto, McAleer, & Roberts, 1996). Researchers came to the conclusion that the specific EF deficiencies varied across the different behavioral disorders (Denckla, 1996; Ozonoff & Jensen, 1999). Moreover, posterior association cortices such as the left superior parietal gyrus are also implicated in EF, which indicates that other areas of the brain besides the frontal lobe are likely involved in higher-order processing whether directly or indirectly via

frontal-parietal connections (Jurado & Rosselli, 2007). Hence, the various disorders could present with executive dysfunction for different reasons. This contributes to the heterogeneous nature of psychopathologies in terms of cognitive, behavioral, and EF dysfunction.

Overall, research supports the idea that EF is a multi-factorial construct, which is comprised of various subskills that develop at different rates throughout childhood and into young adulthood. The differences in timing are often related to the acquisition of skills that are used as building blocks for higher level cognitive functions. These functions arise from the frontal lobes and other supporting areas due to the interconnectivity of these areas of the brain. For example, improvements in the areas of language, memory, and processing speed help to enhance the overall performance of the frontal region on EF tasks. It is important to continue researching the relationship between brain structure and function in order to better understand the development of EF in children. Although deficits in EF are common in other childhood psychiatric disorders, much attention has been given to the role of EF as a primary deficit in attention-deficit/hyperactivity disorder (ADHD; Barkley, 1997; Berlin, Bohlin, & Rydell, 2003). Specific EF deficits related to ADHD will be outlined in greater detail in the subsequent section.

Attention-Deficit/Hyperactivity Disorder

Diagnosing Attention-Deficit/Hyperactivity Disorder

Attention-Deficit/Hyperactivity Disorder (ADHD) is a persistent, pervasive, and impairing neurodevelopmental disorder that is characterized by developmentally inappropriate levels of inattention and/or hyperactivity/impulsivity (APA, 2000). Prevalence estimates have shown that ADHD affects approximately 3-7% of school-age children, making it one of the most common reasons for clinical and educational referrals in the United States (APA, 2000; Gordon et al., 2006; Nigg, 2006). A recent meta-analysis of approximately 100 studies suggested that

the worldwide prevalence rate for children and adults is estimated at 5% (Polancyzk et al., 2007). The Diagnostic Statistical Manual—Fourth Edition (DSM-IV; APA, 1994) breaks the diagnostic category of ADHD down into three subtypes: Predominantly Inattentive Type (PI), Predominantly Hyperactive-Impulsive Type (H/I), and Combined Type (C). According to the DSM-IV, a diagnosis of either ADHD-PI or ADHD-H/I is warranted if a minimum of six out of nine symptoms are endorsed in either symptom category (Inattentive or Hyperactive/Impulsive); ADHD-C is diagnosed when individuals meet criteria for both the PI and H/I subtypes. An example of a statement endorsed with regard to inattention is "Often has difficulty sustaining attention in tasks or play activities." A statement with regard to hyperactivity/impulsivity states "Is often 'on the go' or often acts as if 'driven by a motor'." In order to meet DSM-IV criteria, the onset of symptoms must be observed prior to the age of seven. However, the identification of children with hyperactivity/impulsivity is more easily done prior to this age because these behaviors are more overt than the more covert inattentive symptoms. The onset of these symptoms is also earlier than inattentive symptoms when taking a dimensional approach (Barkley & Biederman, 1997), as will be discussed subsequently. Moreover, in order to meet DSM-IV criteria for ADHD, impairment must be present in at least two settings, typically at home and school for children (Mash & Barkley, 2003). Thus, clinicians often combine information from several sources including the affected individual, parents, teachers, and/or medical or mental health providers in order determine if impairment is occurring in multiple settings. Some of the most widely used screening and diagnostic tools for ADHD include the Behavioral Assessment System for Children, 2nd ed. (BASC-2; Reynolds & Kamphaus, 1992); the ADHD Rating Scale, 4th ed. (ADHD Rating Scale-IV; DuPaul et al., 1998); the Conners' Rating Scale-Revised (CRS-R; Conners, 2000); and the Achenbach Child Behavior Checklist

(CBCL), Teacher Report Form (TRF) and Youth Self Report (YSR; Achenbach, 1978). The aforementioned rating scales are multidimensional and provide information that can be linked to the three diagnostic subtypes outlined in the DSM-IV. There are no medical tests to diagnose ADHD; the diagnosis is a behavioral description. While research is underway to develop biological methods to test for ADHD using information gathered from genetic studies and brain imaging studies, behavioral measurement such as that from behavior observations and questionnaires remains the gold standard diagnostic tool at present. Neuropsychological data also can be helpful.

Problems with Using DSM-IV Criteria

Although the DSM-IV is commonly used to diagnose ADHD in children, several problems exist with this tool that should be addressed. First, the characteristics associated with the PI subtype often do not manifest until 8-9 years of age (symptoms of H/I should be present by age 7); however, it is common to use the cutoff of 7 years of age despite the lack of any empirical support for this particular age (Barkley, 1997). The H/I symptoms are more overt, making them easier to identify than PI symptoms, as noted earlier. Second, few children are diagnosed with the H/I subtype past preschool. In fact, most children who are initially diagnosed with the H/I subtype end up exhibiting inattentive symptoms by the age of 8-12, thus meeting criteria for ADHD-C (Barkley, 2003). This leads to the question of whether or not there should even be an H/I subtype. It may be merely an early manifestation of ADHD-C. More research is needed in this area. Given the lack of research support for the ADHD-H/I subtype in the 8-12 age group, only the ADHD-PI and ADHD-C subtypes will be discussed and included in the subsequent analyses.

The next major concern relates to the categorical nature of the DSM-IV, and the fact that

Inattention and Hyperactivity/Impulsivity are likely two different dimensions of behavior and not categorical like the DSM-IV presumes. Consistent with being separable dimensions, research has suggested that children with ADHD-C, who are high on both dimensions, are rated as being more aggressive and are more likely to have comorbid oppositional behaviors. In contrast, children with ADHD-PI, who are only high on Inattention, may have more difficulty in social and academic situations as opposed to conduct problems (Barkley, 2003). Related to the categorical problems, as previously mentioned, children must exhibit six or more symptoms in either subtype in order to warrant a diagnosis of ADHD. This categorical approach fails to address the issue of severity such that a child who exhibits five symptoms but is more impaired on behavioral rating scales would not meet criteria for ADHD, whereas a child who possesses six symptoms, and has an overall milder presentation, would meet criteria. In light of these drawbacks associated with the DSM-IV, it is important to increase the number of diagnostic studies on ADHD using a dimensional approach.

Theoretical Models

Delay Aversion in ADHD. Many models have been proposed to elucidate the potential sources of ADHD. Three neuropsychological theories that are commonly studied and cited include delay aversion, poor state regulation, and executive dysfunction. Children with delay aversion are more likely to choose a smaller, more immediate reward rather than waiting for a larger reward in order to decrease the delay time between action and reward (Sonuga-Barke, Taylor, Sembi, & Smith, 1992). This theory has been shown to hold more promise for describing problems related to hyperactivity/impulsivity than inattention (Castellanos et al., 2006; Thorell, 2007). Deficits on a delay aversion task are thought to generalize to a broader motivational style/deficit (Sonuga-Barke et al., 1992). This theory has support from studies of

brain circuitry, especially the dopamine reward pathway, which involves the basal ganglia, and specifically the nucleus accumbens. It is theorized that children with ADHD who are not able to avoid a delay were "conditioned" to see a delay setting as resulting in a future failure (Sonuga-Barke, Dalen, & Remington, 2003). These children choose to attend to environmental stimuli that subjectively pass time more quickly rather than experiencing an aversive delay interval. Thus, this subset of children prefers to choose immediate rewards rather than waiting for a bigger reward in order to avoid the negative emotions associated with waiting, or perceived failure. Effect size estimates from two separate meta-analyses (Martinussen et al., 2005; Willcutt et al., 2005), with d-values ranging from 0.6-0.8, suggested that delay aversion only accounted for a subset of the cases of ADHD and was not sufficient to be used diagnostically. As such, the delay aversion theory failed to account for the heterogeneity of ADHD; however, it does show more promise in accounting for some of the variance related to H/I symptoms.

Poor State Regulation in ADHD. Two theories of poor state regulation exist in relation to ADHD: one by Douglas (1980, 1983) and the other by Sergeant (2000, 2005). Douglas (1980, 1983) was the first to propose a model of ADHD that did not rely as heavily on deficits in attention or motivation alone. He believed that difficulties in self-regulation were directly related to poor performance in ADHD on tasks involving cognitive components such as processing speed. In 1999, Douglas outlined that a theory explaining the cognitive difficulties in ADHD must take into consideration various aspects including difficulties in attention and response inhibition, a dampened ability to regulate arousal, an atypical response to reward stimuli, and more variable behavioral characteristics including effort and impulsivity. Douglas' theories were the first to attempt to incorporate poor state regulation with the previously studied cognitive deficits in ADHD, including difficulty sustaining attention, response inhibition, and

aspects of memory such as working memory. More recently, Douglas (2008) updated the model to better account for the fact that having better complex "effortful control" processes contributes to improved attentional states and fewer difficulties related to behavioral inhibition in children with ADHD. As defined by Douglas, effortful control is a term that is related to more commonly used concepts of self-regulation and executive function (Martel & Nigg, 2006; Rothbart, Ellis, Rueda, & Posner, 2003). Although much of the research on effortful control is behavioral, some neuroimaging studies have implicated various brain regions. Raichle and colleagues (1994) used PET to demonstrate that novel tasks such as a semantic association task required the involvement of the left frontal and posterior cortex, the anterior cingulate, and the right cerebellum. After rehearsing the paired word associations, activation shifted to the anterior insula, suggesting that attentional processes involved in novel tasks require input from the frontal and posterior regions, whereas more automated tasks do not draw resources from these regions. It is important to note that the poor state regulation model has not been empirically validated likely due to the difficulty defining the construct of self-regulation. However, it shows some promise given that it focuses on many of the deficits seen in ADHD.

Another model, the cognitive-energetic model, originally outlined by Sanders in 1983, was later adapted to describe children with ADHD (Sergeant 2000, 2005) and is similar to Douglas' model of poor state regulation. These deficits could be observed in a research setting by more variable and increased reaction time required to complete a task when compared to controls. The C. E. Model of ADHD addresses three main areas of impairment: 1) difficulties in the cognitive processes of motor output (e.g., a specific behavioral response), with encoding and central processing (e.g., searching for information and selecting a response) remaining intact (Sergeant, 1990); 2) deficits associated with the energetic pools, indicating that children with

ADHD have poor state regulation, which is described as "difficulty in controlling effort, arousal, and activation"; and 3) deficiencies related to EF, including working memory and goal-directed behavior. In general, the poor state regulation theory suggests that children with ADHD have difficulty with recognizing errors that have been made and subsequently fail to assess the error and its ramifications after it occurred. Rather than identifying a single cognitive deficit, the cognitive-energetic theory places more emphasis on "effortful control" and other "regulatory concepts." Sergeant (2000) proposed that the difficulties seen in ADHD break down at the level of the "evaluation mechanism," which is responsible for self-correction. Rodent models used as models for ADHD have implicated mesocortical dopaminergic activity in the frontal cortex (Hendley, 2000).

In summary, both Douglas and Sergeant provide theories related to poor state regulation in ADHD. Douglas (1983, 1999, 2008) has described the main deficit in ADHD as a difficulty in providing sufficient effort in order to complete a task. Sergeant (2000) used the term effort to describe a specific mechanism that is deficient, which breaks down at the level of providing self-correction. Much like the delay aversion theory, the poor state regulation model may provide a better account of hyperactive/impulsive symptoms than inattentive symptoms (Verté, Geurts, Roeyers, Oosterlaan, & Sergeant, 2006). Children with symptoms of hyperactivity/impulsivity may be reacting quickly rather than taking time to focus on the problem and ways to prevent it in the future. Moreover, Barkley (1997) has described ADHD in terms of difficulties with self-regulation. However, in contrast to the theories by Douglas and Sergeant, Barkley claimed that difficulties with behavioral inhibition are central to ADHD, and that poor inhibitory control leads to secondary deficits in certain executive functions, including what he terms "regulation of arousal" and "motivation" (Barkley 1997). Although the aforementioned theories of ADHD all

involve mechanisms of regulatory control, the focus of this paper will be on EF in ADHD as the caudate is implicated in EF. This literature will be outlined in detail in the subsequent section, with particular emphasis on the link between ADHD and poor frontostriatal functioning, which is the focus of this study.

Executive Functioning in ADHD. ADHD is a heterogeneous disorder with multiple contributing factors. One of these factors may be executive dysfunction. A large body of research suggests that ADHD is due in large part to deficits in EF (for a review see Barkley, 1997; Berlin, 2003). However, when researchers used complex neuropsychological measures such as the WCST to test for executive dysfunction, results showed that approximately 30% of individuals with ADHD exhibited these deficits (Biederman et al., 2006). Despite this, Barkley and colleagues (Barkley, 2006; Barkley, 1997; Barkley, Murphy, & Fischer, 2008) and Brown (2000, 2006) have argued that EF deficits are characteristic of all individuals with ADHD. Poor frontostriatal functioning is likely the cause of EF problems in children with ADHD (see Barkley, 2006 for a review). According to Pennington & Ozonoff (1996), the results of a meta-analysis of eighteen studies, which included 60 EF tasks, showed that children with ADHD (PI and C) had more difficulty with 67% of EF tasks measured, especially those involving motor/response inhibition, when compared to children with autism, conduct disorder, and controls. In this study, the children with ADHD did not outperform the control sample on any measures of EF. In a separate study, approximately 35-50% of children and adults had EF deficits on traditional neuropsychological measures, but this number rose to 86-98% when a questionnaire addressing EF deficits was used (Barkley, 2011c). Even though Barkley and colleagues and Brown argue that EF deficits are present in most, if not all, individuals with ADHD, Nigg and colleagues (2005) reported that EF may be spared in approximately 20% of

children with ADHD. Thus, more work on the prevalence of executive dysfunction in ADHD is necessary. Lastly, limited research on sex differences in executive functioning exists; however, when comparing boys and girls with ADHD, there are no differences in executive dysfunction (for a review see Gershon, 2002; Houghton et al., 1999).

Other studies have reported similar findings of children with ADHD performing worse than controls on EF tasks. Shallice and colleagues (2002) found that children with ADHD (subtype not specified) did worse on measures of interference (Number Stroop Task), commission and omission errors (Sustained Attention Reaction Time), working memory (N-Back Working Memory Task), and problem-solving tasks (Junior Brixton Spatial Rule Attainment Test). In another study, Spanish-speaking children with ADHD, ranging in age from 7 to 12, had difficulties on measures of problem solving and had higher rates of perseveration on the WCST (Cepeda, Cepeda, & Kramer, 2000). Similarly, Pineda (1998) showed that boys with ADHD performed worse on EF tasks such as the WCST, the Controlled Oral Word Association Test (COWAT), which is a measure of verbal fluency, and the Picture Arrangement subtest of the WISC-R when compared with control boys. Another study done by Marzocchi and colleagues (2008) reported that children with ADHD had difficulties with interference control on the Test of Everyday Attention for Children-Opposite Worlds (TEA-Ch; Manly, Robertson, Anderson, & Nimmo-Smith, 1998) when there was interference (i.e., performing an attentional control/switching task), but "prepotent and ongoing response suppression" was spared. This suggests that claims of deficient response inhibition in ADHD may reflect a more generalized deficit in attention and cognitive control, which was impaired in children with ADHD on the TEA-Ch task and is supported by a recent meta-analysis (Alderson, Rapport, & Kofler, 2007). In addition, Marzocchi and colleagues also reported that children with ADHD had deficits

related to visual working memory, planning, cognitive flexibility, and phonetic fluency compared to controls. In comparison, children diagnosed with developmental dyslexia were only impaired on measures involving phonetic fluency. The authors found that children with ADHD did worse than those with developmental dyslexia on planning measures. Unlike the first two theories (delay aversion and poor state regulation), several studies have shown that deficits in cognitive aspects of executive functioning are more often found in children with inattention rather than those with predominantly hyperactive/impulsive symptoms, being linked to the inattention dimension (Castellanos et al., 2006; Chhabildas, Pennington, & Willcutt, 2001; Thorell, 2007; Willcutt et al., 2005). Moreover, the study by Chhabildas and colleagues suggests that there are not distinct neuropsychological profiles between children with ADHD-PI and ADHD-C as both present with inattention, which is linked with cognitive deficits often found in the disorder.

Studies of the central executive component of working memory have been mixed to date. Roodenrys, Koloski, and Grainger (2001) reported that children with comorbid ADHD (subtype not specified) and developmental dyslexia were outperformed by children with dyslexia alone and controls on measures of the central executive, suggesting the deficit in central executive was specific to ADHD. Karatekin (2004) and Martinussen & Tannock (2006) found similar impairments in central executive functioning in children with ADHD (PI & C) compared to controls. In contrast, Kibby & Cohen (2008) reported that verbal working memory and long-term memory were intact in ADHD but found deficits in visual-spatial short-term memory. In addition, children with developmental dyslexia showed deficits in verbal short-term memory (specifically related to poor phonetic coding), but not the central executive, visual short-term memory, or long-term memory.

In terms of other tasks, some research suggests that the WCST is a useful tool to measure problem solving and set shifting skills in children with ADHD (Li et al., 2008; Romine et al., 2005; Vaurio, Riley, & Mattson, 2008). In contrast, other studies have found that the WCST is ineffective at distinguishing between children with and without ADHD (Weyandt et al., 1998). Schmitz and colleagues (2002) suggest that adolescents with different ADHD subtypes perform differently on the WCST such that children with ADHD-C, but not ADHD-H/I, perform worse than controls. Culbertson & Zillmer (1998) measured the construct validity of the Tower of London (TOL), an EF task used to measure planning, in children with ADHD. They found that this subtest loaded best onto the Executive Planning/Inhibition factor out of the four factors extracted. Nigg and colleagues (2002) reported that children with ADHD-C had greater difficulty with the TOL task compared to those with ADHD-PI and controls. Recently, a genetic study done by Karama and colleagues (2008) showed differences in the genotype of the dopamine transporter when investigating a group of 196 children with ADHD using the TOL to measure planning. More specifically, children with the 9/10 genotype had more difficulties on the TOL compared to those with the 10/10 genotype. In contrast, two studies using the TOL failed to show differences between children with and without ADHD (Houghton et al., 1999; Sonuga-Barke et al., 2002). The Tower of Hanoi (TOH), another measure of planning, is another common neuropsychological measure used; however two studies using the TOH failed to show a difference between children with and without ADHD (Sonuga-Barke et al., 2002; Weyandt et al., 1998).

Limitations of Research Investigating Executive Functioning

Barkley (1997) brought to light the fact that researchers either failed to note which subtype of ADHD their participants with ADHD had or lumped them together into the same

group rather than dividing them into the PI and C subtypes (Berlin et al., 2003; Cepeda et al., 2000; Pennington & Ozonoff, 1996; Pineda et al, 1998; Shallice et al., 2002). Barkley himself studied children with ADHD-C but not the other subtypes. This missing information or aggregation across subgroups may account for the discrepancy in results reported on EF in children with ADHD. Differences in the severity of ADHD symptoms, as well as age due to developmental changes in brain maturation, also may add to the variability in the reported results of EF in ADHD. Another limitation in the field is the tendency for researchers to study males in the studies of ADHD. In the future, more studies of children with the PI subtype and girls with both subtypes are needed.

Cognitive, Behavioral, and Emotional Deficits in ADHD subtypes

Research has shown that the ADHD-PI and ADHD-C subtypes may differ in cognitive, behavioral, and emotional functioning (Castellanos & Tannock, 2002), as well as age of onset and gender breakdown. In one study with only female participants, children with ADHD-C had more errors of commission and omission on the Conners' Continuous Performance Test compared to those with ADHD-PI (Hinshaw, 2002). Solanto and colleagues (2007) investigated 34 children with ADHD-C, 26 children with ADHD-PI, and 20 typically developing controls on various measures of neurocognitive functioning to better understand the differences between subtypes. The domains studied included attention, learning, and executive functioning. They reported that, after co-varying for IQ, results from the Continuous Performance Test, which measures sustained attention and impulsivity, and the Tower of London, a measure of planning, differed by subtype such that children with ADHD-C performed worse than those with ADHD-PI and controls. In contrast, the participants with ADHD-PI had more difficulty on the Processing Speed Index of the WISC-III than those with ADHD-C. There were no group

differences in terms of learning and working memory when using the Buschke Selective Reminding Test and measures developed by Posner and Sternberg. In contrast, a study by Bauermeister and colleagues (2005) did not find any significant cognitive, behavioral, or emotional differences between subtypes or when compared to typically developing children on measures of attention, inhibition, externalizing behavior, child-related family stress, and social impairment. Both the PI and C subtype were impaired on measures of academic achievement, and the children with ADHD-PI were described as having a more "sluggish cognitive tempo" than children with ADHD-C and controls.

More recently, a study investigated the differences in executive functioning in a sample of children with ADHD (PI and C), Asperger's Syndrome, and typically developing controls (Semrud-Clikeman et al., 2010). Results showed that children with ADHD-C and Asperger's Syndrome exhibited greater difficulty with behavioral regulation and emotional regulation compared to the ADHD-PI and control groups. The problems with emotional regulation replicated previous findings (Mahone & Hoffman, 2007; Martel & Nigg, 2006). Behaviorally, the authors reported that children with ADHD-PI were rated as being more lethargic and having a higher tolerance for frustration, which was also consistent with a previous study on this topic (Martel & Nigg, 2006). Children with symptoms of hyperactivity and impulsivity had more difficulty with set-shifting and behavioral inhibition as compared to the ADHD-PI and control groups. In addition, research has demonstrated that difficulties with behavioral regulation and higher levels of impulsivity were related to sex differences such that boys with ADHD-C were more impaired on a stop task compared to boys with ADHD-PI. No such differences were found in females (Nigg et al., 2002).

Overall, the differences between ADHD subtypes suggest that individuals with ADHD-C

have more difficulty with inhibitory control on the stop-signal reaction time task (Nigg et al., 2002), have more errors of commission and omission on the Continuous Performance Test (Hinshaw, 2002; Huang-Pollock, Nigg, and Halperin, 2006), have greater difficulties with set-shifting tasks such as the WCST (Schmitz et al., 2002), and have difficulties with behavioral/emotional regulation (Semrud-Clikeman et al., 2010). In contrast, individuals with ADHD-PI may have greater difficulty completing tasks quickly that measure processing speed such as a visual-motor or visual search task and nonverbal and verbal fluency (Chhabildas et al., 2001; Lane, 2004; Nigg et al., 2002). Nonetheless, research by Bauermeister and colleagues (2005) and Martel and Nigg (2006) suggests that ADHD-PI & C are similar on cognitive executive functioning tasks, only differing on measures of behavioral inhibition. It is clear that more research is needed in this area.

Biological Factors Associated with ADHD

Family-based studies, including twin and adoption studies, suggest high heritability estimates in MZ and DZ twins and first-degree biological relatives with ADHD (Thapar, Langley, Owen, & O'Donovan, 2007). Recent studies of children and adults with ADHD-PI and ADHD-C report heritability estimates ranging from 0.3 to 0.8 for DZ and MZ twins, respectively (Haberstick et al., 2008; Heiser et al., 2006; Polderman et al., 2006). Results from these studies show that genetic influences had moderate effects on a given population's risk; however, environmental factors also play a role in the development of ADHD symptomatology. In addition, both subtypes had similar genetic contributions, and there were no differences between males and females. Results from adoption studies have shown consistent results to the twin studies, suggesting that adopted children were less similar to their adoptive parents than they were to their biological parents (Alberts-Corush et al., 1986; Cantwell, 1975; Cunningham et al.,

1975; Sprich et al., 2000). Molecular genetic studies attempting to identify susceptibility genes have shown promise in isolating certain genetic contributors. A recent meta-analysis by Li and colleagues (2006) showed an association with a variant in the dopamine D4 and D5 receptor genes in individuals with ADHD (results were collapsed across subtypes). The dopamine transporter (DAT1) also has been implicated (Hawi et al., 2010), but the results from meta-analyses are variable (Palmer et al., 1999). These genetic findings in ADHD provide further evidence for involvement of the frontostriatal circuit, which is rich in dopamine connections and the target of many stimulant medications (Lacey, Mercuri, & North, 1990). The frontostriatal circuit will be discussed in greater detail in a later section.

Comorbidity Between ADHD & Learning Disability

Children with ADHD often have difficulties that adversely affect several areas of daily functioning including peer and family relationships, self-esteem, self-confidence, and academic performance (Bailey & Owens, 2005). In fact, the majority of children with ADHD have academic problems as evidenced by their lower scores on standardized tests when compared to same-age children despite having at least average intelligence (Mash & Barkley, 2003). Academic demands, including focusing for extended lengths of time without breaks and sitting still in one's chair, may prove difficult for children with ADHD-PI and ADHD-C. Studies have shown that academic difficulties may go beyond the impairments caused by ADHD symptoms alone, and may be compounded by the difficulties resulting from a comorbid learning disability. In fact, children are more likely to receive a comorbid diagnosis of ADHD and developmental dyslexia than one would expect given prevalence rates for either disorder. Specifically, 25-40% of children with ADHD also have developmental dyslexia (Dykman & Ackerman, 1991; Semrud-Clikeman et al., 1992), while 15-35% of children with developmental dyslexia also have

a diagnosis of ADHD (Gilger, Pennington, & DeFries, 1992; Shaywitz, Fletcher, & Shaywitz, 1995; Willcutt & Pennington, 2000). In addition, nearly 80% of children who were more than two grades behind their peers on measures of academic performance had ADHD and a learning disability. Of those children, 16-39% had a Specific Learning Disability in Reading (Mash & Barkley, 2003). Given the high comorbidity between these two common and impairing childhood disorders, with both having elements of cognitive dysfunction, there is evidence to suggest that there may be shared neurobiological links that underlie these disorders (Willcutt et al., 2005).

When evaluating the sex differences within each group, it is important to note that boys are more likely than girls to be diagnosed with each disorder, which is not surprising given the high comorbidity between ADHD and developmental dyslexia. In fact, boys are four to nine times more likely to be diagnosed with ADHD than girls in clinical samples (APA, 1994). At the subtype level, boys were more likely to be diagnosed with ADHD-C than PI, whereas girls were more likely to be diagnosed with ADHD-PI than C. Hawke, Olson, Willcutt, Wadsworth, and DeFries (2009) reported that sex differences in developmental dyslexia vary widely depending on the referral source, and range from approximately 1:1 to 15:1 (males: females) in research and clinic-referred populations, respectively. Sex ratios seem to be higher when symptom severity is greater (Rutter et al., 2004). Willcutt & Pennington (2000) reported that the comorbidity between ADHD and developmental dyslexia was higher in children with ADHD-PI than ADHD-C. Follow-up analyses by these authors investigated the potential influence of sex differences and showed that developmental dyslexia was significantly associated with inattention in both girls and boys, but it was associated with the hyperactivity/impulsivity subtype only in boys. Overt hyperactive and impulsive behaviors in boys with developmental dyslexia are likely

to cause more problems in school and lead to more clinic referrals than the more covert, inattentive behaviors (Barkley, 1997).

Executive Functioning in Comorbid ADHD/Developmental Dyslexia

Studies of executive functioning, measured through the use of neuropsychological test batteries, have shown that individuals with ADHD/developmental dyslexia are impaired on measures of working memory such as mental arithmetic, as well as spelling and reading (Kibby & Cohen, 2008). They found that children with comorbid ADHD/developmental dyslexia had working memory deficits consistent with both disorders as mentioned in each of the separate ADHD and developmental dyslexia sections (i.e., reduced verbal short-term memory in developmental dyslexia and reduced visual-spatial short-term memory in ADHD). In general, studies tend to find that those with ADHD/developmental dyslexia present with deficits consistent with both ADHD and developmental dyslexia (de Jong et al., 2009; Pennington, 2006), as noted subsequently.

Double Dissociation Model of ADHD and Developmental Dyslexia

Since ADHD and developmental dyslexia diagnoses are comorbid with each other in an estimated 15-40% of the cases as previously mentioned, it is important to investigate the overlapping and dissimilar neuropsychological deficits that are found between the two disorders. Originally, Pennington, Groisser, and Welsh (1993) described the impairment between ADHD and developmental dyslexia as a "double dissociation." In this case, children with ADHD and developmental dyslexia were believed to show distinct profiles in two neuropsychological domains, "each of which is hypothesized to be central to one disorder and not the other" (p. 512). ADHD was found to be associated with lower scores on EF measures, and developmental dyslexia on phonological measures. In addition, it is important to note that the developmental

dyslexia group did not differ from the control sample on measures of EF, and the ADHD group did not differ from the control sample on measures of phonological skills. Consistent with this, the two disorders may share some etiologies, as noted in the subsequent section. As the comorbidity does not appear to be greater than 40%, there are likely dissimilar etiologies as well. Relatedly, a study done by Willcutt and colleagues (2001) showed that the comorbid group performed worse than the ADHD only and developmental dyslexia only group on all the measures of EF used in their study, including set-shifting, inhibition, and working memory, along with phoneme awareness. The ADHD only group showed impairments on measures of inhibition on the Continuous Performance Test (Rosvold et al., 1956) and the Stopping Task (Logan & Cowan, 1984), and speeded verbal naming, but not interference from the Stroop Color and Word Test (Golden, 1978); the developmental dyslexia only group performed poorly on phoneme awareness tasks (Pig Latin Test; Olson et al., 1989; Phoneme Deletion Task; Olson et al., 1994; Lindamood Auditory Conceptualization Test; Lindamood & Lindamood, 1971); and the comorbid ADHD/developmental dyslexia group was most notably impaired on measures of set shifting (WCST; Heaton, 1981; Contingency Naming Test; Taylor, 1988) and verbal working memory (Sentence Span task; Siegel & Ryan, 1989; Counting Span task; Case, Kurland, & Goldberg, 1982).

More recently, Willcutt and colleagues (2005) reported an unexpected result that both ADHD and developmental dyslexia were associated with deficits on an orthographic coding measure. They also reported that both ADHD only and developmental dyslexia only groups had difficulty with tasks that measured verbal working memory; however, the ADHD only and developmental dyslexia only groups did not differ on measures of response inhibition, processing speed, or set shifting. Overall, the developmental dyslexia only group had deficits in verbal

working memory, processing speed, and response inhibition; the ADHD only group had deficits in response inhibition, processing speed, some reading measures, and verbal working memory; and the ADHD/developmental dyslexia group showed deficits from both the ADHD only group and the developmental dyslexia only group. Slow and variable processing speed was evident in all three groups, and the authors highlighted the need for more research on this shared deficit.

When studying ADHD/developmental dyslexia groups, Purvis & Tannock (2000) suggested that the nature of the co-occurring deficits in this disorder is additive and not more extreme than what one would expect from each disorder alone, suggesting that ADHD/developmental dyslexia is a comorbid condition of both rather than a separate disorder or subtype. In only one instance the comorbid ADHD/developmental dyslexia group performed worse than would be expected from deficits associated with each disorder alone when found together. In this case, children with both disorders had more errors of omission on the Continuous Performance Test. On all other measures, the comorbid group showed deficits in an additive way. Overall, Purvis & Tannock concluded that there should not be a distinct category for children with comorbid ADHD/developmental dyslexia, as it is likely not a separate diagnosis or subtype. Another study by Willcutt and colleagues (2001) reported that ADHD was most likely associated with deficits related to response inhibition, whereas individuals with developmental dyslexia tended to have deficits related to phoneme awareness and verbal working memory. They found that the comorbid ADHD/developmental dyslexia group was impaired on nearly all of the measures of phoneme awareness and EF that were included in their study, but the deficits were additive. Willcutt and colleagues also found evidence to support the hypothesis that the ADHD/developmental dyslexia group has deficits consistent with both disorders, but it is not a separate disorder. More specifically, they showed that children with

comorbid ADHD/developmental dyslexia had more deficits related to inhibition, working memory, and naming letters and numbers than children with each disorder alone. They did not have any additional deficits, however.

Overall, individuals with comorbid ADHD/developmental dyslexia are impaired in several abilities including processing speed (Rucklidge & Tannock, 2002; Tannock et al., 2000), and EF domains such as verbal working memory (Willcutt et al., 2003), cognitive flexibility (Weyandt et al., 1998), planning (Klorman et al., 1999), and response inhibition (Purvis & Tannock, 2000; Willcutt et al., 2003). The conclusion on whether or not the comorbid ADHD/developmental dyslexia group is a separate disorder is not complete. Some studies showed that there were unique impairments seen in the comorbid group (Pennington et al., 1993), whereas others have shown that ADHD/developmental dyslexia does not appear to be a separate disorder (Seidman et al., 2001; Willcutt et al., 2001). The bulk of the literature supports the latter point of view. More research is needed in this area to determine if the measures being used in the studies are sensitive enough to detect if there is a significant interaction between ADHD and developmental dyslexia.

Shared Contributors to ADHD & Developmental Dyslexia

Given that both disorders are polygenetic, multi-factorial, and tend to be highly comorbid, it is not surprising that they may share common contributors. Prior research has implicated processing speed specifically as the shared cognitive deficit that underlies the comorbidity between these two disorders. In these studies, children with either disorder require an increased amount of time to complete tasks with a "speeded component" (Shanahan et al., 2006; Willcutt et al., 2005). Shanahan and colleagues found that processing speed deficits were underadditive in the comorbid group (i.e., deficits were not as impairing as one might expect

given the impairments in processing speed in each group alone) and when it was partialled out, the relationship between ADHD and developmental dyslexia weakened. These studies suggest that processing speed may be one of the shared contributors to both disorders. Given the polygenetic/multifactorial nature of both disorders, there are likely others as well.

Underlying structural abnormalities in the brain also may be responsible for the comorbidity between the two disorders, which would lead to the disruption of the corresponding cognitive functions that the disorders share (Ramus, 2004). Biological risk factors for both disorders include family history of ADHD and/or developmental dyslexia, particularly in first-degree biological relatives, increasing the likelihood that offspring are diagnosed with either or both disorders (Mash & Barkley, 2003). Given the comorbidity between these two disorders, it is possible that there is an overlap in affected areas of the brain including the temporal, parietal, and/or frontal lobes. Specific brain regions that are implicated in these disorders will be discussed in more detail in a later section. Furthermore, as noted previously, cognitive deficits of those with comorbid ADHD/developmental dyslexia typically are additive and include those of both ADHD, described earlier, and developmental dyslexia, which will be described in more detail subsequently.

Developmental Dyslexia

Diagnosis

According to the DSM-IV, Reading Disorder is characterized by reading achievement, as measured by accuracy, speed, and/or comprehension, that falls below what is expected given an individual's chronological age, measured intelligence, and education level. Most researchers, however, use the medical term, "dyslexia," and focus at the word level on the inability to identify words. The definition of dyslexia has evolved over time beginning with the label of "word

blindness" in the late 1800s, to being known as "minimal brain dysfunction" in the 1960s, to a more heterogeneous disorder often called "specific reading disability" that varies by type and severity (Doris, 1993; Gillon, 2004; Hammill, 1990). The definition has changed over time from being more of an exclusionary one to a more inclusionary one. In 1968, the World Federation of Neurology defined dyslexia as "a disorder manifested by difficulties in learning to read despite conventional instruction, adequate intelligence, and socio-economic opportunity. It is dependent upon fundamental cognitive disabilities, which are frequently of constitutional origin" (Critchley, 1970, p. 11). A broadening of the diagnosis in the DSM-IV has allowed for the inclusion of children with speech/language impairment and other cognitive deficits, which may add to or intensify a reading disability. As the definition stands, a discrepancy between IQ and reading achievement cannot be due to sensory problems or mental retardation (APA, 2000).

Discrepancy Diagnosis and the Poor Reader Definition of Developmental Dyslexia

Until recently, a diagnosis of a learning disability in the school system required a discrepancy between IQ and achievement as outlined in the Individuals with Disability in Education Act (IDEA) in 1977 (Fletcher et al., 2002). Shaw and Cullen (1995) have criticized the discrepancy definition because it does not consider agreed upon cognitive deficits associated with reading difficulty including poor phonological processing. Arguments against the use of the discrepancy definition are four-fold: 1) Clinicians who are not adequately trained or are restricted by time or money to administer only a limited number of measures may put too much weight on the IQ and/or achievement scores. The problem with the limited assessment is that it may not be capturing a good measure of the individual's IQ or reading ability with fewer tests, making the problem go from bad to worse. A proper diagnosis includes a well-rounded battery of cognitive tests, information gathered from interviews and parent and/or self-report

questionnaires, and an overall conceptualization based on behavioral observations during the test administration. 2) A related criticism of the discrepancy diagnosis is the limited measurement of areas underlying reading ability actually assessed in most diagnostic assessments. Specifically, the literature supports poor phonological awareness as a core deficit in developmental dyslexia (Lyon et al., 2003), as well as difficulties with rapid automatized naming (Wolf & Bowers, 1999), deficits in verbal working memory (Rucklidge & Tannock, 2002), and reductions in short-term storage capacity for phonological material (Kibby et al., 2004; Roodenrys et al., 2001); however, these components are not taken into consideration when making a formal diagnosis of developmental dyslexia. 3) Poor readers with below average IQ may not meet IQ/achievement discrepancy criteria, but they are still having significant difficulty with reading and need help; this is the nature of the bell curve. 4) Relatedly, and arguably the most important, the requirement of an IQ discrepancy can be detrimental to the student in need of reading remediation. They are functioning below average in reading, but do not meet discrepancy criteria due to below average IQ. Moreover, research has shown that IQ scores and the use of IQ discrepancy were not related to long-term outcomes in learning disabilities (Fletcher et al., 2002). In 2004, four reports on special education were filed to petition to reduce the severity of the definition with the following stipulations: not requiring an IQ discrepancy as well as the option to not include a measure of IQ as part of the diagnosis process, allowing research-based definitions as an option, and allowing States to include response to instruction (RTI) criteria as part of the identification process. The RTI criteria allowed for a more prevention-focused approach via RTI rather than a “wait to fail” approach afforded by traditional diagnostic approaches, which was the default condition used in many schools.

Along with this change in the IDEA definition in 2004, there has been a move to use the

"poor reader" definition of dyslexia. Children who are identified as having reading problems, regardless of their IQ score, often exhibit difficulties in phonological processing, short-term and working memory, and "syntactic awareness" (Siegel, 1992). Siegel argued that, based on these findings, there was no reason to separate individuals with dyslexia meeting the IQ discrepancy requirement from "poor readers." One obvious benefit to the use of low achievement scores alone for diagnosis was that it allowed for more individuals who struggled with reading to receive appropriate services despite not meeting the requirement for the IQ discrepancy.

Nonetheless, those who argue against the use of a "poor reader" definition stated that there are fundamental differences between the groups of children who meet the discrepancy criteria and those who are simply poor readers (Bishop & Snowling, 2004; Fawcett, Nicolson, & Maclagan, 2001). Specifically, Fawcett, Nicolson, and Maclagan (2001) reported that children who met criteria for the discrepancy definition had more difficulty on a task of cerebellar functioning than a comparison group of children who were identified as "poor readers" without a discrepancy. Studies such as this argue that there may be underlying neuropsychological differences between these groups. In addition, Bishop & Snowling (2004) reported that a review of the literature indicated that children who met criteria for the IQ discrepancy definition had more difficulty with phonological coding and/or phonological short-term memory than children with specific language impairment and poor readers. These deficits have been shown to be heritable, which implies an underlying biological basis. Similarly, the authors also suggested that milder and less specific forms of developmental dyslexia such as those resulting from the poor reader definition were more likely due to environmental factors including low SES, whereas neurobiological contributors such as genetics are more influential in cases of developmental dyslexia with a discrepancy and phonological impairment and those that are more severe.

Heterogeneity of Developmental Dyslexia

There is substantial evidence to support developmental dyslexia as a dimensional disorder with single word reading being at the tail end of a normal distribution, rather than being a categorical disorder as implied by the DSM-IV definition (Willcutt et al., 2005). The difficulty with disorders that exist on a continuum lies in determining appropriate cutoff points for diagnostic purposes (Shaywitz et al., 1992). Typically, scores that are below one standard deviation from the mean are considered to be aberrant in the "poor reader" definition, whereas a two standard deviation difference between IQ and achievement was required for the discrepancy definition by the DSM-IV. Most states followed IDEA law and required a 1-1.5 standard deviation difference prior to 2004. Stanovich (1988) described developmental dyslexia with the phonological-core-variable-difference model, suggesting that developmental dyslexia, much like ADHD and most other childhood psychiatric disorders, is not an "all-or-none" disorder. There is a core deficit across children with this disorder along with variable additional deficits in some. In developmental dyslexia, the core deficit is believed to be poor phonological processing. Developmental dyslexia is thought to be the most common learning disability, with an estimated 10-17.4% of school-age children being diagnosed (Benton, Pearl, & National Institute of Mental Health (DHEW), 1978). The wide range in prevalence is likely due to the aforementioned fact that there is no clear cutoff point that is agreed upon in the field.

For the purposes of this study, both the IQ-achievement discrepancy and the poor reader definitions will be used for the developmental dyslexia group. Pennington (2009) suggested that researchers may be able to use both definitions given that there is a lack of external validity for the difference between the two definitions, both groups have deficits in phonological processing,

and the discrepancy definition often excludes the individuals who are struggling the most with reading.

Common Deficits

Poor Phonological Processing Model. Research indicates that there are several neuropsychological deficits associated with developmental dyslexia. The most common deficit reported in the literature is difficulties related to phonological processing (Willcutt et al., 2005). Phonological processing is an auditory processing skill, which refers to the "use of phonological information, especially the sound structure of one's oral language, for processing written and oral information" (Wagner, Torgesen, Laughon, Simmons, & Rashotte, 1994, p. 78). Difficulties may manifest through errors in the production of speech (e.g., poor articulation) and/or the inability to perceive phonemes well. Difficulties in phonological decoding are related to the difficulty in breaking down words into their phonemes and then blending them to form words. Understanding the phonological components in a given language is a prerequisite to "basic reading, reading comprehension, spelling, and written expression" (Shankweiler & Liberman, 1989).

Several other deficits associated with developmental dyslexia have emerged in recent studies. Kibby and Cohen (2008) studied a sample of children with ADHD, developmental dyslexia, and comorbid ADHD/developmental dyslexia using the Children's Memory Scale. Results showed that children with developmental dyslexia had greater difficulty with short-term memory tasks requiring verbal rather than visual material. In addition, they showed intact central executive and long-term memory ability. Upon further analysis, the deficits in verbal short-term memory appeared to be related to difficulties in phonetic coding of material. Their short-term memory for material encoded semantically was intact. Martinussen & Tannock

(2006) reported that children with developmental dyslexia and language impairment with or without comorbid ADHD had decreased performance on tasks involving the use of verbal and visual-spatial working memory when compared to controls. This finding suggested that these storage problems were related to reading and/or language problems rather than necessitating the presence of ADHD.

Some children with developmental dyslexia exhibit difficulties with non-phonetic language functioning, including) difficulties in the ability to understand and express language (Scarborough, Dobrich, & Hager, 1991). Those difficulties are more common when the poor reader definition is used (Bishop & Snowling, 2004). Schulz and colleagues (2008) used functional magnetic resonance imaging (fMRI) and event-related potential (ERP) to study semantic and syntactic processing in a small sample of children with developmental dyslexia. Children were classified as being dyslexic if they scored below the 10^{th} percentile on a German orthographic measure. The authors reported that children with developmental dyslexia had decreased activation on the tasks requiring sentence reading (i.e., syntax) in the inferior parietal and frontal regions and decreased activation for semantic processing in inferior parietal regions. Other studies demonstrated deficits in auditory processing, which may involve a disruption in the translation of information presented through auditory pathways (Gaab, Gabrieli, Deutsch, Tallal, & Temple, 2007; McAnally & Stein, 1996; McArthur, Atkinson, & Ellis, 2009; Tallal, Stark, Kallman, & Mellits, 1980). Moreover, developmental dyslexia has been linked to difficulties with the rapid automatic naming of material presented visually called rapid automatized naming or rapid naming (Jones, Branigan, & Kelly, 2009; Semrud-Clikeman et al., 2000; Wolf & Bowers, 2000).

Executive Functioning in Developmental Dyslexia. Many studies on developmental dyslexia do not focus on executive functioning; however, there are a few studies that have mentioned its potential role in this disorder. Specifically, difficulties have been shown in the areas of verbal working memory, set shifting, planning, response inhibition, learning novel sequences, initiation and perseveration, and abstract reasoning in children with developmental dyslexia (Willcutt et al., 2005). Based on the current research, children with developmental dyslexia may have deficits related to cognitive EF tasks such as problem-solving, verbal working memory, planning, set-shifting, and verbal and non-verbal fluency; however, they may not have difficulty with behavioral regulation and inhibition (Asbjornsen, Helland, Obrutz, & Boliek, 2003; Berninger, 2001; Kelly, Best, & Kirk, 1989; Klorman et al., 1999; Willcutt et al., 2001). Other researchers have reported that they may have difficulty with cognitive regulation, which affects planning, self-monitoring, and editing during learning or problem solving (Pressley, Levin, & McDaniel, 1987). Lastly, children with developmental dyslexia may have trouble integrating information and coordinating component skills in order to effectively read the material presented to them (see Meltzer, 1991). One central problem with the inconsistent reporting in the literature of executive dysfunction in children with developmental dyslexia is the lack of uniformity in task selection in published studies (Booth, Boyle, & Kelly, 2010).

A study done by Kelly, Best, and Kirk (1989) used a sample of 12-year-old males with and without developmental dyslexia to investigate whether or not performance on neuropsychological measures of posterior functioning involving the parietal lobes could be differentiated from performance on the typical measures of frontal functioning used to study EF. Results from a discriminant analysis demonstrated that measures of prefrontal functions such as selective and sustained attention, response inhibition, set shifting, and cognitive flexibility

differentiated between the two groups better than measures of posterior functions. This study was one of the earlier ones to postulate that children with developmental dyslexia also may have difficulties in EF, and that the prefrontal cortex is implicated in executive dysfunction.

Klicpera (1983) and Waber and Bernstein (1995) used the Rey-Osterrith Complex Figure in order to measure visual-spatial abilities, memory, planning ability and use of strategy in a sample of children with developmental dyslexia. This task required the participant to reproduce a complicated figure by first copying it and then later recalling it from memory. The authors reported that children with developmental dyslexia were less efficient at completing this task when relying on memory and were less likely to rely on semantics in their approach. Using the same measure, Waber and Bernstein showed that children with developmental dyslexia did not show the same improvements with age based on what would have been expected from a control sample, especially during the time between 7-9 years of age. Interestingly, the children with developmental dyslexia never seemed to catch up, exhibiting 8-year-old levels of functioning even at the age of 14. Based on these results, the authors suggested that planning may be sensitive to age-related brain maturation in children with developmental dyslexia given that these children did not improve to the level of controls by middle childhood.

Several researchers have implicated the central executive to be a source of dysfunction in children with developmental dyslexia. Swanson (1999) used Baddeley's model of working memory (1986) in a study of children with developmental dyslexia and found that these children were impaired on measures of central executive functioning. Others have found similar results (de Jong, 1998; Swanson & Ashbaker, 2000). In contrast, some researchers have shown that the central executive is not impaired in this population. For example, after controlling for deficits in phonological short-term memory, Kibby and colleagues (2004, 2008) found that the central

executive and the visuospatial sketchpad were intact when using Baddeley's model, but the phonological loop was impaired. Roodenrys, Koloski, and Grainger (2001) reported that children with comorbid ADHD and developmental dyslexia had difficulty with verbal working memory tasks, but those with developmental dyslexia only did not. Specifically, they found that children with developmental dyslexia had poor functioning of the phonological loop but were spared on measures tapping the central executive when they did not have comorbid ADHD. Those with comorbid ADHD/developmental dyslexia had deficits on both the tasks measuring the phonological loop and the tasks measuring the central executive.

Everatt, Warner, Miles, and Thomson (1997) found that children with developmental dyslexia had greater difficulty on the Stroop Interference task when compared to a control group. Specifically, this group, comprised of children around 10 years of age, had difficulty inhibiting the response of naming the color in which the word was printed when the text was a different color name (e.g., saying "blue" when the text of the word "red" is printed in blue ink). The responses by these children were more similar to a comparison group of children who were chosen based on similar reading level (i.e., that of an 8-year-old). A study done by Donfrancesco, Mugnaini, and Dell'Uomo (2005) reported that children with developmental dyslexia had deficits in "cognitive impulsivity" when compared to children with a spelling disability on a measure called Matching Familiar Figures Test. The authors concluded that these children behaved much like one would expect a child with ADHD would and suggested that this impairment was likely due to frontal/prefrontal deficits, or executive dysfunction.

Helland & Asbjørnsen (2000) and Asbjørnsen, Helland, Obrzut, and Boliek (2003) used a dichotic listening task in conjunction with measures of EF (WCST and Stroop) and were able to predict a correct diagnosis in 90% of the overall sample and 100% of the sample of 12-year-olds

with developmental dyslexia. This approach only incorrectly predicted the diagnosis for three children in the control group. The groups all had equal difficulty on the dichotic listening task, but the children with developmental dyslexia were more impaired on the Stroop test and the WCST, suggesting that the dichotic listening task was not the best way to differentiate between the groups.

In contrast, some studies have found no difference in the performance of children with developmental dyslexia when compared to controls on measures of EF. For example, McGee, Brodeur, Symons, Andrade, and Fahie (2004) investigated executive functions in children with developmental dyslexia and controls and found no difference in performance on tasks of working memory and the Continuous Performance Test. Furthermore, Swanson, Sáez, Gerber, and Leafstedt (2004) conducted a large-scale study assessing the predictive value of phonological and executive functioning on reading performance. As part of this study, children who scored at least one standard deviation below the mean on a task of word reading were compared to those who scored above this cut-off score on a battery of tasks of working memory and also random generation tasks, which are designed to measure inhibition. No significant difference on task performance was found between these two groups on these measures.

A meta-analysis by Booth, Boyle, and Kelly (2010) attempted to clarify the conflicting literature, noting that some studies reported executive dysfunction in developmental dyslexia, while others reported intact performance on EF measures. With data from 48 studies, an overall effect size of 0.57 was obtained, which suggests that children with developmental dyslexia have moderately impaired performance on EF tasks. The authors reported that the effect sizes varied considerably across studies, however, suggesting that the impairment is not uniform. A moderator analysis demonstrated that the type of task and the use of the IQ-achievement

discrepancy definition of developmental dyslexia influenced the strength of the effect, with those not meeting the discrepancy criteria having a higher mean effect size (i.e., worse performance). The authors note that different types of assessments were used for each definition, and when accounting for the different methodologies, individuals who met the discrepancy criteria did not differ from those who did not, which also has been demonstrated in another meta-analysis using both discrepant and non-discrepant groups (Stuebing et al., 2002). Moreover, age and gender did not have an impact on effect size. This suggests that the variation in effect size may be due to the wide variety of EF tasks used and their varying tasks demands, as well as measures and the definition used for inclusionary purposes.

In summary, children with developmental dyslexia have been shown to have difficulties with EF even without the presence of ADHD symptoms. Working memory deficits have been implicated in developmental dyslexia, and specifically verbal working memory is thought to be important for efficient reading (Kibby, 2009a; Kibby & Cohen, 2008; Snowling, 1991). This deficit in verbal working memory is likely related to poor phonological processing and phonological storage of verbal material; however, semantic coding of material seems unaffected in developmental dyslexia (Kibby et al., 2004; Kibby, 2009a; Kibby & Cohen, 2008; Lee & Obrzut, 1994; Roodenrys et al., 2001). Other EF deficits that have been implicated in developmental dyslexia include problem solving, planning, set shifting, and verbal and nonverbal fluency (Asbjørnsen et al., 2003; Berninger, 2001; Kelly et al., 1989; Klorman et al., 1999; Weyandt et al., 1998; Willcutt et al., 2001). Lastly, given the high comorbidity of ADHD and developmental dyslexia, it is possible that overlapping deficits in EF may be response for some of the shared etiology in these disorders.

Biological Factors Associated with Developmental Dyslexia

Reading problems have been shown to run in families and across generational lines (Mash & Barkley, 2003). Reviews of twin and family studies, gene linkage studies, and studies investigating environmental factors have provided considerable evidence that reading disabilities have a heritable component (Grigorenko, 2001; Pennington, 1999). In fact, children who have parents with a reading problem are eight times more likely to have a reading disability themselves (Pennington, 1999). In fact, children who have parents with reading struggles were 30-60% more likely to be diagnosed with a reading disability than their same-age peers (Grigorenko, 2001). In addition, an estimated 25-60% of parents who had children with reading problems also reported similar difficulties in reading. Fathers were more likely to have endorsed this statement compared to mothers (46% and 33%, respectively). Moreover, evidence from twin studies has demonstrated that monozygotic (MZ) twins had an 80% concordance rate. This was compared to a 50% concordance between dizygotic (DZ) twins. The difference between the rates of concordance between MZ and DZ twins is thought to approximate the heritability of a given disorder. Lastly, gene linkage studies have been used to investigate potential genetic contributors to developmental dyslexia. A few specific locations in the genome have been implicated including chromosome 6, which has been replicated by separate research groups, and 1, 2, and 15, which have yet to be replicated (Grigorenko et al., 1997; Smith, Pennington, Kimberling, & Ing, 1990). These studies support the idea that developmental dyslexia is a heritable disorder with an underlying biological cause.

Frontostriatal Circuitry

Evidence from several research studies indicates that underlying problems associated with a diagnosis of ADHD have been linked to dysfunction in pathways that use dopamine and

noradrenaline (Biederman & Spencer, 1999; Castellanos, 1997; Giedd, Blumenthal, Molloy, & Castellanos, 2001). These pathways, which are thought to be involved with executive functions, are located in prefrontal and subcortical areas, as well as other areas. Two of the most popular psychostimulant medications used to treat ADHD include methylphenidate and amphetamine, which are more commonly known by their trade names as Ritalin, Metadate, Concerta and Adderall (Volkow et al., 2002). The proposed mechanism of action for these stimulants includes increasing the concentration of dopamine in the extracellular space, especially near sites that are abundant in dopamine receptors and transporters, including the striatum (Roman et al., 2004).

The striatum, given its name due to its striped appearance when stained in certain ways, is broken down into two distinct, but highly interrelated, anatomical structures: the caudate and the putamen, which are separated by the internal capsule (see Figure 1). The striatum is believed to mainly receive input from the cerebral cortex via the caudate, with inputs from the frontal, parietal, and temporal lobes, and via the putamen, with inputs from the motor and somatosensory areas. When the globus pallidus, substantia nigra, and subthalamic nucleus are included with these structures, they are together referred to as the basal ganglia (Brodal, 2010). The basal ganglia are part of the extrapyramidal motor system and are linked to several neuronal pathways related to emotion, motivation, and cognitive functioning (Herrero, Barcia, & Navarro, 2002). The interconnections of the basal ganglia structures with the cortex provide a link through which messages related to executive functions are thought to pass. One such circuit is the prefrontal-basal ganglia-thalamic loop outlined by Alexander, DeLong, and Strick (1986), which will be a focus of this project.

Not much is known about the quality of the frontostriatal circuit in developmental dyslexia; however, given the deficits related to executive functioning found in this population, it

is hypothesized that anatomical correlates of executive dysfunction may be found in developmental dyslexia. In addition, frontal lobe size has been shown to be smaller in developmental dyslexia (Filipek et al., 1995; Hynd et al., 1990; Pennington et al., 1999), and the striatum may be affected as well (Brown et al., 2001; Eckert, 2010; Hoeft et al., 2007). The frontostriatal circuit in ADHD and developmental dyslexia will be discussed more thoroughly in later sections.

Caudate Nucleus

The ventral striatum (i.e., nucleus accumbens) is a main target of the limbic frontostriatal circuits, and the dorsal striatum (i.e., caudate and putamen) is the main striatal relay of the frontostriatal circuit, specifically the caudate nucleus. The ventral striatum is typically related to "hot" cognitive processes, whereas the dorsal striatum is linked to "cool" cognitive processes. The caudate nucleus has inputs to and from the prefrontal cortex, parietal and temporal lobes, frontal eye fields, and cerebellum, and to the thalamus via the globus pallidus (Leh et al., 2007; Lehericy et al., 2004). Animal models have shown that lesions to the striatum cause problems with memory and difficulties with tasks requiring response inhibition (Alexander et al., 1986). Several fMRI studies have linked the caudate nucleus with cognitive measures of EF. Activation of the caudate nucleus has been found in planning tasks such as the Tower of London (Beauchamp et al., 2003; Dagher et al., 1999; Rowe et al., 2001; van den Heuvel et al., 2003) and during the WCST (Monchi et al., 2001). Working memory is a very important component in planning tasks, and the caudate nucleus has been found to be active during tasks that require working memory (Manoach et al., 2003). Specifically, the left caudate has been implicated in verbal working memory (Narayanan et al., 2005), whereas the right caudate, especially the body of the right caudate, has been implicated in tasks requiring spatial working memory (Geier et al.,

2007). Lastly, Possin and colleagues (2009) reported reductions in the volume of the caudate nucleus in a population of individuals with neurodegenerative diseases. More specifically, an increase in the number of Rule Violation errors correlated with caudate volume loss bilaterally and the lateral middle and inferior frontal gyri when compared to controls. This suggests that the frontostriatal circuit may be involved in error monitoring.

Neuroanatomic Findings in ADHD

Neuroimaging studies have attempted to better understand the anatomical underpinnings of ADHD. A growing literature supports the integral involvement of the frontostriatal region and the cerebellar hemispheres as likely contributors to the pathophysiology of ADHD (Castellanos et al., 1994, 1996, 2001, 2002; Filipek et al., 1997; Hynd et al., 1993; Reading et al., 2004; Semrud-Clikeman et al., 1994). Since the caudate nuclei receive inputs from cortical regions implicated in two of the hallmark symptoms of ADHD, executive dysfunction and inattention, it is not surprising that brain areas such as the frontostriatal circuit have been the focus of numerous neuroanatomic studies of children with ADHD. Children with ADHD often have deficits in spatial working memory (Kibby & Cohen, 2008; Nigg, 2005), which further supports the link between the caudate nucleus and ADHD. Recently, fMRI studies have shown decreased activity in the right caudate in children with ADHD while performing a spatial working memory task (Vance et al., 2007a). The cerebellum also has been implicated in the pathophysiology of ADHD given its involvement in cognitive functions, including attention, via the cerebello-thalamo-prefrontal circuit (Berquin et al., 1998); however, it is not the focus of this project.

MRI has been a popular tool for measuring brain structures since the 1990s due to its enhanced spatial resolution when compared to computerized tomography (CT). The typical

methodology used to analyze the volume of specific hypothesized areas is called region of interest (ROI) analysis. Using ROI analyses, several structural brain abnormalities have been found when studying the brains of individuals with ADHD.

Cerebral Hemispheres

A meta-analysis of MRI results from studies of children with ADHD done by Valera and colleagues (2007) reported that, of the commonly studied brain areas, differences were seen in total and right cerebral volume, the cerebellum, the splenium of the corpus callosum, and the right caudate nucleus. Several studies found that children with ADHD had decreased overall cerebral hemisphere volume in both gray and white matter, with a 3-8% reduction in cerebral volume being found, particularly in males with ADHD-C (Mostofsky et al., 2002; Silk, Vance, Rinehart, Bradshaw, & Cunnington, 2009; Willcutt et al., 2005). More specifically, Castellanos (1994) reported a total cerebral volume reduction in males with ADHD (PI and C) at a rate of approximately 5% after controlling for age, height, weight, and IQ. A reduction of 3.2% of total cerebral volume also was found in another study done by Castellanos and colleagues (2002) using males and females with ADHD (PI and C). Kibby (2009) found a possible explanation for the reduced cerebral volume, believing it may be mediated by reduced receptive language function, which occurred in some but not all of the sample, but was consistent with the reduced cerebral volume when found.

When examining total cerebral volume, frontal regions assessed in two studies also showed large significant differences. A study by Durston and colleagues (2004) reported that children with ADHD and their unaffected siblings had 4% right prefrontal gray matter volume reductions, as well as left occipital gray matter reductions of 7.4% and 9.1% for participants with ADHD and their siblings, respectively. In addition, white matter reductions in the left occipital

cortex were seen in 3.6% and 6.6% of participants with ADHD and siblings, respectively. These findings in unaffected siblings suggest that there is an increased risk for the disorder within families. However, a study by Filipek and colleagues (1997) did not find a reduction in overall cerebral hemisphere gray matter volume in ADHD. Rather, they reported that children with ADHD who responded well to stimulant medication had reductions in white matter in the frontal and parieto-occipital regions. To ensure effects related to the striatum in ADHD are not due to cerebral volume differences, cerebral volume will be used as a covariate in this study.

Frontostriatal Circuit

In regard to the frontostriatal circuit, a recent review has shown that numerous studies implicate abnormalities in the frontal lobes and the striatal circuit as potential sources of ADHD behaviors (Van Mier & Petersen, 2002). Specifically, children with ADHD-C are thought to have difficulties with response inhibition, a hallmark characteristic of executive dysfunction, which can be directly linked to dysfunction in the frontostriatal circuit (Barkley, 1997). The evidence from brain imaging research has increasingly supported a role for the basal ganglia specifically in individuals diagnosed with ADHD. The caudate nucleus and the circuits with which it is associated have been implicated in ADHD for some time (Pontius, 1973). Researchers have demonstrated differences in volumes and asymmetry in the caudate nucleus between ADHD and control groups, but these findings have been variable. A review of the literature showed that nine out of thirteen studies reported reduced total caudate volumes, or in the caudate head specifically, either on the right (31% of studies) or left (69% of studies) side (Castellanos et al., 1994, 1996, 2001, 2002; Filipek et al., 1997; Hynd et al., 1993; Mataro et al., 1997; Semrud-Clikeman et al., 1994), including smaller total caudate volumes in affected rather than unaffected monozygotic twins discordant for ADHD (Castellanos et al., 2003).

Castellanos and colleagues (1994, 1996) studied the brains of males aged 5-19 years with ADHD (PI and C) compared to controls using structural MRI scans. They reported not seeing the typical right-over-left asymmetry in caudate volume in the sample of boys with ADHD. The volume of the right caudate was somewhat smaller than the control group, but there were no differences in the left caudate volume. Lastly, for the typically developing boys, there was an age-related decrease in the volume of the caudate over time (13%), as well as a right-over-left asymmetry, but there was no age-related change in the ADHD group. Relatedly, a surprising finding emerged in the article by Castellanos and colleagues (2002), who examined the differences in brain volume in children and adolescents with ADHD (PI and C) compared to controls. They found that by age 19, there were no longer any significant differences in caudate volume between males with ADHD compared with typically developing controls. Females showed the same normalization pattern in caudate volume as males by age 16, which was the upper age limit for the females scanned. Castellanos and colleagues (2001) used structural MRI to investigate the differences in caudate volume between girls with ADHD and female controls. The authors argued the need to separate girls from boys when analyzing brain imaging data given that most brain volumes are 10% smaller in girls, which is why this study only included females with ADHD and controls. This pattern is true for many structures; however, the caudate nucleus is not one of them. Control girls tended to have larger caudates than boys (Filipek et al., 1994; Giedd et al., 1996). Nonetheless, this study reported that girls with ADHD had smaller caudate volumes on the left and in total than female controls, which is consistent with the hypothesis that the caudate is implicated in ADHD. In contrast, Qiu and colleagues (2009) found no differences in caudate volume in girls with ADHD (PI and C) compared to female controls.

Hynd and colleagues (1993) reported that 72.7% of typically developing control subjects had a “left-over-right” asymmetry in the caudate nucleus, whereas 63.6% of children with ADHD (diagnosed using the DSM-III-R) showed a “right-over-left” asymmetry. This indicated that the overall volume of the left caudate is reduced in the sample of children with ADHD compared to controls. Other studies found the same result (Filipek et al., 1997; Semrud-Clikeman et al., 2000). Thus, there are discrepant findings on the caudate for both ADHD and controls. Possible sources of this discrepancy will be discussed subsequently.

A more recent study done by Qiu and colleagues (2009) found that, after controlling for total cerebral volume and general intelligence (IQ), children with ADHD had smaller left basal ganglia volumes when compared to controls. Further analysis showed that boys with ADHD had decreased basal ganglia volumes when compared to girls with ADHD; however, there were no volumetric differences or asymmetry shown in girls when compared to controls. When breaking analyses down by subtype, children with ADHD-C had smaller left basal ganglia volumes (including caudate, putamen, and globus pallidus volumes) relative to controls. Children with the ADHD-PI subtype had smaller left caudate and bilateral globus pallidus volumes relative to controls. No group differences in basal ganglia volumes were found when comparing the ADHD-PI and ADHD-C subtypes. Thus, ADHD subtype may influence findings when compared to controls.

Reports on the studies of the right caudate have been variable and are similar to those of total caudate volume. One study found a reduction in the volume of the right caudate in ADHD (PI and C) children (Castellanos et al., 1996), whereas another study reported an increase (Mataró et al., 1997). Mataró, Garcia-Sanchez, Junque, Estevez-Gonzalez, and Pujol (1997) reported a greater right-over-left asymmetry in the caudate when comparing adolescents with

ADHD (PI and C; diagnosed using the DSM-III-R) to controls, which supports Castellanos' findings. They reported that this accounted for 17% of the variance in parent ratings of inattention and 4% of the variance in ratings of hyperactivity/impulsivity (Schrimsher, Billingsley, Jackson, & Moore, 2002). Tremols and colleagues (2008) suggested a new method for segmentation of the caudate nucleus and body rather than only reporting both together (i.e., head+body). Results from this study showed that the right body and right head+body of the ADHD (PI and C) group was significantly smaller than in the control group, although the right caudate head was bigger in ADHD. The authors noted that there were no differences by subtype in the ADHD group. In addition, controls showed a significantly larger left caudate head and a significantly bigger caudate right body and right head+body. Thus, this new segmentation method for the caudate nucleus was able to show differential abnormalities of the right caudate head and body in the ADHD group, which may help to explain previous conflicting findings in the literature. It also helps to explain the conflicting findings on controls.

In summary, previous reviews of structural and functional magnetic resonance imaging (MRI) studies of ADHD have implicated abnormalities in the frontostriatal circuit, specifically in relation to caudate volume and asymmetry. Studies such as these shed light on the implications of having larger or smaller caudate volumes. Larger or more gray matter may be related to a lack of pruning (Alexander et al., 1986), whereas a smaller volume may be related to a delay in typical brain developmental in those with ADHD (Castellanos et al., 1994, 1996). Most studies of the caudate nucleus in ADHD have included boys age 4-18 (Castellanos, 1997; Durston, 2003; Seidman et al., 2005); however, the few studies that have included girls did not report similar asymmetry findings to those found in boys with ADHD (Castellanos et al., 2001, 2002; Qiu et al., 2009). It is important to note that the vast majority of neuroimaging studies of children with

ADHD focus not only on males, but specifically males with a diagnosis of ADHD-C. There is a paucity of research comparing ADHD-PI to ADHD-C. Of these studies, it was found that children with ADHD-PI had smaller left caudate and bilateral globus pallidus volumes compared to controls and children with ADHD-C had smaller left basal ganglia volumes compared to controls (Qiu et al., 2009). Lastly, despite the fact that several studies investigate both the caudate and the putamen, which together make up the striatum, only the caudate nucleus head and body will be traced for this project due to time constraints related to tracing and attaining reliability. The caudate also is the part of the striatum believed to receive input from the frontal lobes.

Neuroanatomic Findings in Developmental Dyslexia

Cerebral Hemispheres

Initially, developmental dyslexia was studied using only behavioral means; however, the advances in neuroimaging technology have allowed the field to investigate neurobiological underpinnings using neuroimaging and electrophysiology studies. Steinbrink and colleagues (2008) found that gray matter volume in the cerebral hemispheres was decreased using voxel-based morphometry (VBM) in a German sample of adults with developmental dyslexia. Another study showed gray matter reductions in several structures including the superior temporal gyrus, fusiform gyrus, and anterior cerebellum bilaterally, and the right supramarginal gyrus in a sample of adolescents using VBM (Kronbichler et al., 2008). In addition, a study of adolescents with developmental dyslexia reported differences in the ratio of gray matter to white matter in the left hemisphere in girls with developmental dyslexia compared to controls (Sandu et al., 2008). More specifically, girls with developmental dyslexia had a significantly higher gray matter to white matter ratio than female controls, which was influenced by a reduction in white

matter volume rather than an increase in gray matter. Two other studies reported that decreased volumes of gray matter were found in the right posterior superior parietal lobule, the left temporal lobe, the precuneus, and the right supplementary motor area using structural MRI and voxel-based morphometry (Eliez et al., 2000; Menghini et al., 2008).

Frontostriatal Circuit

Data from functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) scans have implicated the aforementioned brain regions, as well as the inferior frontal lobes (Paulesu et al., 1996; Rumsey et al., 1997; Shaywitz et al., 1998), in developmental dyslexia. Paulesu, Frith, Snowling, and Gallagher (1996) used PET to study developmental dyslexia and found that there was decreased activation in the supplementary motor area and the premotor cortex on a rhyming task and a phonological short-term memory task. Shaywitz and colleagues (1998) used fMRI and found decreased activation in the posterior regions of the brain, including Wernicke's area, the angular gyrus, and the striate cortex on word and pseudoword reading tasks. In contrast, they reported an increase in activity in the inferior frontal gyri bilaterally. Rumsey and colleagues (1999) used PET and found decreased blood flow compared to controls in the bilateral parietal areas, temporal regions, and precuneus region, as well as the right pre- and postcentral gyrus, while completing phonological tasks. Interestingly, they found increased blood flow to the left inferior occipital gyrus, the left medial temporal cortex, the right insula, the left pre- and postcentral gyrus, and the right frontal area during those same tasks. Hence, it has been proposed that the inferior frontal region may be used in phonological tasks in developmental dyslexia to compensate for a dysfunctional posterior region (Shaywitz et al., 1998). In contrast, individuals with developmental dyslexia had deactivations compared to controls in the left inferior frontal region when completing

orthographic tasks. Duffy, Denckla, Bartels, and Sandhini (1980) used ERP to investigate the frontal lobes in developmental dyslexia. They found significant differences in the bilateral medial frontal and left lateral frontal lobe when comparing children with and without developmental dyslexia on measures of reading and speech.

Limited research has been conducted on the frontal lobes in developmental dyslexia using structural neuroimaging techniques. Eckert and colleagues (2003) have reported that differences in the structure of the pars triangularis (anterior region of the Sylvian fissure) such as size and asymmetry have been of interest due to the variability of the posterior Sylvian fissure morphology in developmental dyslexia. Foundas, Weisberg, Browning, and Weinberger (2001) classified the different morphologies of the anterior Sylvian fissure into four distinct types: V, U Y, and J, although the study only included right-handed males without psychiatric or learning problems. They found V/U were the most common types. Eckert and colleagues (2003) reported reductions in the volume of the pars triangularis bilaterally in children with developmental dyslexia in grades 4-6 as compared to controls. In a recent study by Kibby (2009) of the pars triangularis in a sample of children with developmental dyslexia and/or ADHD, groups did not differ in the pars triangularis volume. Nonetheless, the length of the right anterior ascending ramus was associated with inattention in the whole sample. In terms of linguistic ability, having an extra sulcus in the left pars triangularis was associated with worse outcome on measures of expressive language. In children without impairment in expressive language, left pars triangularis length was related to phonological awareness, phonological short-term memory and rapid automatic naming. The length of the right pars triangularis was associated with rapid automatic naming and processing semantic information.

Few studies have examined frontal lobe structure in dyslexia outside of the pars

triangularis. In an earlier study using CT, Hynd, Semrud-Clikeman, Lorys, Novey, and Eliopulos (1990) reported reduced frontal asymmetry in developmental dyslexia as a result of reduced right hemisphere width. This same result also was found in children with ADHD. Another study that used parcellation techniques with MRI showed that children with developmental dyslexia may have reductions in bilateral frontal volumes but larger anterior and posterior opercular regions (Pennington et al., 1999).

Studies using functional neuroimaging have added to the literature on frontal volume in developmental dyslexia. An early ERP study demonstrated differences between children with and without developmental dyslexia in the medial frontal and left lateral frontal lobe as noted earlier (Duffy et al., 1980). An early PET study showed reduction in the typical right-over-left asymmetry in the prefrontal cortex during an oral reading task (Gross-Glenn et al., 1991). Hoeft and colleagues (2007) reported hypoactivation in left parietal and bilateral fusiform cortices and hyperactivation in left inferior and middle frontal gyri, left caudate, and left thalamus when using fMRI to investigate differences between children with developmental dyslexia and age-matched controls during a visual word rhyme judgment task compared with a visual cross-hair fixation rest. Thus, literature on the activation of the inferior frontal region is varying, with some studies showing no differences in activation when compared to controls during rhyming and short-term memory tasks (Chiron, 1999; Paulesu et al., 1996; Rumsey et al., 1997), others reporting hyperactivation in the frontal cortex during rhyming tasks, visual-spatial tasks, phonological processing tasks, and orthographic tasks as a way to compensate for reduced activation in posterior areas of the brain (Hoeft et al., 2007; Pugh et al., 2000; Shaywitz et al., 1998), and still others demonstrating hypoactivation during phonological tasks (Georgiewa et al., 1999).

Brown (2001) explored specific areas within the lobes that may be associated with

developmental dyslexia. He used voxel-based morphology with a sample of 16 men with developmental dyslexia and 14 matched controls and found decreases in gray matter of the left orbital frontal gyrus and frontal pole and bilateral inferior and superior frontal gyri. When looking at the subcortical nuclei, individuals with developmental dyslexia had bilateral reductions in gray matter in the head of the caudate nucleus and the thalamus. Data from a personal communication (Eckert, personal communication, December 7, 2010) showed that gray matter reductions in the caudate and cerebellar vermis have been most consistently implicated in developmental dyslexia relative to controls when using voxel-based comparisons.

Overall, data on the role of the frontostriatal circuit in developmental dyslexia is limited. Studies using VBM reported decreases in gray matter in the head of the caudate bilaterally (Brown et al., 2001) and the caudate in general (Eckert, personal communication, December 7, 2010). Functional neuroimaging has shown hyperactivity in the caudate of children with developmental dyslexia during a rhyming task (Hoeft et al., 2007). The present study will add to the limited research in the field of developmental dyslexia on structure of the caudate nucleus and its relation to EF.

The Present Study

Given the limitations in the literature related to the study of the frontostriatal circuit in ADHD and developmental dyslexia, more research is needed to isolate specific regions that may be implicated in these disorders. Specifically, more focus should be placed on the structure-function relationship between the striatum, specifically the caudate nucleus, and developmental dyslexia, especially given the high rate of comorbidity between ADHD and developmental dyslexia, the research implicating the frontostriatal circuit in ADHD, and the findings of executive dysfunction in both groups. Thus, the present study aims to address the limitations in

the understanding of the caudate nucleus in these disorders and its relation to executive functioning. In addition, this study will add novel information to the structural MRI literature on the caudate in developmental dyslexia.

More specifically, the purpose of this study is to better understand the brain-behavior relationships between the volume of the caudate nucleus, part of the frontostriatal network, and measures of executive functioning in a community-based sample of children ages 8-12 years with ADHD and/or developmental dyslexia and controls. Relationships between right and left caudate nuclei head and body volumes and measures of executive functioning will be examined in the hopes of adding to the research on the anatomical correlates that may underlie executive dysfunction in this population. The head and body of the caudate was segmented using the method outlined by Filipek and colleagues (1997). This study will add to the research on a potential neurobiological process that may underlie the high comorbidity between these two common childhood disorders.

Specific Hypotheses

Hypothesis 1: It was hypothesized that there would be a reduction in caudate volume in the ADHD and developmental dyslexia groups compared to those without each disorder and that there would be right-over-left asymmetry in the head of the caudate and left-over-right asymmetry in the body of the caudate for children with ADHD, as well as left-over-right asymmetry in the head of the caudate and right-over-left asymmetry in the body of the caudate for controls. This was based on the findings by Tremols and colleagues (2008). An asymmetry variable was computed for head and body volumes separately using the formula (Right volume – Left volume)/[(Right volume + Left volume)/2] initially described by Hynd and colleagues (1990). Using this computation, a positive value indicated a right-over-left asymmetry, whereas a

negative value indicated a left-over-right asymmetry. These asymmetry variables were used as outcome measures for analyses that included the volume of the caudate head and body. Research on the caudate in developmental dyslexia demonstrated a reduced bilateral caudate head volume using voxel-based morphometry (Brown et al., 2001), but there have been no studies investigating the asymmetry or studies using structural MRI with region of interest analysis. Therefore, differences in caudate volume and asymmetry in developmental dyslexia compared to controls were exploratory in this study.

Hypothesis 2: It was hypothesized that both the ADHD and the developmental dyslexia groups would be impaired compared to those without each disorder on EF domains, but comparable to each other. More specifically, Hypothesis 2a stated that both the ADHD and developmental dyslexia groups would exhibit impairment compared to controls on cognitive executive functioning domains including working memory, set shifting, planning, and non-verbal fluency (Klorman et al., 1999; Willcutt et al., 2001), but would be comparable to each other given the high comorbidity between these disorders (Shaywitz, Fletcher, & Shaywitz, 1995; Willcutt & Pennington, 2000) and the prevalence of executive dysfunction in these disorders (Willcutt et al., 2001). In contrast, I expected that ADHD would be affected on inhibitory tasks (Hinshaw, 2002; Nigg et al., 2002) compared to those without ADHD. Given that attention could be affecting performance on these measures and the fact that the caudate nucleus may be related to these executive functioning measures because of decreased attention, a measure that required attention but not executive functioning was also assessed (i.e., a verbal long-term memory measure [Stories Delayed Recall] from the Children's Memory Scale) to see if there was a dissociation between it and the executive functioning findings.

Hypothesis 2b stated that the relationship between diagnostic group membership and other EF tasks would still be significant after controlling for working memory and caudate volume. This was justified because working memory impairments were characteristic of both ADHD (Rubia et al., 1999; Vaidya et al., 1998) and developmental dyslexia (Kibby & Cohen, 2008; Snowling, 1991), working memory influenced performance on other EF tasks (Barkley, 1997; Miyake et al., 2000), and research has demonstrated decreased caudate volumes compared to controls in both ADHD (Castellanos et al., 2002; Filipek et al., 1997) and developmental dyslexia (Brown et al., 2001; Eckert, personal communication, December 7, 2010). Hence, it was of interest to determine if there was a relation between clinical group membership and the other executive functioning measures when working memory and caudate volume were controlled.

Hypothesis 3*:* It was hypothesized that working memory would mediate the relationship between caudate volume and performance on other executive functioning tasks given that working memory impairments have been shown in both ADHD and developmental dyslexia. More specifically, hypothesis 3a stated that verbal working memory would mediate the relationship between the left caudate volume and performance on the NEPSY Tower and the WCST because the left caudate has been implicated in verbal working memory (Narayanan et al., 2005). In addition, the activation of the caudate nucleus has been linked to a Tower planning task (Beauchamp et al., 2003; Dagher et al., 1999; Rowe et al., 2001; van den Deuval et al., 2003) and the WCST (Monchi et al., 2001). Lastly, working memory has been shown to be crucial in the successful performance of planning tasks (Manoach et al., 2003; Monchi et al., 2001, 2006b). Hypothesis 3b stated that spatial working memory would mediate the relationship between the right caudate volume and performance on the NEPSY Tower, WCST, and NEPSY

Design Fluency given that the right caudate has been implicated in spatial working memory (Vance et al., 2007a).

CHAPTER THREE

METHODS

Participants

Participants were recruited as part of a larger, ongoing research study investigating the neuropsychological functioning of children ages 8-12 years with ADHD and/or developmental dyslexia, and controls, which is funded by the National Institutes of Health (NIH/NICHD R03 HD048752; NIH/NICHD R15 HD065627). Children were recruited through the local school systems and by posting recruitment flyers in doctors' offices and public places such as libraries and grocery stores in the Southern Illinois region. As an incentive, families received a full-length neuropsychological report at no charge that outlined their child's neuropsychological strengths and weaknesses and diagnosis, if applicable, based on the measures given on the evaluation day, along with providing recommendations for the child's parents and teachers based on these findings. Children who had diagnoses of ADHD, developmental dyslexia, or ADHD/developmental dyslexia and typically developing controls without any psychiatric or neurological disorders were included in the analysis. Children with language impairments without ADHD or developmental dyslexia were excluded from the study. Language deficits were allowed in the clinical groups given their comorbidity with these disorders. The sample included 105 children, 19 with ADHD-Predominantly Inattentive Type (PI), 16 with ADHD-Combined Type (C), 18 with developmental dyslexia, 17 with comorbid ADHD/developmental dyslexia, and 35 controls. In the comorbid group, there were 10 children with ADHD-PI and 7 children with ADHD-C (see Table 6).

Parental consent and child assent were obtained prior to both the neuropsychological and imaging portions of the study. The Southern Illinois University Institutional Review Board approved this study.

Inclusionary Criteria—ADHD

Children were diagnosed with ADHD-PI or ADHD-C based on data collected from a developmental parent interview and questionnaires that were given to parents and teachers as part of the study. Specifically, data from the Behavioral Assessment System for Children, 2nd edition (BASC-2; Reynolds & Kamphaus, 2004) was collected from parents and teachers, and a questionnaire that maps onto the ADHD items and criteria from the DSM-IV was given to the parent to complete. Scores on the Attention Problems and Hyperactivity scales from the BASC-PRS and BASC-TRS, in conjunction with DSM-IV criteria for ADHD-PI or ADHD-C, were used to arrive at a diagnosis of ADHD. More specifically, DSM-IV criteria for ADHD were followed in general. However, if a child met 5 instead of 6 symptoms for a given subtype but had corresponding elevations on BASC Attention Problems/Hyperactivity of at least 1 SD, then the child was diagnosed with ADHD given the continuous nature of inattention and impulse control. It should be noted that there are no children with ADHD-H/I included in this study. This ADHD subtype is commonly seen in children who are of preschool or early elementary school age (Barkley, 2003), which is out of the range for this study (i.e., 8-12 years). Children on stimulant medication were included in the study; however, they were required to be medication-free for 24 hours prior to the testing session to allow for a washout period. Children on other medications, except for allergy treatment, were excluded from the study.

Inclusionary Criteria—Developmental Dyslexia

For the purposes of this study, two definitions of developmental dyslexia were used: the discrepancy definition and the poor reader definition. Academic achievement was measured by the Woodcock Johnson, 3rd edition (WJ-III) for both definitions. For the discrepancy definition, the Basic Reading Cluster needed to be significantly below the child's best IQ on the WISC-IV using the IL discrepancy table, which uses a regression-based approach. Best IQ was the child's FSIQ unless there was a significant discrepancy between the Verbal Comprehension Index (VCI) and Perceptual Reasoning Index (PRI), in which case the higher of the two was used given that it was believed to be a better estimate of their intellectual potential. An IQ/achievement discrepancy was required by IDEA prior to the changes made in 2004. According to this definition, the IQ/achievement discrepancy could not be due to underlying neurological conditions such as seizure disorders or acquired brain injury, poor academic instruction, or disadvantaged socio-economic status. With the revised IDEA (2004) law, other empirically supported definitions have to be considered; clinicians can no longer rely on the discrepancy definition alone. In accordance with this, the poor reader definition also was used, in which developmental dyslexia was diagnosed if best IQ is greater than or equal to 80 and the Basic Reading Cluster was less than 85 (Siegel, 1992). This procedure was followed as Pennington (2009) noted that the two groups are comparable in many cognitive deficits including poor phonological processing, the 'core' deficit in developmental dyslexia. For the purposes of this study, children who met criteria for either the IQ/achievement discrepancy definition or the poor reader definition of developmental dyslexia were included.

To determine if diagnostic groups differed where expected, a series of ANOVAs were run to test group differences on WISC FSIQ, academic achievement (i.e., WJ-III), and behavioral

ratings (i.e., BASC-2 parent report). Groups differed on WISC FSIQ scores, $F(4, 104) = 4.30$, $p < .05$ and PRI scores, $F(4, 88) = 3.65$, $p < .05$ such that the ADHD/DD group performed worse than controls on both WISC FSIQ and PRI scores. Groups initially differed on TONI-3 IQ, $F(4, 104)$; however, groups were not significantly different at the post-hoc level. There were no group differences on VCI; all groups performed in the Average range. On the WJ-III, groups differed on Letter-Word Identification, $F(4, 104) = 24.53$, $p < .05$, Word Attack, $F(4, 104) = 20.59$, $p < .05$, Passage Comprehension, $F(4, 104) = 8.30$, $p < .05$, and Spelling, $F(4, 104) = 21.57$, $p < .05$. More specifically, the developmental dyslexia and ADHD/developmental dyslexia groups performed worse than the ADHD-PI, ADHD-C, and control groups on Letter-Word Identification, Word Attack, and Spelling. On Passage Comprehension, the comorbid ADHD/developmental dyslexia group did worse than controls, and the developmental dyslexia group did worse than controls and those with ADHD-PI. Groups also differed on Hyperactivity ratings from the BASC-2, $F(4, 102) = 19.00$, $p < .05$. More specifically, children with ADHD-C scored higher on hyperactivity than those with developmental dyslexia, ADHD-PI, and controls. Children with ADHD-PI scored higher than controls, and those with comorbid ADHD/developmental dyslexia scored higher than controls and children with developmental dyslexia. Lastly, children also differed on the Attention Problems scale, $F(4, 102) = 51.81$, $p < .05$. More specifically, children with comorbid ADHD/developmental dyslexia, ADHD-PI, and ADHD-C had higher ratings than children with developmental dyslexia on the BASC-2. Those with developmental dyslexia also had more symptoms than controls, although they still scored in the Average range (see Table 7).

Exclusionary Criteria

Children were excluded from the study at two separate points: at intake and following administration of the neuropsychological test battery. At intake, children were excluded from the study if they were outside of the identified age range, had a history of neurological problems (e.g., TBI, tics, seizures), medical problems (e.g., heart defect), were born prematurely (less than 34 weeks), or were the product of a complicated birth requiring treatment with oxygen or a lengthy stay in the hospital. Children meeting criteria for psychiatric disorders such as Conduct Disorder, Major Depressive Disorder, Bipolar Disorder, Generalized Anxiety Disorder, or Schizophrenia also were excluded from the study due to the fact that these disorders also are related to cognitive dysfunction. More specifically, conduct problems are associated with deficits in verbal language ability, executive functioning, and perceptual organization; depression is associated with slowed processing speed, psychomotor slowing, reduced motivation, and mild attentional and working memory problems; severe anxiety is related to problems with attention, retrieval due to poor encoding, working memory, and processing speed; and childhood schizophrenia is associated with attention problems, slowed processing speed, memory deficits, problems learning new material, abstract reasoning, and executive dysfunction (Reynolds & Fletcher-Janzen, 2009). After testing was completed, children were excluded for these disorders and other substantial medical complications if these were not identified at intake (sometimes problems were revealed during the parent interview and/or during testing). Furthermore, children scoring below 80 in intellectual functioning (when using the child's best IQ) were excluded from the study. Exclusion criteria applied to all participants.

Measures

Questionnaires

Behavior Assessment System for Children—2nd Edition. The Behavior Assessment System for Children (BASC-2) is a questionnaire-based diagnostic tool used to assess the presence of internalizing and externalizing behaviors in school-age children (Reynolds & Kamphaus, 2004). Data can be collected through the Parent Report Scale (PRS), the Teacher Report Scale (TRS), and other measures; however, for the purposes of this study, data were only collected from the PRS and the TRS to gather information about how the children behave at home and school, respectively. The questionnaires are broken down by age into three groups: preschool (2-5), school-age (6-11), and adolescence (12-21). Thus, the latter 2 forms were used for this study. Information on the reliability and validity for the parent and teacher forms for the Attention Problems and Hyperactivity scales are as follows:

The Attention Problems subscale, which measures how easily a child is distracted and how much difficulty the child is having concentrating for long periods of time, has an alpha reliability coefficient for the PRS of .82 for children and .81 for adolescents and has coefficients of .93 for children and .91 for adolescents on the TRS. The Hyperactivity subscale, which measures a child's tendency to be very active, hastily complete school tasks or other activities, and act impulsively, has an alpha reliability coefficient for the PRS of .74 for children and adolescents and .93 for children and adolescents on the TRS. All scores on the BASC-2 are reported as T scores, with a mean of 50 and a standard deviation of 10. Concurrent validity of the Achenbach System of Empirically Based Assessment--Child Behavior Checklist (ASEBA; Achenbach & Rescorla, 2001) with the BASC PRS is .75 for the Attention Problems scale and

.61 for the Hyperactivity scale. On the TRS, the concurrent validity is .64 for the Attention Problems scale and .69 for the Hyperactivity scale.

Behavior Rating Inventory of Executive Functioning. The Parent Form of the Behavior Rating Inventory of Executive Functioning **(**BRIEF) was completed by parents as a measure of their child's executive functioning abilities in the home (Gioia, Isquith, Guy, & Kenworthy, 2000). Teachers completed the BRIEF Teacher form as a measure of the child's EF at school. The forms are comprised of 86 items that make up two index scores: the Behavioral Regulation Index (BRI) and the Metacognition Index (MI). The BRI measures a child's ability to regulate emotional and behavioral responses and inhibit inappropriate behavioral responses. It is comprised of the following subscales: Inhibit, Shift, and Emotional Control. The MI is a measure of a cognitive control and, specifically, a child's ability to monitor his/her own behavior and use planning and organization skills. It is comprised of the following subscales: Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor subscales. These indices are summed to derive the Global Executive Composite (GEC). Standard scores are reported as T scores with a mean of 50 and a standard deviation of 10; scores elevated above 65 are considered to be clinically significant. Internal consistency for the Parent Form ranges from .80 to .97 for the normative sample and from .82 to .98 for the clinical sample of children ages 8-12, which is comprised of children with ADHD, learning disabilities, or Pervasive Developmental Disorders. Internal consistency for the Teacher Form ranges from .90 to .98 for the normative sample and from .84 to .98 for the clinical sample, which also is comprised of children with ADHD, learning disabilities, or Pervasive Developmental Disorders. Inter-rater reliability coefficients for the Parent and Teacher Forms on the BRI and MI are .31 and .34, respectively (Gioia et al., 2000). A study done by Mahone and colleagues (2002) showed that

the BRIEF has good concurrent validity with parent ratings and interviews such as the Child Behavior Checklist (CBCL) Attention Problems scale (r = .82), Diagnostic Interview for Children and Adolescents, 4th Edition (DICA-IV) ADHD Scale (r = .78), and the ADHD Rating Scale IV (inattention symptoms r = .79, hyperactivity/impulsivity symptoms r = .69).

DSM-IV Questionnaire. This parent questionnaire requires dichotomous responses (i.e., yes/no) to questions relating to several common childhood psychiatric disorders including ADHD, Dysthymia, Major Depressive Disorder, Separation Anxiety, Oppositional Defiant Disorder, Conduct Disorder, Generalized Anxiety Disorder, Social Phobia, Obsessive Compulsive Disorder, and Schizophrenia (APA, 2000). The format of the questionnaire maps directly onto DSM-IV criteria including all the symptoms and questions related to onset, duration, settings, and impairment from the endorsed symptoms. This measure includes the DSM-IV symptoms/items verbatim with APA permission; its reliability is unknown.

Education Scale of the Four-Factor Index of Social Status. Maternal education from the Education Scale of the Four-Factor Index of Social Status (Hollingshead, 1975) was selected as a measure of socioeconomic status (SES) given that it has been shown to be a reliable predictor of socioeconomic status (Belsky et al., 2007). It is common to use the number of years of schooling completed as a way to quantify education level. Magnuson (2007) found that mother's education level was related to children's academic success; he also indicated that coding the highest degree completed might be the most useful way to code education level in relation to SES rather than number of years of education. He believed that other variables such as financial resources and intrinsic factors may confound the relationship between time to degree conferment and highest level of education completed.

For the purposes of this study, SES was coded using a modification of the Hollingshead (1975) measure recommended by Magnuson, Ruhm, & Waldfogel (2007). As a part of the Hollingshead measure, the highest level of education obtained is rated as follows: 1 = less than 7th grade, 2 = junior high school, 3 = partial high school, 4 = high school diploma or GED, 5 = partial college or Associate's degree, 6 = Bachelor's degree, 7 = Master's degree, and 8 = Doctorate. One of the modifications to the original Hollingshead is the inclusion of separate groups for Master's degree and Doctoral degree recipients.

Cognitive/Achievement Tests

Wechsler Intelligence Scales for Children, 3rd Edition. The Wechsler Intelligence Scales for Children, 3rd Edition **(**WISC-III) was administered to a subset of children tested in the beginning of the study as a measure of their intellectual functioning (Wechsler, 1991). The WISC-III is comprised of four index, or factor, scores, including the Verbal Comprehension Index (VCI), the Processing Speed Index (PSI), the Perceptual Organization Index (POI), and the Freedom from Distractibility Index (FDI). All factor scores are reported with a mean of 100 and a standard deviation of 15. The inter-rater reliability coefficients were .90 and above. Table 7 shows the number of participants who were administered the WISC-III.

A Full-Scale Intelligence Quotient (FSIQ) was derived according to the procedures outlined in the WISC-III manual. The test-retest reliability coefficient for the FSIQ score in a sample of children ages 10-11 is .95, and the concurrent correlation coefficient between the WISC-III and the previous version, the WISC-R (Wechsler, 1974) is .96 (Wechsler, 1991). Scores for the FSIQ and all indices are reported with a mean of 100 and a standard deviation of 15. The index scores used as part of this study are broken down in the following paragraph.

The Verbal Comprehension Index (VCI), which measures verbal reasoning and acquired knowledge, is derived from a child's scores on the following subtests: Information, Similarities, Vocabulary, and Comprehension. The split-half reliability coefficient for children and adolescents ages 6-16 is .94, and the test-retest reliability for children ages 10-11 is .93. The Perceptual Organization Index (POI), which measures nonverbal reasoning and visual-spatial processing, is derived from a child's performance on the following subtests: Picture Completion, Picture Arrangement, Block Design, and Object Assembly. The split-half reliability coefficient is .90, and the test-retest reliability for children ages 10-11 is .87 (Wechsler, 1991). As noted earlier, the FSIQ was used for diagnostic purposes unless there was a significant discrepancy between POI and VCI.

Wechsler Intelligence Scales for Children, 4th Edition. The Wechsler Intelligence Scales for Children, 4th Edition (WISC-IV) was administered in order to measure intellectual functioning starting in 2006 and is currently the measure being used in the lab (Wechsler, 2004). A Full-Scale Intelligence Quotient (FSIQ) is derived from scores on the Verbal Comprehension Index (VCI), Perceptual Reasoning Index (PRI), Working Memory Index (WMI), and Processing Speed Index (PSI). The test-retest reliability of the FSIQ is .93. The FSIQ of this edition has a concurrent correlation of .89 with the previous edition (WISC-III). The VCI, a measure of verbal reasoning and acquired knowledge, is derived from scores on the following subtests: Similarities, Vocabulary, and Comprehension. The internal consistency coefficient for the VCI is .94, and its concurrent validity with the WISC-III is .88. The PRI, a measure of nonverbal reasoning and visual-spatial processing, is derived from scores on the following subtests: Block Design, Matrix Reasoning, and Picture Concepts. The internal consistency coefficient for the PRI is .92, and its concurrent validity with the WISC-III is .72 (Flanagan & Kaufman, 2004).

Similar to the WISC-III, the FSIQ was used as the best IQ for diagnostic purposes unless there was a significant discrepancy between VCI and PRI; however, the Test of Nonverbal Intelligence, 3rd edition (TONI-3), which is described below, would have been used as a covariate in the subsequent analyses if groups differed on IQ. The TONI-3 was not used for diagnostic purposes because it is a single subtest test. In contrast, the WISC-III and the WISC-IV were used only for diagnostic classification purposes in this study; therefore, they were not included in the list of potential covariates. A one-way ANOVA showed no significant differences between the FSIQ from the WISC-III and the WISC-IV when collapsing across diagnostic groups (see Table 6).

The Test of Nonverbal Intelligence, 3rd Edition. The Test of Nonverbal Intelligence, 3rd Edition (TONI-3) is a language-free measure of nonverbal intelligence and abstract reasoning abilities (Brown, Sherbenou, & Johnsen, 1997). This measure requires no reading, writing, speaking, or listening on the part of the participant, requiring only a point to indicate the desired response choice. Children are presented with abstract figures that represent a pattern and are gestured to choose one response choice from the options at the bottom of each page to complete the pattern. The internal consistency reliability coefficients range from .89-.93 for children ages 8-12. Median discrimination coefficients for validity range from .33-.51 for children ages 8-12. This variable would be used as a covariate in the analyses rather than the best estimate IQ from the WISC-III or WISC-IV if groups differ in IQ given that the TONI-3 is a nonverbal measure of IQ, is not timed, and thus has minimal processing speed and language demands. This is important given that both ADHD and developmental dyslexia can have comorbid language impairment and processing speed deficits. In addition, the different versions of the WISC (i.e., III and IV) were normed on different samples and comprised of different measures; therefore,

using the TONI-3 as a potential covariate in the analyses precluded the need to discuss the problems associated with using two different versions of the WISC. TONI-3 results are presented in Table 7.

Woodcock-Johnson III Tests of Achievement. Select portions of the Woodcock-Johnson III Tests of Achievement (WJ-III), a measure of academic achievement, were administered as part of the testing day to assess reading and spelling ability (Woodcock, McGrew, & Mather, 2001). This study includes scores for basic reading, reading comprehension, and spelling abilities. Scores on the WJ-III subtests are reported using a mean of 100 and a standard deviation of 15.

The Letter-Word Identification subtest assesses the ability to identify single words in isolation, which increase in difficulty until a maximum score is achieved. Children and adolescents 5-19 years of age had a mean test-retest reliability of .91. The Word Attack subtest assesses the ability to decode phonetic non-words, or pseudowords, in isolation. Children and adolescents 5-19 years of age had a mean test-retest reliability of .87. The Passage Comprehension subtest assesses reading comprehension by having children read a short passage with a missing word. The children are asked to provide the missing word based on information from the passage. Children and adolescents 5-19 years of age had a mean test-retest reliability of .83. The Spelling subtest is a measure of the ability to correctly spell words that are orally presented. Children and adolescents 5-19 years of age had a mean test-retest reliability of .89 (Woodcock, et al., 2001). WJ-III scores are reported in Table 7.

Wisconsin Card Sorting Test-64 Card Version. The Wisconsin Card Sorting Test-64 Card Version (WCST-64) is an abbreviated computerized version of the 128-card task; however, the concepts measured are comparable (Kongs, Thompson, Iverson, & Heaton, 2000). Children

are presented with one card at a time from a deck and are asked to match the card from the deck to the appropriate stimulus card above. There are four types of stimulus cards by which they can be matched: shape, color, the number of objects, and other (doesn't match). They receive feedback ("right" or "wrong") after the placement of each card. The children are supposed to notice a change in the pattern, or rules, for how the stimulus cards are accurately matched. This happens after the child has completed 10 consecutive matches. The WCST is believed to measure problem-solving skills and set shifting. Reliability and validity data are not available for the computerized version, but the generalizability coefficient for the card version ranges from .60-.85, with a mean of .74. Cicchetti & Sparrow (1981) and Mitchell (1979) reported that a value of .60 or higher on generalizability coefficients are considered very good. Raw scores are reported in the manual for samples of school age children with ADHD and developmental dyslexia and are noted below in the subsequent sections describing each index reported in the output and used in this study. Standard scores for the WCST have a mean of 100 and a standard deviation of 15.

The Categories Completed subscale is believed to measure problem solving ability and is an indication of how many of the categories (e.g., match to color, match shape, etc.) the child successfully completed. Child/adolescent samples with frontal lesions can be discriminated from controls using this index score (Kongs et al., 2000). In a sample of school age children with ADHD (M = 2.60, SD = 1.35), participants did not appear to differ from controls (M = 2.96, SD = 1.10) when comparing performance out of 5 potential categories. Similarly, the performance of school age children with developmental dyslexia (M = 2.58, SD = 1.12) was indistinguishable from controls (M = 2.74, SD = 1.15). It should be noted, however, that inferential statistics were not reported in the manual comparing these samples (Kongs et al., 2000).

The Perseverative Errors subscale is a measure of a child's ability to shift mental set after receiving feedback that they were incorrect. Child/adolescent samples with frontal lesions can be discriminated from controls using this index score (Mather & Woodcock, 2001). In a sample of school age children, participants with ADHD (*M* = 14.34, *SD* = 10.88) made more perseverative errors than controls (*M* = 9.77, *SD* = 4.42). Similarly, the school age children with developmental dyslexia (*M* = 14.84, *SD* = 7.77) made slightly more perseverative errors than controls (*M* = 12.11, *SD* = 5.68). Again, inferential statistics were not reported in the manual comparing these samples (Kongs et al., 2000).

A Developmental Neuropsychological Assessment. Select subtests from the Developmental Neuropsychological Assessment (NEPSY) were administered as measures of executive functioning, including the Tower, Tower Rule Violations, and Design Fluency (Korkman, Kirk, & Kemp, 1998). The scores for Tower and Design Fluency are reported with a mean of 100 and a standard deviation of 15. Scores for the Tower Rule Violations are subsequently described.

The Tower subtest is a measure of planning ability. Children are given a wooden board with 3 pegs of different heights that can hold one, two, or three balls, which are different colors. The child is told to copy a pattern from the stimulus book in a certain number of moves. The Tower subtest had an internal consistency of .82 for children 5-12 years of age according to the manual. The Rule Violations section of the Tower subtest counts the number of times a child violates the rules given by the examiner such as only moving one ball at a time and keeping all of the balls on the pegs when not moving them. Rule violations are tallied throughout the subtest administration and are believed to measure poor response inhibition. A percentile range is calculated based on the number of rule violations and coded as follows: 1 = <2%, 2 = 3-10%, 3 =

11-25%, 4 = 26-75%, 5 = >75%. Inter-rater agreement for Rule Violations is .79 according to the manual.

The Design Fluency subtest measures non-verbal fluency. Children are given 2 tasks, one with a structured array of 5 dots and the other with a random array of 5 dots. The children are asked to generate as many novel designs as they can within a 1-minute period of time for each array. Only novel designs are given full credit. The Design Fluency subtest had an internal consistency of .59 for children 5-12 years of age (Korkman et al., 1998).

Children's Memory Scale. The Children's Memory Scale (CMS) is a measure of children's memory capacity for visual and verbal information, assessing short-term, long-term, and working memory (Cohen, 1997). Specifically, the Numbers and Sequences subtests were used to measure verbal working memory in the larger study, Picture Locations was used to measure visual working memory, and Stories was used to measure verbal long-term memory. The split-half reliability coefficients for the Numbers and Sequences subtests are .80 and .81, respectively. The CMS Attention/Concentration Index, which uses the scores from the Numbers and Sequences subtests, has a criterion-related validity correlation of .73 with the FDI from the WISC-III (Cohen, 1997). The split-half reliability coefficient for the Picture Locations subtest is .81. The split-half reliability coefficient for the Stories Delayed subtest is .75. Standard scores are reported with a mean of 100 and a standard deviation of 15.

The Numbers subtest requires the children to repeat back a sequence of numbers that the examiner reads to them either in the forward direction (Numbers Forward) or in the reverse order in which they were presented (Numbers Backward), similar to Digit Span on the WISC. The Sequences subtest requires the children to complete tasks that involve the retrieval of rote sequences from LTM such as stating the days of the week or months of the year in forward order

then in backward order, as well as counting aloud in increments such as counting by 2s from zero to 20. This subtest requires the use of the central executive and the phonological loop for completion. The Picture Locations subtest requires the children to view a stimulus page with pictures placed in certain locations within a larger rectangle. The stimulus page is removed from view, and the children are asked to place chips on a response grid in the same locations that they saw the pictures on the stimulus page (Cohen, 1997). This subtest was used as a measure of visual working memory. The immediate verbal memory portion of the Stories subtest requires children to repeat back two stories verbatim. In the long-term recall portion (Stories Delayed), children are asked to repeat the two stories that they heard following a 30-minute delay. The Stories Delayed subtest was used in this study as a measure of verbal long-term memory that is a non-executive functioning task. For a list of all neuropsychological measures to be used in the analyses for this project, see Table 8.

Procedures

All children included in this study participated in a full-day neuropsychological evaluation and a structural magnetic resonance imaging (MRI) scan at the local hospital as part of a larger study as noted previously. Measures of executive functioning that were collected as part of the neuropsychological testing battery were used for the current study and included the tests outlined in the previous section. Parents and teachers completed questionnaires about the child, including the DSM-IV questionnaire, the Behavioral Assessment System for Children (BASC), and the BRIEF. The first two were used to diagnose ADHD. Reading-specific measures comprising the Basic Reading Cluster from the WJ-III were used to determine whether or not children met criteria for developmental dyslexia. For the second part of the study,

children completed an 8-minute anatomical MRI scan on a 1.5T Philips Intera scanner at the local hospital.

MRI Acquisition

This sample includes only those participants with magnetic resonance imaging (MRI) scans. All children were scanned on the same Philips Intera 1.5 Tesla scanner for 8 minutes at the local hospital in Carbondale, IL. T1-weighted images (TR = 30, TE = 4.6, FOV = 22, flip angle = 35, pixel matrix = 256 x 256) with 200 axial slices spaced .8mm apart (thickness is 1.6 mm) were acquired to form a 3-D structural magnetic resonance imaging scan. The child's head was stabilized with padding to reduce movement artifacts, and the child was allowed to listen to music through noise-dulling headphones for the duration of the 8-minute scan.

MRI Processing

Analyze 7.0 or 10.0 (Rochester, MN) were used to load and align the brains along the axis connecting the anterior commissure and the posterior commissure (AC-PC), as well as along the longitudinal fissure and the optic area by other graduate students and me after checking out with Dr. Kibby. This ensured that the MR images were aligned in all three planes prior to the region-of-interest (ROI) analysis. The aligned brain images were used from this point forward for all subsequent segmentation and tracing. Another graduate student and I used Analyze 10.0 to calculate the total cerebral brain volume for each participant, which is a semi-automated procedure. Total cerebral volume was used as a covariate in all of the subsequent analyses involving the volume of the caudate nucleus.

Reliability for Tracing the Caudate Nucleus

Prior to tracing the dataset, I established inter-rater reliability on 10 consecutive brains with Dr. Kibby. Paired samples t-tests were used to compare the volume of each tracer's caudate

nucleus, slice-by-slice, which generated inter-rater reliability correlation coefficients for the left caudate ($r = .95$, $p < .001$) and the right caudate ($r = .95$, $p < .001$). Once inter-rater reliability was established (blind to group membership), I attained intra-rater reliability by tracing 10 brains twice (separated in time) and then comparing the slice volumes using paired samples t-tests for the left caudate ($r = .94$, $p < .001$) and the right caudate ($r = .92$, $p < .001$). Next, I completed the tracing for all of the participants' caudates. Following the completion of the tracing for the entire dataset, intra-rater reliability of 10 consecutively traced brains was re-established for the right caudate ($r = .93$, $p < .001$) and the left caudate ($r = .93$, $p < .001$). The last round of intra-rater reliability was calculated by comparing a newly traced set of the same 10 brains to the second set of measurements used for intra-rater reliability initially. The second set was chosen because it was the set most recently traced in time.

MRI Tracing Method

I traced the caudate nucleus manually using the ROI Module of Analyze 10.0. The caudate was traced in the transverse, or axial, plane according to the methods outlined by Looi et al. (2008) who also used Analyze to manually trace the caudate nucleus. The authors' tracing protocol is as follows: the beginning point is when the head of the caudate is clearly visible, bounded by the frontal white matter anteriorly, anterior commissure posteriorly, internal capsule laterally, and thin band of frontal white matter medially; and the ending point is when the gray matter of the body of the caudate is no longer distinguishable from the wall of the lateral ventricle. Boundaries of the caudate nucleus were verified with a neuroanatomy textbook (Damasio, 2005). Measurements were conducted in the transverse plane.

The head and body of the caudate were segmented according to the method outlined by Filipek et al. (1997). The anterior commissure served as the boundary between the head and

body of the caudate; the tail was not included due to the fact that it is difficult to visualize, rarely included in the analyses of previous studies tracing the caudate nucleus, and not believed to be involved with EF. The authors defined the head of the caudate nucleus as any slice in the sagittal plane that is anterior to the anterior commissure, and the body of the caudate as any slice posterior to the anterior commissure. A semi-automated procedure was used in Analyze 10.0 in order to segment the head and body of the caudate nucleus. See Figure 2 for an example of a slice that shows a traced caudate nucleus bilaterally.

Reliability for Segmenting the Caudate Nucleus

Prior to segmenting the dataset, I established inter-rater reliability on 10 consecutive brains with Dr. Kibby. Dr. Kibby and I segmented the same set of traces. Paired samples t-tests were used to compare the volume of each tracer's caudate nucleus following segmentation into head and body, slice-by-slice. This generated inter-rater reliability correlation coefficients for the left caudate head ($r = .99$, $p < .001$), the left caudate body ($r = .99$, $p < .001$), the right caudate head ($r = .99$, $p < .001$), and the right caudate body ($r = .99$, $p < .001$). Once inter-rater reliability was established, I attained intra-rater reliability by segmenting 10 different brains twice (separated in time) and then calculating the reliability coefficients using paired samples t-tests as outlined previously. This generated intra-rater reliability coefficients for the left caudate head ($r = .99$, $p < .001$), the left caudate body ($r = .98$, $p < .001$), the right caudate head ($r = .99$, $p < .001$), and the right caudate body ($r = .98$, $p < .001$). Next, I completed the segmentation into head and body for all of the participants' caudates. See Figure 3 for an example of a slice that shows a segmented caudate nucleus into head and body.

CHAPTER FOUR

RESULTS

Preparation for Main Analyses

Skewness and Kurtosis Statistics

Descriptive statistics were run on all dependent variables to check skewness and kurtosis prior to running any analyses. Variables that were positively skewed (i.e., a positive value for a given skewness statistic was greater than two times the standard error) were square rooted, and variables that were negatively skewed (i.e., a negative value for a given skewness statistic was greater than two times the standard error) were squared to normally distribute each skewed variable. Table 9 shows the skewness and kurtosis statistics and standard errors, as well as corrected statistics for all dependent variables used in subsequent analyses.

Covariates

Between-subjects ANOVAs were run to determine if there were any diagnostic group differences (i.e., ADHD, developmental dyslexia [DD], both groups [ADHD/DD], and controls) in TONI-3 IQ, age, and handedness. Chi square tests were conducted to examine diagnostic group differences in sex, ethnicity, and SES (i.e., maternal education). These analyses were run because previous research indicated these variables may affect brain volume and/or executive functioning (Ankney, 1992; Buchel, Raedler, Sommers, Sach, Weiller, & Koch, 2004; Nyborg, 2005; Toga, Thompson, & Sowell, 2006; Witelson, Beresh, & Kigar, 2006). Total cerebral volume was used as a covariate regardless of group differences to ensure any differences in the volume of the analyzed region were not due to differences in overall brain volume.

Results initially indicated that the groups differed on TONI-3 IQ scores, $F(4, 104) = 2.59$, $p = .04$; however, post-hoc tests did not reveal any significant differences between clinical

groups and controls (*p*s > .05). A priori comparisons were tested using the TONI-3 as a covariate given that the omnibus test was significant; however, the results were not affected. Therefore, TONI-3 IQ was not used as a covariate in subsequent analyses. Groups did not differ in age, $F(3, 104) = .55$, $p = .65$; handedness, $F(4, 96) = .45$, $p = .77$; sex, X^2 (3, $N = 105$) = 1.22, $p = .75$; ethnicity, X^2 (12, $N = 105$) = 5.46, $p = .94$; or maternal education, X^2 (18, $N = 93$) = 16.50, $p = .56$ (see Tables 6 and 7). In summary, only total cerebral brain volume was used as a covariate in the main analyses.

ADHD Subtypes

A MANOVA was used to test the differences between ADHD-PI and ADHD-C on EF measures. Results showed that these groups differed by subtype, Wilks's $\Lambda = .47$, $F(11, 23) = 2.40$, $p = .04$; however, follow-up ANOVAs showed that ADHD-C and ADHD-PI only differed on Tower Rule Violations from the NEPSY, $F(1, 33) = 5.45$, $p = .03$. This finding is expected given that children with ADHD-C exhibit more impulsive behavior than children with ADHD-PI. Therefore, the ADHD subtype groups were collapsed into one in all subsequent analyses using cognitive executive functioning measures (see Table 8).

Creating Composite Executive Functioning Scores

An exploratory factor analysis was run using the Statistical Package for Social Sciences (SPSS version 17.0) on the EF measures included in the dataset as a way to reduce the number of dependent variables tested in the analyses. These areas included problem solving (Categories Achieved from the WCST), planning (Tower from the NEPSY), working memory (Numbers, Sequences, Picture Locations from the CMS), rapid generation of novel ideas/fluency (Design Fluency from the NEPSY), behavioral inhibition (Tower Rule Violations from the NEPSY), set shifting/perseveration (Perseverative Errors from the WCST), cognitive control (i.e., self-

monitoring, planning, organization; Metacognition Index from the BRIEF), and regulation of emotional and behavioral responses (BRI from the BRIEF).

An exploratory factor analysis was run in two stages: factor extraction and factor rotation. Factor extraction was done using the Principal Components method. Any factor that had an Eigenvalue greater than 1 was included in the subsequent factor analysis. The scree plot was used to verify the accuracy of the Eigenvalue cutoff (i.e., any value in the sharp decent of the scree plot was considered a factor). Based on this method, three factors were extracted.

Factor rotation was run using the three factors determined from the Eigenvalue and scree plot test. The Maximum Likelihood extraction method was used along with oblique rotation. Oblique rotation was chosen because the selected variables are believed to be related to each other given that they have been shown to measure various aspects of executive functioning to various degrees.

The rotated solution yielded three interpretable factors: executive functioning abilities in the home, problem solving/perseveration, and working memory/fluency. Following extraction, executive functioning abilities in the home accounted for 23.73% of the variance, problem solving/perseveration accounted for 15.41% of the variance, and working memory accounted for 17.15% of the variance. Of note, Tower and Tower Rule Violations did not load on to any factor; therefore, the factor analysis was re-run without these variables. The resulting three component variables from the rotated factor matrix were used as outcome variables in the main analyses. The results from the factor analysis from the Pattern Matrix are shown in Table 10.

Testing Main Hypotheses

Hypothesis 1: Differences in Caudate Volume

It was hypothesized that the volume of the caudate would be reduced in the clinical groups compared to those without each disorder and that there would be rightward asymmetry in the caudate head in the ADHD group, leftward asymmetry in the caudate body, and the opposite pattern for those without ADHD. The asymmetry pattern in the developmental dyslexia group was exploratory. The dependent variables used in the volumetric analysis were the volumes of the right and left caudate head and body. For the asymmetry analysis, the dependent variables were the asymmetry scores that were computed separately for the caudate head and body as described in the Specific Hypotheses section. Two 2 (ADHD or not) x 2 (developmental dyslexia or not) MANOVAs were conducted to investigate potential differences in caudate volume and asymmetry (see Figure 4 for a description of the 2 x 2 design). Total cerebral volume was used as a covariate in these analyses.

In terms of the results from the volumetric analysis, the ADHD group did not differ on caudate volume compared to those without ADHD, Wilks's $\Lambda = .92$, $F(4, 97) = 2.12$, $p = .08$. The developmental dyslexia group also did not differ from those without it, Wilks's $\Lambda = .94$, $F(4, 97) = 1.45$, $p = .22$, nor was the interaction significant, Wilks's $\Lambda = .98$, $F(4, 97) = .39$, $p = .81$ (see Table 11).

In terms of the asymmetry analysis in the ADHD group, both the rightward caudate head asymmetry and the leftward caudate body asymmetry were significantly different than zero, $t(51) = 6.39$, $p < .001$ and $t(51) = -2.16$, $p = .04$, respectively. Those without ADHD had rightward caudate head asymmetry that was significantly different from zero, $t(52) = 2.05$, $p = .05$, as well as significant leftward asymmetry of the caudate body, $t(52) = -3.36$, $p < .001$. In the

developmental dyslexia group, the rightward asymmetry of the caudate head was significantly different from zero, $t(34) = 3.17$, $p < .01$; however, the leftward asymmetry of the caudate body was not significantly different from zero, $t(34) = -1.21$, $p = .24$. Those without developmental dyslexia had rightward caudate head and body asymmetry that was significantly different from zero, $t(69) = 4.66$, $p < .001$ and $t(69) = -3.80$, $p < .001$, respectively (see Table 12).

Hypothesis 2: Cognitive Deficits Associated with Executive Functioning (EF)

It was hypothesized that those with ADHD and those with developmental dyslexia would be impaired on measures of cognitive executive functioning. The dependent variables used in this analysis were the three latent variables from the exploratory factor analysis. In order to test Hypothesis 2a, a 2 (ADHD or not) x 2 (DD or not) MANOVA was run to see if performance on cognitive EF measures differed by diagnostic group. The outcome measures were the three component EF variables generated from the previous factor analysis. Those with and without ADHD and those with and without developmental dyslexia were significantly different on EF measures, Wilks's $\Lambda = .67$, $F(3, 99) = 15.97$, $p < .001$, and Wilks's $\Lambda = .77$, $F(3, 99) = 9.86$, $p < .001$, respectively. More specifically, the ADHD group was more impaired than those without ADHD on executive functioning abilities in the home and working memory/fluency, $F(1, 101) = 44.23$, $p < .001$, and $F(1, 101) = 9.76$, $p = .002$, respectively. Similarly, the developmental dyslexia group was more impaired on the same measures, executive functioning abilities in the home, $F(1, 101) = 7.07$, $p = .01$ and working memory/fluency, $F(1, 101) = 26.70$, $p < .001$. Lastly, the multivariate test was not significant for the interaction, Wilks's $\Lambda = .95$, $F(3, 99) = 1.84$, $p = .15$ (see Table 13).

Given that there was no dissociable inhibition factor resulting from the factor analysis, a separate univariate ANOVA was run to see if the ADHD-C group was more affected on

inhibition (i.e., Tower Rule Violation corrected score) compared to the rest of the clinical groups and controls as hypothesized. This relationship was significant, $F(4, 100) = 2.73$, $p = .03$. Follow-up tests showed that those with ADHD-C ($M = 17.32$, $SD = 6.57$) did not have more rule violations on the NEPSY Tower than those with ADHD-PI ($M = 11.56$, $SD = 7.05$), $p = .07$ as expected; however, low power may have affected the ability to find a significant effect in this analysis. No other group differences approached significance.

Given that all cognitive tests involve a certain amount of attentional control to complete, it is important to rule out differences in attention as the driving factor behind group differences. Therefore, another univariate ANOVA was run to see if diagnostic groups differed on a non-executive functioning task (i.e., Stories Delayed Recall from the Children's Memory Scale [CMS]). The groups did not differ on Stories, $F(4, 99) < 1.0$. This shows a dissociation between performance on complex tasks with and without an executive functioning component such that diagnostic groups differ on EF tasks but not on non-EF tasks. This suggests that attention is not driving the effects reported for the diagnostic groups. See Table 8 for descriptives.

To test Hypothesis 2b, a 2 (ADHD or not) x 2 (DD or not) MANCOVA was used, adding the three working memory measures (i.e., Sequences, Numbers, and Picture Locations) and caudate head and body asymmetry scores as covariates. The asymmetry variables were used as covariates given that they were significantly different from zero for the ADHD group in Hypothesis 1. The dependent variables included all of the EF measures that were added to the factor analysis, which were on the same scale (i.e., $M = 100$, $SD = 15$), and included Categories Achieved and Perseverative Errors from the WCST, Design Fluency from the NEPSY, and the Metacognitive Index and Behavioral Regulation Index from the BRIEF. After controlling for working memory and caudate head and body asymmetry scores, the ADHD group was still more

impaired than those without ADHD on EF measures, Wilks's $\Lambda = .58$, $F(5, 92) = 13.28$, $p < .001$. More specifically, the ADHD group was more impaired than those without ADHD on the Metacognitive Index, $F(1, 96) = 61.98$, $p < .001$ and the Behavioral Regulation Index, $F(1, 96) = 30.46$, $p < .001$. There was not a significant relationship between ADHD and Categories Achieved, $F(1, 96) = 1.07$, $p = .30$, Perseverative Errors, $F(1, 96) < 1$, or Design Fluency, $F(1, 96) = 2.55$, $p = .11$. The relationship between those with developmental dyslexia and those without was not significant on EF measures controlling for working memory and caudate asymmetry scores, Wilks's $\Lambda = .95$, $F(5, 92) = 1.04$, $p = .40$, nor was the interaction, Wilks's $\Lambda = .93$, $F(5, 92) = 1.40$, $p = .23$. Sequences, a verbal working memory measure, was a significant covariate in this analysis, Wilks's $\Lambda = .87$, $F(5, 92) = 2.76$, $p = .02$; however, Numbers and Picture Locations were not significant, Wilks's $\Lambda = .98$, $F(5, 92) < 1$ and Wilks's $\Lambda = .91$, $F(5, 92) = 1.94$, $p = .10$, respectively. The caudate head and body asymmetry scores were not significant covariates, Wilks's $\Lambda = .94$, $F(5, 92) = 1.16$, $p = .34$ and Wilks's $\Lambda = .89$, $F(5, 92) = 2.25$, $p = .06$, respectively (see Table 14).

Given that verbal working memory appeared to be driving the potential mediation effect for those with developmental dyslexia versus those without it, a separate 2 x 2 MANCOVA was run with only verbal working memory as a covariate. Similar to the first analysis using the three working memory measures and caudate volume as covariates, the ADHD group differed from those without ADHD, Wilks's $\Lambda = .58$, $F(5, 96) = 13.80$, $p < .001$ and verbal working memory was a significant covariate, Wilks's $\Lambda = .80$, $F(5, 96) = 4.83$, $p = .001$. Furthermore, the same pattern emerged as reported earlier such that the ADHD group was more impaired than those without ADHD on the Metacognitive Index and the Behavioral Regulation Index from the BRIEF, $F(1, 100) = 63.41$, $p < .001$ and $F(1, 100) = 36.09$, $p < .001$, respectively. There was no

significant difference between those with and without developmental dyslexia on EF measures when only controlling for verbal working memory, Wilks's $\Lambda = .97$, $F(5, 96) < 1$. The interaction also was not significant, Wilks's $\Lambda = .93$, $F(5, 96) = 1.47$, $p = .21$.

Hypothesis 3: Brain-Behavior Relationships

It was hypothesized that verbal and spatial working memory would mediate the relationship between left and right caudate volume, respectively, and performance on EF measures. The dependent variables were performance on NEPSY Tower, NEPSY Design Fluency, and the WCST. In order to test Hypothesis 3a, the brain-behavior relationship between left caudate volume and performance on NEPSY Tower (i.e., planning) and WCST Categories Achieved (problem solving), a mediator model outlined by Baron & Kenny (1986) was used. The full mediation model is below:

To test this mediation, separate analyses must be run in steps as outlined by Baron & Kenny (1986). Step 1: It is necessary to show that the initial variable (i.e., left caudate volume) is correlated with the outcome (i.e., performance on the NEPSY Tower and the WCST). Performance on the NEPSY Tower and the WCST were used as the outcome variable in the two regression equations and left caudate volume was used as a predictor (this estimated and tested path c).

The relationship between left caudate volume and performance on the NEPSY Tower was not significant, $F(2, 102) < 1.0$, nor was the relationship with WCST Categories Achieved, $F(2, 102) < 1.0$. The failure to establish an effect between the initial variable and the outcome variables precludes any further analysis of a mediation between caudate volume and performance on these EF measures.

In order to test Hypothesis 3b, the same steps outlined in 3a were used, but spatial working memory was substituted for verbal working memory and right caudate volume was substituted for left caudate volume.

The relationship between right caudate volume and performance on NEPSY Tower was not significant, $F(2, 102) < 1.0$, nor was the relationship with WCST Categories Achieved, $F(2, 102) < 1.0$, or the relationship with NEPSY Design Fluency, $F(2, 102) < 1.0$ (path c).

The failure to establish an effect between the initial variable and these outcome measures precludes any further analysis of a mediation between caudate volume and performance on these EF measures.

Exploratory Analyses

Given the negative findings testing the brain-behavior relationship in Hypothesis 3, exploratory analyses were run to further investigate the relationship between caudate volume and performance on working memory measures. This is justified given the fact that the caudate head volume was significantly related to a diagnosis of ADHD and working memory was related to performance on EF measures in Hypotheses 1 and 2. Prior literature also suggests the caudate is involved with working memory. Bivariate correlations were run using the volume of the right and left caudate head and performance on the three working memory measures from the Children's Memory Scale (i.e., Sequences, Numbers, and Picture Locations; see Table 16). Results showed that the left caudate head volume was not significantly correlated with Sequences, a verbal working memory measure ($r = .182$, $p = .06$); however, low power may have affected the ability to detect a significant effect. Given the left side of the brain's influence on verbal measures (Frost et al., 1999), this relationship deserves further investigation following an increase in power. This relationship is more specific in comparison to the general relationship

between caudate volume and EF performance that was tested in Hypothesis 3, which was non-significant.

CHAPTER FIVE

DISCUSSION

The current study investigated brain-behavior relationships between the caudate nucleus, part of the frontostriatal circuit, and measures of executive functioning in children with ADHD, developmental dyslexia, both disorders, and controls. The review of literature outlined cognitive deficits commonly seen in these childhood disorders such as working memory, set shifting, planning, and nonverbal fluency (Klorman et al., 1999; Willcutt et al., 2001). Given the high rate of comorbidity between ADHD and developmental dyslexia (Willcutt & Pennington, 2000), this study aimed to address limitations in the understanding of the caudate nucleus and its relation to executive dysfunction in these disorders.

Differences in Caudate Volume by Diagnosis

Hypothesis 1 tested the differences in caudate volume and asymmetry in children with ADHD, developmental dyslexia, both disorders, and controls. It was hypothesized that there would be a reduction in caudate volume in clinical groups compared to controls and right-over-left asymmetry in the head of the caudate and left-over-right asymmetry in the body of the caudate nucleus for children with ADHD, as well as a left-over-right asymmetry in the head of the caudate nucleus and a right-over-left asymmetry for controls based on findings by Tremols and colleagues (2008). The investigation of symmetry of the caudate nucleus in children with developmental dyslexia was exploratory.

After controlling for total cerebral volume, there were no differences in caudate volume compared to controls in the ADHD or developmental dyslexia groups. This is consistent with prior research showing no reduction in the volume of the total caudate nucleus (Mataro et al., 1997). Given that other studies have reported a reduction in total volume (Giedd et al., 1994;

Lou et al., 1989), the inability to find differences in the current study were likely related to the fact that the caudate head is the critical region related to executive dysfunction; therefore, combining the head and body in analyses may have washed away the effects of the head alone. Therefore, asymmetry analyses separating the head and body were performed in the current study. Results showed that there was rightward asymmetry in the caudate head of children with ADHD as expected. Those without ADHD also had right-over-left asymmetry, in contrast to the findings of Tremols and colleagues (2008). However, this finding is consistent with prior research, which found rightward asymmetry in controls (Castellanos et al., 1994, 1996). The relationship between caudate body asymmetry and group membership was not significant for those with and without ADHD. Both groups had leftward asymmetry. This is consistent with findings of leftward asymmetry of the total caudate volume in those with ADHD compared to controls by Castellanos and colleagues (1996). Further, children with developmental dyslexia did not differ significantly from those without it, which suggests that caudate volume/symmetry is not related to developmental dyslexia.

The current finding for the head of the caudate in children with ADHD is commensurate with those reported by Tremols and colleagues (2008), as well as other studies measuring the same structure (Filipek et al., 1997; Hynd et al., 1993; Semrud-Clikeman et al., 2000). More specifically, the volumes measured in the current study for head and body fall between those of Tremols and colleagues and Filipek and colleagues (1997). It is likely that differences in total volume and volume of the head and body are due to methodological differences given that Tremols and colleagues used a semi-automated tracing method that did not follow anatomical boundaries and Filipek and colleagues used anatomic segmentation following normalization.

Methods that segment the head and body rather than grouping them together provide a unique opportunity to investigate the differential functions of these anatomical structures. Segmentation also allows for the ability to explain the conflicting research on caudate volume in ADHD. Some authors found rightward asymmetry in the left caudate head and in total caudate volume in those with ADHD compared to controls (Filipek et al., 1997; Hynd et al., 1993; Semrud-Clikeman et al., 2000), whereas one study found leftward asymmetry in total right caudate volume but symmetry for the total caudate volume when comparing those with ADHD to controls (Castellanos et al., 1996). Using a new segmentation methodology may help to explain the differences reported in the literature given that the head and body of the caudate nucleus may have differential functions. More specifically, the head is part of the dorsolateral prefrontal, lateral orbitofrontal, and anterior cingulated circuits of Alexander (Alexander et al., 1986). In contrast, the body of the caudate is believed to be related to Alexander's oculomotor circuit. In terms of functional relationships, Seger and Cincotta (2005) reported that the caudate head was associated with executive functions such as feedback processing, and the caudate body was associated with successful learning. In light of the findings from the current study showing a relationship between caudate head asymmetry and ADHD, more research is needed to support the differential functions of the caudate head and body in ADHD.

Given that no other study has looked at the symmetry of the caudate nucleus in those with developmental dyslexia, these findings added to the literature in this area. Limited research has implicated the caudate nucleus in developmental dyslexia, especially using structural imaging techniques; however, considerable research has implicated other brain structures, including posterior regions of the brain such as Wernicke's area, the angular gyrus, and the striate cortex (Shaywitz et al., 1998). In light of these findings, the inability to find a reduction in caudate

nucleus volume or asymmetry in the current study could have acted as a buffer against the dysfunction seen in phonological tasks in developmental dyslexia. In addition, other frontostriatal regions such as the inferior frontal cortex, which was not assessed in this study, may be implicated in developmental dyslexia rather than the caudate nucleus and deserves further investigation.

Cognitive Deficits Associated with Executive Functioning

Hypothesis 2 investigated the relationship between cognitive deficits associated with executive dysfunction and diagnostic group membership (i.e., ADHD, developmental dyslexia, both disorders, and controls). Results from the exploratory factor analysis using the measures of executive functioning assessed in the current study indicated three factors: executive functioning in the home, problem solving/perseveration, and working memory/fluency. Planning and inhibition did not load onto any of the factors; therefore, they were included as a separate variable. Results showed that children with ADHD and children with developmental dyslexia were more impaired than those without on executive functioning abilities in the home and working memory/fluency. These findings are consistent with the work of Gioia, Isquith, Guy, and Kenworthy (2002) who showed that children with ADHD and children with developmental dyslexia have shared cognitive deficits in working memory and on subscales from the BRIEF, which measures executive functioning abilities in the home (i.e., Plan/Organize and Monitor). Similar to the current study, previous studies using the Tower of London and the Tower of Hanoi as a measure of planning also failed to show differences between children with and without ADHD (Houghton et al., 1999; Sonuga-Barke et al., 2002; Weyandt et al., 1998). This study added to the literature on cognitive executive functioning in ADHD and developmental dyslexia

by implicating working memory as a potential source of comorbidity between these two common childhood disorders.

Children with ADHD-C did not differ from other clinical groups and controls on behavioral inhibition as expected; however, a power analysis indicated a ß of .48 with the current sample size of 105 children. Therefore, low power likely affected the ability to find a significant effect when all five groups were compared. With a conservative effect size of .25, a sufficient sample size should be 220 children. Previous literature suggests that children with ADHD-C have more difficulty on a stop-signal reaction time (SSRT) task (Nigg et al., 2002) and have more errors of commission and omission on the CPT (Huang-Pollock, Nigg, & Halperin, 2006) than those with ADHD-PI. Thus, future research should include more traditional measures of inhibition such as the SSRT task and the CPT to assess ADHD and developmental dyslexia.

Given that the ADHD-PI and ADHD-C groups were similar on measures of cognitive executive functioning and may have differed on behavioral inhibition given a sufficient sample size, this supports the fact that there are likely two ADHD dimensions, Inattention and Hyperactivity/Impulsivity, rather than being categorical diagnoses as the DSM-IV implies. The findings in the current study related to the two subtypes are consistent with previous research by Barkley (2003) showing that children with ADHD-C, who are high on both dimensions, have more difficulty with behavioral regulation than those with ADHD-PI. In addition, work by Chhabildas and colleagues (2001) suggest that there are not distinct neuropsychological profiles when comparing children with ADHD-PI to those with ADHD-C because both groups present with difficulties related to inattention. Thus, future studies should use a dimensional approach when investigating cognitive deficits associated with ADHD.

The findings from the current study suggest that cognitive executive functioning may be a potential source of comorbidity between ADHD and developmental dyslexia. Children in both groups were impaired on executive functioning abilities in the home and working memory/fluency. The current findings of deficits in working memory are commensurate with previous literature showing that individuals with comorbid ADHD/developmental dyslexia are impaired on a mental arithmetic task, which is a measure of working memory (Kibby & Cohen, 2008). In addition, Willcutt and colleagues (2001) showed that children with comorbid ADHD/developmental dyslexia had more deficits related to working memory, inhibition, and naming letters and numbers than children with each disorder alone. Lastly, other authors have reported that individuals with comorbid ADHD/developmental dyslexia are impaired on verbal working memory (Rucklidge & Tannock, 2002; Willcutt et al., 2003). Consistent with previous research, it appears that the comorbid group has additive deficits from both diagnostic groups and does not represent a unique disorder. Given the high rate of comorbidity in these two common childhood disorders, further research is needed to investigate the role of cognitive executive functioning, especially working memory, as a potential source of comorbidity between ADHD and developmental dyslexia.

Given that all cognitive tests involve a certain amount of attentional control to complete, it is important to rule out differences in attention as the driving force of diagnostic group differences in the current sample. In order to compare the diagnostic groups on a complex task that requires attention but not executive functioning, an ANOVA was run using the Stories Delayed Recall subtest from the Children's Memory Scale (CMS) with one group level factor (i.e., ADHD, developmental dyslexia, ADHD/developmental dyslexia, and controls). No group differences were found, suggesting a dissociation in performance on complex tasks that require

attention with and without executive demands. Therefore, the cognitive deficits assessed in the diagnostic groups studied in the current study appear to be specific to executive functioning and not likely due to inattention alone.

Hypothesis 2b examined the relationship between performance on cognitive executive functions, using the three factor scores from the exploratory factor analysis as outcome measures, and diagnosis after controlling for working memory and caudate head volume. Children with ADHD and children with developmental dyslexia both exhibited impairments in executive functioning abilities in the home and working memory/fluency, which is consistent with the hypothesis and past research showing that both ADHD (Chamberlain & Sahakian, 2007; Rubia et al., 1999) and developmental dyslexia (Kibby & Cohen, 2008; Snowling, 1991) are associated with impairments in working memory, as well as other cognitive executive functioning tasks. A subsequent analysis included working memory as a covariate given that it is believed to influence performance on other executive functioning tasks such as planning (Manoach et al., 2003; Monchi et al., 2001, 2006b). Furthermore, caudate head volume rather than total caudate volume was used as a covariate given that it was related to a diagnosis of ADHD in Hypothesis 1 and in prior literature (Filipek et al., 1997; Tremols et al, 2008).

When including working memory and caudate volumes as covariates, the difference between those with ADHD and those without ADHD was still significant. This suggests that deficits in executive functioning go beyond working memory and caudate volume in ADHD. In contrast, the difference between children with developmental dyslexia and those without it was not significant on executive functioning measures when working memory was included as a covariate despite prior significance. Covariate findings suggest that caudate asymmetry is not related to executive functioning measures in this analysis. Therefore, working memory may be

the main factor driving the impairment in executive functioning in developmental dyslexia. Previous literature supports working memory as the main cognitive executive functioning deficit in developmental dyslexia (Kibby, 2009; Kibby & Cohen, 2008; Snowling, 1991; Swanson & Ashbaker, 2000), and working memory influences performance on other executive functioning tasks (Barkley, 1997; Miyake et al., 2000) as noted earlier. Verbal working memory in particular may be driving the effect given its importance in reading (Swanson & Ashbaker, 2000) and its relation to poor phonological processing (Kibby et al., 2004) and phonological storage of verbal material (Kibby, 2007). Given that verbal working memory is impaired in developmental dyslexia and the fact that working memory influences the performance on other executive functioning tasks, future studies should investigate the relationship between developmental dyslexia and performance on other executive functions using verbal working memory as a mediator. This study added to the literature the fact that working memory is a common impairment in both ADHD and developmental dyslexia and may be a source of comorbidity between these disorders given the shared neuropsychological and behavioral deficits.

Brain-Behavior Relationships

Hypothesis 3 tested the brain-behavior relationship between caudate volume and performance on executive functioning measures. Given that both children with ADHD and children with developmental dyslexia have been shown to have impairments in working memory and the caudate has been shown to be active during working memory tasks (Beauchamp et al., 2003; Monchi et al., 2001; van den Deuval et al., 2003), verbal and spatial working memory were hypothesized to mediate the brain-behavior relationship between left and right caudate volume with verbal and spatial abilities, respectively. Activation of the caudate nucleus has been linked to performance on a Tower planning task (Beauchamp et al., 2003; van den Deuval et al.,

2003) and the WCST (Monchi et al., 2001); therefore, the NEPSY Tower and the WCST were used in the current study as outcome measures. The relationship between left caudate volume and performance on the NEPSY Tower and the WCST was not significant; therefore, the mediation model was not tested further.

This negative finding and that of the previous analysis when the caudate was used as a covariate suggests that caudate volume may not directly influence function on these executive functioning tasks; however, different measures of executive functioning may be more sensitive to caudate structure than the ones available for the current study. Moreover, it should be noted that previous studies reported positive findings using functional neuroimaging techniques, whereas the current study used structural MRI. Methodological differences likely affected the ability to detect an effect. Thus, in this instance, caudate functioning at the synapse level may play a more important role in these executive functioning tasks than caudate size/asymmetry.

Similarly, the relationship between the right caudate volume and performance on executive functioning tasks (i.e., NEPSY Tower, WCST, and NEPSY Design Fluency) was not significant. As a result, the analysis using spatial working memory as a mediator was not tested further. Given that neither of the hypotheses testing brain-behavior relationships was significant, an exploratory analysis was run to test the relationship between the volumes of the caudate heads bilaterally and performance on working memory measures in the total sample. The volume of the left caudate head was not significantly correlated with performance on a verbal working memory measure (i.e., Sequences from the CMS); however, a power analysis revealed a power of .59; therefore, low power likely affected the ability to find a significant effect. This relationship deserves further research given that the frontostriatal circuit has been implicated in both ADHD and developmental dyslexia and both groups have verbal working

memory deficits. It also is warranted given prior functional neuroimaging research showing activation of the caudate during working memory tasks (Manoach et al., 2003; Monchi et al., 2006b).

Moreover, the interconnections of the frontostriatal circuit may be more complicated than those assessed in the current study. Given that there are two divergent pathways in the basal ganglia, a "motor" circuit and a "prefrontal" circuit (Alexander et al., 1986), more research is needed on the functional nature of identified circuits (i.e., dorsolateral prefrontal circuit), rather than focusing on specific nuclei (i.e., caudate nuclei). Although there were no volume differences found in the caudate nucleus, the asymmetry findings in the sample of children with ADHD further supported the role of the frontostriatal circuit dysfunction in the pathophysiology of ADHD. More sophisticated analyses of the interconnection of the prefrontal cortex and the caudate head are needed given the link between executive dysfunction and the dorsolateral prefrontal cortex and the research linking atypical caudate volume, especially the head, in ADHD.

Strengths

There are several strengths to the current study that should be highlighted. First, the current study adds to the limited research in the area of caudate volume and its relation to ADHD when using a newer segmentation approach. Given that the findings in the current study are consistent with the asymmetry seen in the caudate head for children with ADHD, the current study helps to rectify the differences found in total caudate volume for ADHD and controls in the previous literature. Second, the sample size of the current study is another strength, with 19 children with ADHD-PI, 16 with ADHD-C, 18 with developmental dyslexia, 17 with comorbid ADHD/developmental dyslexia, and 35 controls included in the analyses. Third, the current

study included several commonly used neuropsychological measures for children, which allows for greater comparison to past and future research. Fourth, children who met either the IQ/achievement discrepancy and poor reader definition of developmental dyslexia were included in the current study given that there is a lack of external validity for the difference between the two definitions (Pennington, 2009). This is important given that poor readers have deficits in reading despite not meeting the IQ/achievement discrepancy. Lastly, children in the current sample were screened so as to provide a dataset that is free from comorbidity with mood and anxiety disorders, schizophrenia, and neurologic disorders.

Limitations

The current study has several limitations that should be addressed when interpreting the findings, particularly those related to group differences. Given that power analyses revealed that small sample size may have impacted the ability to find significant effects in the current study, it is recommended that the analyses be repeated or modified following an increase in sample size in the clinical groups to investigate whether the relationships become significant. An increase in sample size in the ADHD group in particular may allow for separate analyses to be run by subtype rather than collapsing across subtypes into a general ADHD group. This breakdown would be especially important when analyzing differences in inhibition given that it is a hallmark characteristic of the ADHD-C subtype and there were no significant differences between those with ADHD-C and other diagnostic groups in the current study. Having a larger sample of children with developmental dyslexia would allow for the ability to see if differences exist between poor readers and those with an IQ/achievement discrepancy.

Another limitation is that the children who participated in the grant-funded study from which the participants for this study were drawn are not a random sample. The children came

from rural communities surrounding the university that are comprised mainly of participants who are Caucasian, which affects the ability to generalize to any population selected from a city or suburban areas and to a more ethnically diverse sample. Moreover, parents who are willing to have their children participate in a study that involves a neuroimaging component may represent a unique group, which also may affect generalizability. Furthermore, children who were able to successfully complete the 8-minute MRI scan with minimal motion may represent a unique group of children who are not as severe in terms of their ADHD diagnosis. Of note, ADHD severity was mild overall in this study.

Lastly, the measures of executive functioning available for analysis were limited as these data were drawn from a larger study focused on other topics. Future research should include more measures of similar constructs, rather than the one or two measures per construct that were used in this study. This would be especially useful if an exploratory factor analysis were used, similar to this study, to collapse measures into common factors. Moreover, experimental measures that are more sensitive to one aspect of executive functioning rather than these complex tasks, which are sensitive to various executive functioning aspects to differing degrees, could be used in future research.

Future Directions

Further research is needed in the area of brain-behavior relationships in children with ADHD and developmental dyslexia due to the high comorbidity between these disorders. Given the implication of the frontostriatal circuit in ADHD and the emergence of literature showing executive functioning impairments in developmental dyslexia, it is important to continue using neuroimaging techniques to elucidate the role of the frontostriatal circuit in these common childhood disorders. Future studies investigating the role of the frontal lobes in executive

dysfunction are needed given that the frontal lobes may be the source of the impairment seen in developmental dyslexia instead. The current study used structural neuroimaging techniques; however, future studies should include functional neuroimaging, electrophysiology, and positron emission tomography techniques in conjunction with structural neuroimaging. Since underlying structure influences fMRI activation, it is important to know if fMRI activation is driven by structure alone or if the activation goes beyond that to involve a more complex interplay of neurochemistry and physiology.

More research is needed on whether the two ADHD subtypes (i.e., ADHD-PI and ADHD-C) should be differentiated when analyzing differences in cognitive functioning. There is a debate as to whether the ADHD subtypes represent distinct disorders or are the same and, therefore, should be collapsed into one group in future analyses (Nigg, 2006). It has been shown consistently that individuals who are diagnosed with ADHD-C have difficulty with behavioral regulation that is not seen in those with ADHD-PI. The current study did not find differences in cognitive executive functioning between subtypes, with the exception of inhibition, which is expected based on the diagnostic criteria for ADHD-C. Given that individuals with ADHD-PI and individuals with ADHD-C are relatively high on Inattention, but those with ADHD-C also are relatively high on Hyperactivity/Impulsivity, this suggests that children with ADHD-C are doubly affected. Thus, ADHD-C may be a more severe form of ADHD than ADHD-PI. This is possible given that Inattention and Hyperactivity/Impulsivity are likely two different dimensions of behavior and are not categorical like the DSM-IV presumes. In light of this, it is important to increase the number of diagnostic studies on ADHD using a dimensional approach.

Given that the focus of this study was on cognitive executive functioning in total, further analysis of the volume of the caudate head in ADHD and its relation to more specific measures

of executive functioning is warranted. More specifically, working memory should be further investigated given the findings from the current study and the fact that no other study has looked at the relationship between caudate structure and working memory despite fMRI studies finding a relationship. In addition, measures of reaction time and response inhibition such as the go/no-go task should be used as outcome measures in future analyses given the literature outlining the impairment in these areas for individuals with ADHD and its link to the frontostriatal circuit.

Clinical Implications

Given that ADHD and developmental dyslexia are two of the most common childhood disorders and the fact that they are highly comorbid with each other, it is important to screen for the presence of one disorder when the other is suspected or diagnosed. Identification and treatment of one disorder and not the other could negatively impact a child's ability to perform to their potential. Given that there are shared cognitive deficits between these disorders, it is important to screen for the presence of both disorders in order to diagnose the correct disorder so as to maximize treatment effectiveness. Current treatments for both ADHD and developmental dyslexia include behavioral treatments and school remediation. Lastly, it is important to test executive functioning in both disorders when a diagnosis is suspected given that both disorders have been shown to be associated with executive dysfunction in a significant proportion of the cases studied.

Furthermore, research into the impact of brain structure as it relates to function may advance the knowledge and usefulness of pharmacotherapies used to treat these disorders. A recent study by Arcos-Burgos and colleagues (2010) reported that Latrophilin 3 gene (LPHN3) variants are expressed in brain regions that are associated with ADHD (i.e., caudate nucleus, amygdala, pontine nucleus, and cerebellar Purkinje cells) and also are associated with response

to stimulant medication. Given that the current main line of defense for treating ADHD is the use of psychostimulants, findings such as this provide a promising avenue for how structure may be related to pharmacotherapy effectiveness. At present, there are no accepted pharmacological treatments for developmental dyslexia. Future research regarding the involvement of the frontostriatal circuit in these disorders may provide insight into targeted pathways for effective treatments that can be used in conjunction with behavioral treatments and school remediation for both disorders. This may be especially true for those with executive functioning deficits.

Table 1

Executive Functions Measured in Previous Literature

Executive Function	Neuropsychological Test Used
Set shifting, problem solving, perseveration	WCST
Set shifting, cognitive flexibility	TMT-B
Response inhibition	SSRT, CPT
Planning	Tower of Hanoi/Tower of London, Rey-Osterrieth Complex Figure Test
Verbal working memory	DSF, DSB
Novel generation of ideas/fluency	Five-Point Test, RFFT

Note. WCST: Wisconsin Card Sorting Test; TMT-B: Trailmaking Test Part B; SSRT: Stop-signal Reaction Time; CPT: Continuous Performance Test; DSF: Digit Span Forward; DSB: Digit Span Backward; RFFT: Ruff Figural Fluency Test.

Table 2

List of Studies of Executive Functioning in ADHD

Author (Year)	Diagnoses	Age (years)/Sex ratio	Executive Functioning Measure Used	Findings
Alderson (2007)	ADHD, controls	6-12; males and females	Meta-analysis on behavioral inhibition as measured by Stop-signal paradigm	Children with ADHD had slower mean reaction time, greater reaction time variability, and slower stop-signal reaction time compared to controls.
Berlin et al. (2003)	ADHD-like symptoms	5-8; males and females	Go/no-go, nonverbal working memory, verbal working memory, self-regulation of affect/arousal, reconstitution	Preschool aged children who had difficulty with inhibition had more ADHD-like behaviors at both home and school (males) and only at school (females).
Biederman et al. (2006)	Executive functioning deficits without ADHD, ADHD, ADHD and executive functioning deficits, controls	18-55; 50% male	Stroop (interference), WCST (perseverative errors & failure to maintain set), Rey-O (copy & delay), Auditory Continuance Performance Test, California Verbal Learning Test, Estimated freedom from distractibility	Significantly more adults with ADHD had deficits in executive functioning (scores 1.5 SD below matched comparison subjects). Deficits also were seen in academic achievement, and they had lower socioeconomic status.
Cepeda et al. (2000)	ADHD-C, controls	6-12; not specified	Mental flexibility	Children who were off medication had more difficulty with a switching task. When on mediation, they did not differ from

				controls.
Chhabildas et al. (2001)	ADHD (C, PI, and H/I), controls	10-12; ~2:1 for ADHD group (male: female) and ~1:1 for controls	Commission and omission errors; inhibitory control task, processing speed, and working memory	ADHD-H/I did not differ from controls. ADHD-C and PI did not differ from each other, but did perform worse than ADHD-H/I and controls.
Culbertson & Zillmer (1998)	ADHD, controls	7-12; 1:1 (male: female)	Modification of Tower of London task to test construct validity of executive planning	The Tower of London modification loaded onto the Executive Planning/Inhibition factor and was separate from factors of Executive Concept Formation/Flexibility, Psychometric Intelligence, and Memory.
Houghton et al. (1999)	ADHD (C & PI), controls	6-12; 1:1 (male: female)	WCST, the Stroop Color-Word Test, the Matching Familiar Figures Test, the Trail Making Test, and the Tower of London	Children with ADHD-PI and C differed from controls on all measures, but children with ADHD-C had specific impairments in perseveration and response inhibition.
Karama et al. (2008)	ADHD, controls	6-12; not specified	Tower of London, Freedom from Distractibility Index & Digit Span (WISC-III), Self-Ordered Pointing Task based on dopamine transporter genotype	Children with the 9/10 genotype performed worse on all measures of executive functioning than those with the 10/10 genotype.
Karatekin (2004)	ADHD, controls	8-15; predominantly male	Verbal and spatial working memory tasks	Children with ADHD are not impaired in working memory overall or verbal/spatial processing; however, they may be

				impaired in the central executive component of working memory.
Kibby & Cohen (2008)	ADHD, Reading Disability (RD), ADHD/RD, controls	6-15; 70-87% male	Verbal short-term memory, visual short-term memory, central executive, and long-term memory	Children with RD performed worse on verbal short-term (STM) memory tasks, but had intact visual STM, central executive (CE), and long-term memory (LTM). Children with ADHD had difficulty on visual-spatial STM, but not CE and LTM. The comorbid group shared deficits with both disorders.
Klorman et al. (1999)	ADHD-C, ADHD-PI, ADHD/CD, or Reading Disability	7-13; 342 males, 17 females	WCST, Tower of Hanoi	Only the ADHD/CD group showed impairments on executive functioning measures.
Li et al. (2008)	ADHD (C & PI), controls	Children; not specified	Response inhibition, phonological working memory, visual working memory, and temporal discounting	Children with ADHD showed impairments in response inhibition, working memory, planning, and set-shifting. No differences were shown between ADHD-C and ADHD-PI.
Martinussen et al. (2006)	ADHD, ADHD+Reading Disability(RD)/Language Impairment(LI); RD/LI, controls	7-13; 50-82% male (clinical groups); 12% male (controls)	Working memory (auditory-verbal, visual-spatial, temporary storage, manipulation of information)	Children with ADHD but not LI showed impairments in visual-spatial storage and central executive functions. Data suggest that neuropsychological impairments are more associated with inattention than hyperactivity/impulsivity.
Marzocchi et al. (2008)	ADHD, Reading Disability (RD), controls	7-12; males and females	Inhibition, visual working memory, planning, cognitive flexibility, and verbal	Children with ADHD were impaired on interference tasks, visual working memory, planning, cognitive flexibility, and phonetic

			fluency	fluency. Children with RD were impaired on phonetic fluency. Planning was the only measure to differentiate the ADHD and RD groups.
Nigg (2005)	ADHD, controls	18-37; males and females	Working memory/cognitive flexibility, set-shifting/interference, problem solving, response inhibition, planning	The ADHD group performed worse than the control group on measures of executive functioning and processing speed. Inattention was related to executive dysfunction and slower speed, whereas hyperactivity/impulsivity was not.
Nigg et al. (2002)	ADHD (C & PI), controls	7-12; males and females	Response inhibition task, planning (Tower of London), interference, set-shifting, go/no-go	Both ADHD groups performed worse than controls; however, the ADHD-C group had a specific deficit in planning, and ADHD-C males did worse on the response inhibition task than ADHD-PI males.
Pennington & Willcutt (2001)	ADHD (C, PI, & H/I)	Twins aged 8-18; 2:1 (males: females) for ADHD and 1:1 for controls	Processing speed, vigilance, and inhibition	Children with inattention were impaired on all measures of executive functioning, whereas children with ADHD-H/I were not impaired on any measures after controlling for inattention.
Pennington (1996)	ADHD, conduct disorder (CD), autism, and Tourette syndrome (TS)	Review article of previous studies of children (males and females)	Global executive functioning deficits (unspecified) and specific deficits such as inhibition and verbal working memory	Executive functioning weaknesses are seen in ADHD (motor inhibition) and autism (verbal working memory), but not in CD and TS.

Pineda et al. (1998)	ADHD, controls	7-12; males only	WCST (problem solving/perseverative errors), verbal fluency, WISC-R Picture Arrangement	Children with ADHD had deficits in the "abstraction/flexibility" factor compared to controls.
Romine et al. (2004)	ADHD, controls	Children and adolescents; males and females	Meta-analysis on use of WCST to identify executive dysfunction in ADHD	Children with ADHD performed worse on the categories Percent Correct, Number of Categories Completed, Total Errors, and Perseverative Errors.
Roodenrys et al. (2001)	ADHD/RD, Reading Disability (RD), controls	Mean age = 10 (ADHD/RD); 9.1 (RD), and 9.11 (controls); 1:1 (male: female)	Working memory processes (phonological loop and central executive)	Children with ADHD/RD performed worse than comparison groups with increasing demands to the central executive.
Schmitz et al. (2002)	ADHD (C, PI, & H/I), controls	12-16; males and females	Set-shifting, problem solving, focused auditory attention	Children with ADHD-C and PI had more difficulty with focused auditory attention and set-shifting compared to controls. Those with ADHD-H/I did not differ from controls.
Shallice et al. (2002)	ADHD	7-12; 94% males	Working memory, verbal fluency, sustained attention, interference	Children with ADHD did worse on all executive functioning tasks except verbal fluency.
Sonuga-Barke et al. (2002)	ADHD-like symptoms	3-5; ~1:1 (male: female)	Response inhibition, working memory, planning (Tower of London)	Young children with ADHD-like symptoms performed worse on response inhibition tasks than tasks involving planning and working memory.
Vaurio et al. (2008)	ADHD, Fetal Alcohol Spectrum Disorder (FASD), controls	Children; not specified	WCST, the Controlled Oral Word Association Test (COWAT), and the	Both the ADHD and FASD groups exhibited impairment on the WCST; however, children with ADHD performed worse than

			Trail Making Test (TMT)	those with FASD on the WCST.
Weyandt (1998)	ADHD, Reading Disability, controls	Mean age: 23.7 (6.7); 26 males, 38 females	Tower of Hanoi, TOVA, WCST, Ravens Progressive Matrices	Children with dyslexia had more perseverative errors on WCST, and ADHD group did not differ from controls on WCST or Tower of Hanoi.
Willcutt et al. (2005)	ADHD, controls	Meta-analysis of male and female children and adolescents with (*N* = 3,374) and without (*N* = 2,969) ADHD	Stop-Signal Task, Porteus Mazes, Tower of Hanoi, and WCST	Executive functioning weaknesses (response inhibition, vigilance, working memory, and planning) are associated with, but not sufficient for, a diagnosis of ADHD.

Table 3

List of Studies of Executive Functioning in Developmental Dyslexia

Author (Year)	Diagnoses	Age (years); Sex ratio	Executive Functions	Findings
Asbjornsen et al. (2003)	Reading Disability with and without Specific Language Impairment	12; 1:1 males: females	WCST, Stroop, dichotic listening task	Dichotic listening task correctly classified 42% of children with Dyslexia. After including EF measures, the correct classification jumped to 90%.
Booth, Boyle, & Kelly (2010)	Reading disability, controls	Median age of 10.5; 74% RD males, 70% control males	Several measures of executive functioning from 48 studies	Meta-analysis reported that children with RD have deficits in executive functioning.
Donfrancesco et al. (2005)	Dyslexia, spelling disorder, controls	6-14; unspecified	Matching Familiar Figures Test	Children with dyslexia performed worse on the task, implying difficulties with cognitive impulsivity.
Everatt et al. (1997)	Dyslexia, controls	Mean age = 10.5; unspecified sex ratio	Stroop	Children with dyslexia show impairments in interference consistent with their reading age.
Helland & Asbjørnsen (2000)	Dyslexia, controls	Mean age = 12; RD group: 36 males, 7 females, controls: 16 males, 4 females	Dichotic Listening Test, Stroop, WCST	Children with dyslexia were impaired on all tasks.
Kelly, Best & Kirk (1989)	RD, controls	12; males only	Verbal fluency, Stroop, WCST	Males with dyslexia performed worse on measures of inhibition and mental flexibility.
Kibby (2009a)	Reading Disability, controls	9-14; groups equated for gender	Verbal short-term memory using Baddeley's model	Children with RD were impaired on measures of phonological awareness and phonological store, which affected verbal short-term memory for phonetically coded

				items.
Kibby et al. (2004)	Dyslexia, controls	9-13; Dyslexia: 3:2 males: females; Controls: 2:3 males: females	Verbal and visual working memory measures, central executive, articulation rate	Dyslexia group showed impairment in the phonological storage system, but had intact visual-spatial sketchpad and central executive functioning.
Klicpera (1983)	Dyslexia, controls	11-14; 33 males	Rey-O Complex Figure Test	Dyslexia group had deficits in planning and strategy use when replicating figure. Focused on details more than gestalt.
Lee & Obrzut (1994)	Children with and without Learning Disabilities	7-12; 1:1 male: female	Semantic memory	Children with LD showed less clustering by frequency in secondary word lists (i.e., child-generated).
McDougall et al. (1994)	Good, average, and poor readers	Elementary school aged children; unspecified	Reading, short-term memory, and phonological skills	Groups differed on measures of phonological ability, rhyming, and phoneme deletion based on reading performance.
McGee et al. (2004)	ADHD, Reading Disability, controls	Mean age = 9; all groups were predominantly male	Working memory, phonological processing, and time perception	Children with RD had deficits in auditory phonological processing.
Nigg et al. (1998)	ADHD, ADHD/ODD, ADHD/CD, ADHD/Reading Disability, controls	6-12; males only	Verbal IQ, Reading measures, Porteus mazes, Rey-O, rapid naming	Children with ADHD/RD had more difficulty with naming. Children with ADHD only had difficulty with motor-planning tasks.
Reiter, Tucha, & Lange (2004)	Dyslexia, controls	10; 26 males, 16 females	Visual working memory, verbal short-term memory, go/no-go, Tower, Stroop, Trails A & B, Five-Point Test, S-	Children with dyslexia performed worse on working memory, inhibition, verbal and figural fluency, and problem solving tasks.

			word and Animals, card sorting	
Snow (1998)	Learning Disability (reading & math)	7-13; 91 males, 28 females	WCST	Children with LD were more perseverative & performed worse on this problem solving task.
Swanson (1999)	Learning disability, controls	Mean age 11.4; 17 males, 1 female in LD groups, 9 males, 9 females in control group	Phonological accuracy, processing speed, LTM, executive processing	LD group was more impaired on all measures of articulation, LTM, and central executive than controls.
Swanson, Sáez, & Gerber (2004)	Children at-risk for Reading Disability	6-8; 3:2 male: female	Rhyming task and semantic association task; reading, letter naming, vocabulary, and IQ measures	Short-term memory performance in Grade 1 predicted basic reading skills and comprehension in Grade 2.
Weyandt (1998)	ADHD, Reading Disability, controls	Mean age: 23.7 (6.7); 26 males, 38 females	Tower of Hanoi, TOVA, WCST, Ravens Progressive Matrices	Children with dyslexia had more perseverative errors on WCST, and ADHD group did not differ from controls on WCST or Tower of Hanoi.

Table 4

List of Studies of Executive Functioning in Comorbid ADHD and Developmental Dyslexia

Author (Year)	Diagnoses	Age (years); Sex ratio	Executive Functions	Findings
de Jong (2009)	ADHD, Reading Disability, ADHD/RD, controls	8-12; 87.5% ADHD males, 75% ADHD/RD males, 38% RD males, 62% control males	Visuospatial working memory, inhibition, lexical decision tasks	Children with ADHD/RD showed improved visuospatial working memory performance and decreased inhibition following atomoxetine treatment. No effects were seen in the ADHD and RD groups.
Pennington, Groisser, & Welsh (1993)	ADHD, RD, ADHD/RD, controls	7-10; 1:1 male: female	WISC-R, Spelling from WRAT, GORT, Tower of Hanoi, Matching Familiar Figures Test, WCST, CPT, Pig-Latin Test, Word Attack	The RD groups had impaired phonological processing, but not EF. ADHD only group had impairments in EF. Comorbid group had impairments similar to RD only group, with secondary ADHD symptoms.
Purvis & Tannock (2000)	ADHD, RD, ADHD/RD, controls	7-11; 1:1 male: female	Inhibitory control and phonological processing measures	RD groups were impaired on all phonological processing measures. ADHD groups were impaired on go-task responding and inhibition. ADHD/RD group showed impairments from both disorders.
Roodenrys, Koloski, & Grainger (2001)	ADHD/RD, RD, controls	Mean age = 9.5; 1:1 male: female	Phonological loop, phonological loop and central executive combined, and central executive functioning	ADHD/RD group performed worse with increasing demands from the central executive.
Rucklidge (2002)	ADHD, RD, ADHD/RD, controls	13-16; 3:2 males: females in ADHD and ADHD/RD group, 1:1	WISC-III, rapid automatized naming, Stroop, and Stop tasks	ADHD and ADHD/RD groups showed poor processing speed, naming of objects, and inhibition.

		male: female in RD and control groups		RD and ADHD/RD groups showed impairment in verbal working memory. ADHD/RD group was slower in naming number and colors.
Tannock, Martinussen, & Frijters (2000)	ADHD, ADHD/RD, controls	8-12; unspecified	Rapid automatized naming	Children with ADHD were slower in naming than controls. Stimulant medication improved color-naming speed, but not naming of letters or digits.
Willcutt et al. (2001)	Twins with Reading Disability, ADHD, ADHD/RD, and controls	8-16; unspecified sex ratio	Measures of phoneme awareness and executive functioning	ADHD group had deficits in inhibition, whereas the RD group had difficulty with phoneme awareness and verbal working memory. ADHD/RD group was impaired on nearly all measures.
Willcutt et al. (2005)	ADHD (C & PI), Reading Disability, ADHD/RD, controls	9-13; 235 males, 202 females	Gordon Diagnostic System, WCST, verbal and spatial working memory, Stroop, WISC-R (PSI)	Children with dyslexia were impaired on all reading, language, and verbal working memory measures. ADHD group was impaired on reaction time tasks and had more commission errors. Comorbid group had deficits consistent with both groups. All groups showed decreased processing speed.

Table 5

Neuropsychological Measures Tested in the Current Study

Cognitive Function Assessed	Cognitive Measure Used
Verbal Working Memory	Numbers, Sequences (CMS)
Spatial Working Memory	Picture Locations (CMS)
Verbal Long-term Memory	Stories (CMS)
Planning	Tower (NEPSY)
Rapid Generation of Novel Ideas/Fluency	Design Fluency (NEPSY)
Inhibition/Impulsivity	Rule Violations (NEPSY)
Problem Solving	Categories Achieved (WCST-64)
Mental Flexibility	Perseverative Errors (WCST-64)
Behavioral Regulation	Behavioral Regulation Index (BRIEF)
Self-monitoring, Planning, Organization	Metacognition Index (BRIEF)

Note. CMS: Children's Memory Scale; NEPSY: A Developmental Neuropsychological Assessment; WCST-64: Wisconsin Card Sorting Test-64 Card Version; BRIEF: Behavior Rating Inventory of Executive Functioning.

Table 6

Demographic Characteristics of the Present Study (N = 105)

	ADHD	DD	ADHD/DD	Control
Total N	35	18	17	35
Females	16	6	7	17
Males	19	12	10	18
Age				
Mean (yrs)	9.70	9.32	9.70	9.82
SD	1.67	1.59	1.40	1.41
Handedness	78.82	72.50	85.71	80.30
Race/Ethnicity				
Caucasian	31	17	15	29
African Amer	2	0	1	2
Asian	0	0	0	1
Hispanic	1	1	0	1
Other	1	0	1	2
Maternal Education				
Mean	5.33	5.36	5.08	5.36
SD	1.58	.93	.95	1.03
WISC FSIQ Test Admin				
III Mean	101.78 (N=9)	102.67 (N=3)	N/A	115.25 (N=4)
IV Mean[a]	94.19 (N=26)	93.13 (N=15)	90.41 (N=17)	103.16 (N=31)

Note. No significant differences were found between groups on sex, age, race/ethnicity, handedness, or maternal education. Handedness is scored on a continuum, ranging from 0 (left-handed) to 100 (right-handed). [a]Controls scored higher on WISC-IV FSIQ than the clinical groups when using ANOVA (*p*s ≤ .05).

Table 7

Descriptive Statistics on Intelligence, Achievement, and BASC-2 Data (N = 105)

	ADHD-PI		ADHD-C		DD		ADHD/DD		Control	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Intelligence										
FSIQ[a]	94.37	13.15	98.25	14.20	94.72	13.65	90.41	12.06	104.54	12.54
TONI-3	101.16	9.12	99.56	13.54	102.50	10.08	98.12	12.14	108.00	13.73
VCI	94.58	14.42	102.88	15.71	96.39	14.68	96.12	16.50	105.43	13.58
PRI[a]	98.57	11.21	99.00	11.56	101.07	11.82	93.41	9.37	107.06	14.69
Achievement										
L-W[b]	103.47	10.38	106.94	10.98	81.72	9.81	86.53	8.62	105.40	11.38
Word Attack[b]	104.11	8.54	107.25	10.83	87.28	7.06	87.53	10.31	104.54	9.87
Passage Comp[c]	97.84	7.02	94.88	15.01	86.39	10.63	88.24	14.58	102.85	10.08
Spelling[b]	103.00	10.62	104.94	13.08	80.11	11.20	78.65	11.13	103.63	14.75
BASC-2 (Parent)										
Hyperactivity[d]	57.53	10.68	70.19	14.76	49.24	5.99	62.13	13.24	45.77	7.68
Attention Problems[e]	68.58	5.23	69.19	6.76	54.53	6.61	70.13	7.23	47.00	8.45

Note. FSIQ: Full-Scale IQ; TONI-3: Test of Nonverbal Intelligence, 3rd ed.; VIQ: Verbal IQ; VCI: Verbal Comprehension Index; PIQ: Performance IQ; PRI: Perceptual Reasoning Index; L-W: Letter-Word Identification; BASC-2: Behavioral Assessment System for Children, 2nd ed.

[a]ADHD/DD < controls

[b]DD, ADHD/DD < ADHD-PI, ADHD-C, controls

[c]DD < controls, ADHD-PI; ADHD/DD < controls

[d]controls < ADHD-PI; controls, DD, ADHD-PI < ADHD-C; controls, DD < ADHD/DD

[e]ADHD/DD, ADHD-C, ADHD-PI > DD > controls

Table 8

Means and Standard Deviations for Cognitive Measures by Diagnosis

	ADHD-PI		ADHD-C		DD		ADHD/DD		Controls	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Categories Achieved (WCST)	90.74	16.38	98.38	14.78	96.78	14.79	101.18	13.76	105.09	17.43
Perseverative Errors (WCST)	100.26	17.97	97.38	23.60	100.28	22.55	98.41	15.34	112.06	27.71
Tower (NEPSY)	102.63	15.13	105.94	16.56	104.72	14.20	100.59	11.71	103.71	13.63
Tower Rule Violations (NEPSY)	4.05	.97	3.19	1.22	3.94	.87	3.41	1.28	3.97	.82
Design Fluency (NEPSY)	87.63	13.37	95.62	17.88	91.39	13.15	89.71	13.52	100.29	12.24
Sequences (CMS)	97.63	14.94	103.44	14.69	88.61	12.93	86.18	16.35	106.43	13.80
Numbers (CMS)	95.79	15.39	94.06	16.66	89.72	14.09	82.35	12.76	98.14	14.66
Picture Locations (CMS)	103.16	17.58	95.94	12.41	96.94	14.05	94.41	15.40	108.29	14.80
Metacognition Index (BRIEF)	69.00	8.14	68.81	9.98	57.22	11.29	71.88	8.00	49.80	11.02
Behavioral Regulation Index (BRIEF)	56.68	10.25	62.12	9.36	50.72	8.68	64.12	15.24	45.66	8.88
Stories Delayed Recall (CMS)	96.32	14.61	100.63	13.53	96.18	14.63	95.88	16.42	100.71	13.01

Note. ADHD-PI and ADHD-C only differ on Tower Rule Violations (p = .03).

Table 9

Skewness and Kurtosis Statistics for Dependent Variables Used in the Current Study

Variable Name	Skewness Statistic	S.E.	Corrected Skewness Statistic	Kurtosis Statistic[a]	S.E.
Categories Achieved	.222	.237		-.618	.469
Perseverative Errors	.137	.238		-.548	.472
Tower	-.195	.237		-.306	.469
Tower Rule Violations	-1.332	.238	-.528	.162	.467
Design Fluency	.229	.236		-.341	.467
Sequences	-.077	.236		-.708	.467
Numbers	.151	.236		-.555	.467
Picture Locations	-.242	.236		-.214	.467
Stories Delayed Recall	.138	.237		-.211	.469
Metacognition Index	-.252	.236		-1.188	.467
Behavioral Regulation Index	.649	.236	.439	-.574	.467
Total Cerebral Volume	-.182	.236		.016	.467
Left Caudate Head Volume	.273	.236		.253	.467
Right Caudate Head Volume	.276	.236		.092	.467
Left Caudate Body Volume	.913	.236	.392	.577	.467
Right Caudate Body Volume	.621	.236	.177	.254	.467
Left Total Caudate Volume	.194	.236		-.231	.467
Right Total Caudate Volume	.230	.236		.102	.467

Note. S.E. = Standard Error. [a]Corrected kurtosis statistics are reported for Tower Rule Violations, Behavioral Regulation Index, Left Caudate Body Volume, and Right Caudate Body Volume.

Table 10

Factor Loadings from the Pattern Matrix for the Exploratory Factor Analysis With Oblique Rotation

Executive Functioning Measure Assessed	Executive Functioning Abilities in the Home	Problem Solving/ Perseveration	Working Memory/ Fluency
Categories Achieved	.046	**1.00**	-.154
Perseverative Errors	-.033	**.600**	.314
Design Fluency	-.026	.055	**.563**
Sequences	.039	.062	**.698**
Numbers	.000	-.084	**.584**
Picture Locations	.055	-.003	**.518**
Metacognition Index	**-.719**	-.028	-.079
Behavioral Regulation Index	**-.997**	.021	.056

Note. Factor loadings > .5 are in boldface

Table 11

Volume Effects of Caudate Head and Body by Diagnostic Group

Diagnostic Group	*F* Value	Significance (*p*)
ADHD or Not	2.12	.08
Dyslexia or Not	1.45	.22
Interaction Term	.39	.81

Table 12

Asymmetry Effects by Diagnostic Group

Diagnostic Group	*t* Value	Significance (*p*)	N
ADHD			
Head Asymmetry	6.39	<.01	52
Body Asymmetry	-2.16	.04	52
No ADHD			
Head Asymmetry	2.05	.05	53
Body Asymmetry	-3.36	.001	53
Dyslexia			
Head Asymmetry	3.17	.003	35
Body Asymmetry	-1.21	.236	35
No Dyslexia			
Head Asymmetry	4.66	<.01	70
Body Asymmetry	-3.80	<.01	70

Table 13

Cognitive Executive Functioning Effects by Diagnostic Group

Diagnostic Group	*F* Value	Significance (*p*)
ADHD or Not	15.97	<.01
Dyslexia or Not	9.86	<.01
Interaction Term	1.84	.15

Table 14

Cognitive Executive Functioning by Diagnostic Group Controlling for Working Memory and Caudate Volume

Diagnostic Group	*F* Value	Significance (*p*)
ADHD or Not	13.28	<.01
Dyslexia or Not	1.04	.40
Interaction Term	1.40	..23

Table 15

Cognitive Executive Functioning by Diagnostic Group Controlling for Verbal Working Memory

Diagnostic Group	*F* Value	Significance (*p*)
ADHD or Not	13.80	<.01
Dyslexia or Not	.70	.62
Interaction Term	1.47	.21

Table 16

Bivariate Correlations between Working Memory and Caudate Volume

Variables	1	2	3	4	5
1. Sequences	--				
2. Numbers	.46**	--			
3. Picture Locations	.35**	.25**	--		
4. Left Head Volume	.18	.12	.12	--	
5. Right Head Volume	.16	.11	.14	.90**	--

** $p < .01$.

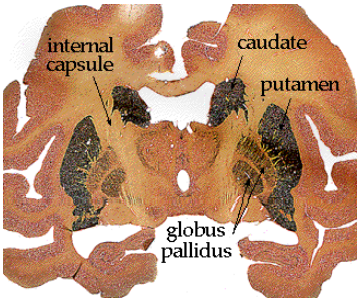

Figure 1. Striatum, which is comprised of the caudate and putamen.

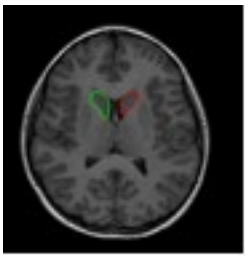

Figure 2. An example of a traced caudate nucleus bilaterally in the transverse view.

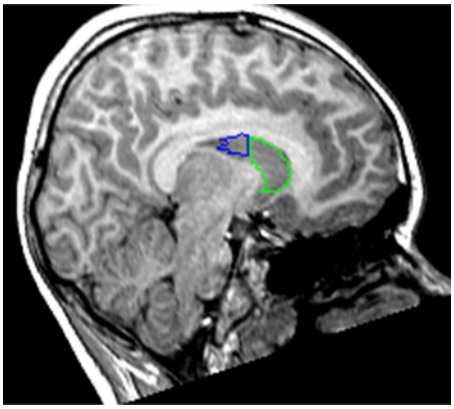

Figure 3. An example of a segmented caudate nucleus into head (green) and body (blue).

	ADHD	Not
Developmental dyslexia	Comorbid group	Developmental dyslexia only
Not	ADHD only	Controls

Figure 4. A 2 x 2 design showing the interaction between diagnostic groups. The upper left quadrant of the table below represents the comorbid ADHD/developmental dyslexia group, or the interaction term, the groups on the diagonal represent the ADHD and developmental dyslexia only groups, and the lower right quadrant represents the control group.

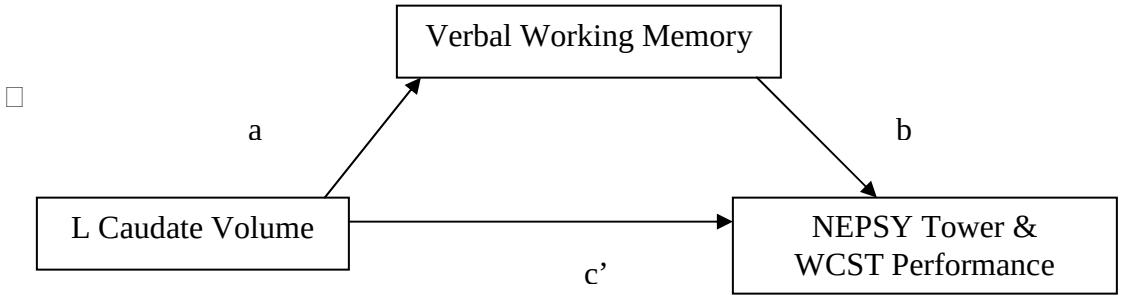

Figure 5. The full mediation model testing the relationship between left caudate volume and performance on NEPSY Tower and WCST with verbal working memory as a mediator.

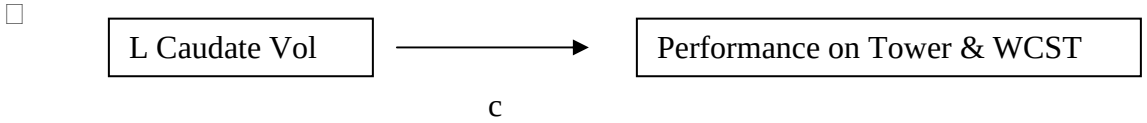

Figure 6. Step 1 in Baron & Kenny's mediation model showing the relationship between the initial variable and the outcome for Hypothesis 3a.

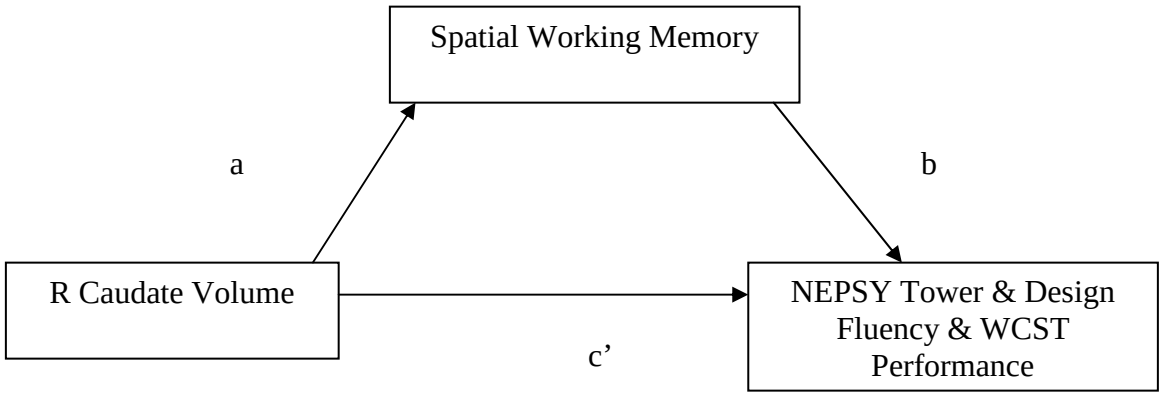

Figure 7. The full mediation model testing the relationship between right caudate volume and performance on NEPSY Tower, NEPSY Design Fluency, and WCST with spatial working memory as a mediator.

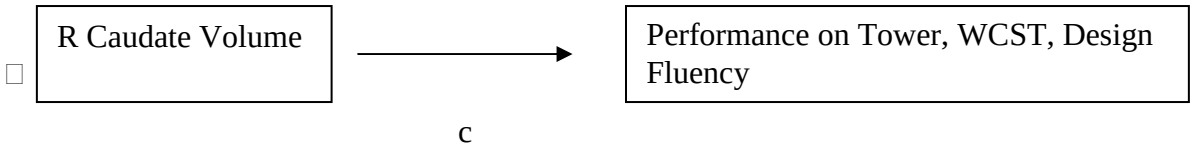

Figure 8. Step 1 in Baron & Kenny's mediation model showing the relationship between the initial variable and the outcome for Hypothesis 3b.

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