Assessing Higher- and Lower-Order Processing in Children With and Without ADHD: A Prospective Longitudinal Study

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ASSESSING HIGHER- AND LOWER-ORDER PROCESSING IN CHILDREN WITH AND WITHOUT ADHD: A PROSPECTIVE LONGITUDINAL STUDY

by

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This manuscript has been read and accepted for the Graduate Faculty in Psychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

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ABSTRACT

Assessing Higher- and Lower-Order Processing in Children With and Without ADHD:

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by

Adina Bitton

Advisor: Jeffrey M. Halperin, PhD

Background: Attention-deficit/hyperactivity disorder (ADHD) is a highly prevalent neurodevelopmental disorder marked by developmentally inappropriate levels of inattention and hyperactivity/impulsivity. ADHD typically emerges during the preschool years, though the developmental course is highly variable across individuals (American Psychological Association, 2013; Faraone et al., 2006). Individuals with ADHD have been shown to have a number of structural and functional brain differences (Bush, Valera, & Seidman, 2005; Castellanos et al., 1996; Durston et al., 2004; Krain & Castellanos, 2006) as well as an array of neurocognitive deficits (Pennington and Ozonoff, 1996; Wilcutt et al., 2005) relative to typically developing peers. Considerable attention has been given to executive functions (EFs) and their role in the etiology of the disorder (Alderson et al., 2010; Barkley, 1997, 2006; Pennington & Ozonoff, 1996). However, there is compelling research to suggest that EFs are not the primary contributors to ADHD symptomatology; rather, deficits in more basic, lower-order cognitive functions may drive executive dysfunction in ADHD (Halperin & Schulz, 2006; Marks et al., 2005; Rommelse et al., 2007). Halperin and Schulz (2006) proposed a model of ADHD etiology wherein subcortical deficits underlie the disorder and improvements in EFs over the course of development compensate for those deficits. In order to properly evaluate this model and EF-
based models of ADHD, rigorous research designs are essential to distinguish EF performance from basic, lower-order cognitive performance (Rommelse et al., 2007). The Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan, & Kramer, 2001) is a battery of EF tests that contain multiple conditions of increasing complexity, moving from lower to higher-order processing. Using selected subtests from the D-KEFS, the current study examined EFs and non-EF cognitive performance in a sample of children at-risk for ADHD and typically developing children from ages 8 to 12 years.

Methods: 160 children (96 labeled as at-risk for ADHD in early childhood) were assessed annually from age 8 to 12 with a selection of D-KEFS measures and their parents filled out ADHD rating forms and completed a clinical interview to assess symptomatology at each year.

Results: Overall, children at-risk for ADHD performed more poorly on tests of higher-order processing and to a lesser extent, approaching significance, on lower-order processing as well. Trajectory analysis on the entire sample, using hierarchical linear modeling, indicated that 1) poorer higher-order functioning at age 8 significantly predicted greater ADHD symptom severity at age 12; 2) poorer lower-order functioning at age 8 was associated with higher ADHD symptom severity at age 12; and 3) improvements in higher-order functioning from ages 8 to 12 significantly predicted lower ADHD symptom severity scores at age 12. Trajectory analysis conducted in the at-risk children only, found that poorer lower-order functioning at age 8 significantly predicted higher ADHD symptom severity at age 12.

Conclusions: Taken together, these results suggest that improvement in higher-order processing is associated with the diminution of symptoms seen across childhood and poorer lower-order processing may be associated with greater symptom severity. As the Halperin and Schulz model suggests, more optimal neural development appears to be associated with greater symp-
tom reduction. Additionally, there is considerable variability in trajectories of neuropsychological functioning as well as symptomatology across childhood, suggesting that ADHD is a highly heterogeneous disorder with likely diverse etiologies. Future research should include moving away from exclusively EF-based models to incorporate a wider range of neuropsychological weaknesses. This, in turn, could facilitate the development of a wider array of treatment alternatives for ADHD.
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My entire family – my sisters, parents- and siblings-in-law, cousins and close friends were invaluable in providing me with support during the long graduate school journey and always believed that I would finish when I, myself, was less sure.
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<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstract</td>
<td>iv</td>
</tr>
<tr>
<td>Acknowledgments</td>
<td>vii</td>
</tr>
<tr>
<td>List of Tables</td>
<td>xi</td>
</tr>
<tr>
<td>List of Figures</td>
<td>xiii</td>
</tr>
<tr>
<td>Specific Aims</td>
<td>1</td>
</tr>
<tr>
<td>ADHD: Phenomenology and Development</td>
<td>7</td>
</tr>
<tr>
<td>Developmental Trajectory</td>
<td>8</td>
</tr>
<tr>
<td>Structural Brain Development</td>
<td>9</td>
</tr>
<tr>
<td>ADHD and Brain Development</td>
<td>10</td>
</tr>
<tr>
<td>Neuroanatomical Correlates of ADHD</td>
<td>10</td>
</tr>
<tr>
<td>Neuropsychological Evidence</td>
<td>13</td>
</tr>
<tr>
<td>Theoretical Perspectives of ADHD</td>
<td>16</td>
</tr>
<tr>
<td>Present Study</td>
<td>23</td>
</tr>
<tr>
<td>Method</td>
<td>30</td>
</tr>
<tr>
<td>Participants</td>
<td>30</td>
</tr>
<tr>
<td>Diagnostic Measures</td>
<td>34</td>
</tr>
<tr>
<td>Procedure</td>
<td>38</td>
</tr>
<tr>
<td>Data Analyses</td>
<td>40</td>
</tr>
<tr>
<td>Results</td>
<td>47</td>
</tr>
<tr>
<td>Hierarchical Linear Modeling</td>
<td>47</td>
</tr>
<tr>
<td>Whole Sample</td>
<td>47</td>
</tr>
</tbody>
</table>
List of Tables

Table 1  Mean (SD) age for the 8 year-old to 12 year-old evaluations across the whole sample and as a function of preschool baseline clinical status 31

Table 2  Mean (SD) preschool baseline demographics as a function of baseline clinical status (At Risk vs. Typically Developing) 32

Table 3  Demographics of participants in current sample vs. those lost to attrition 33

Table 4  Mean (SD) K-SADS (0-36) symptom severity score for the whole sample and as a function of preschool baseline clinical status from age 8 through 12 years 35

Table 5  “Bottom up” performance at age 8 as a predictor of ADHD symptom severity at age 12 and of rate of change of ADHD symptom severity from 8 through 12 years for the whole sample 48

Table 6  “Top down” performance at age 8 as a predictor of ADHD symptom severity at age 12 and of rate of change of ADHD symptom severity from 8 through 12 years for the whole sample 49

Table 7  Rate of change of “bottom up” performance and rate of change in “top down” performance from 8 through 12 years as predictors of ADHD symptom severity at age 12 and of rate of change of ADHD severity from 8 through 12 years for the whole sample 51

Table 8  “Bottom up” performance at age 8 as a predictor of ADHD symptom severity at age 12 and of rate of change of ADHD symptom severity from 8 through 12 years for the at risk sample 53

Table 9  Mean (SD) “bottom up” performance across the whole sample and as a function of preschool baseline clinical status 56
Table 10  Mean (SD) “top down” performance across the whole sample and as a function of preschool baseline clinical status
<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1</td>
<td>Individual growth trajectories of ADHD symptom severity from age 8 through age 12 years</td>
<td>47</td>
</tr>
<tr>
<td>Figure 2</td>
<td>Individual growth trajectories of ADHD symptom severity from age 8 through age 12 years for children identified as at risk for ADHD during preschool</td>
<td>52</td>
</tr>
<tr>
<td>Figure 3</td>
<td>“Bottom up” performance as a function of preschool baseline clinical status</td>
<td>55</td>
</tr>
<tr>
<td>Figure 4</td>
<td>“Top down” performance as a function of preschool baseline clinical status</td>
<td>56</td>
</tr>
</tbody>
</table>
Specific Aims:

Attention-deficit/hyperactivity disorder (ADHD) is a highly prevalent neurodevelopmental disorder characterized by developmentally inappropriate levels of inattention, impulsivity and overactivity that impair daily functioning in multiple settings (American Psychological Association, 2013). Symptoms of ADHD typically emerge during the preschool years and, for many, persist through adolescence and into adulthood (APA, 2013; Barkley, Fischer, Edelbrock, & Smallish, 1990; Biederman et al., 1996b; Biederman, Petty, Evans, Small, & Faraone, 2010; Campbell, 1995; Faraone et al., 2006). Further, ADHD is associated with variable patterns of comorbid disruptive behavior disorders, anxiety disorders, mood disorders, learning disorders and an array of neuropsychological deficits (Barkley, Fischer, Smallish, & Fletcher, 2006; Currie & Stabile, 2006; Daley & Birchwood, 2010; Fischer & Barkley, 2006; Massetti et al., 2008; Spira & Fischel, 2005; Wilcutt et al., 2005). Accordingly, the clinical presentation of ADHD is highly variable between individuals and across development.

Structural and functional magnetic resonance imaging (MRI) studies implicate neural circuits involving the prefrontal cortex (PFC), basal ganglia and cerebellum, as well as subcortical structures (Bush, Valera, & Seidman, 2005; Bussing et al., 2007; Durston et al., 2004; Hill et al., 2003; Kates et al., 2002; Krain & Castellanos, 2006; see Bush, 2010 and Cubillo, Halari, Smith, Taylor, & Rubia, 2012 for review). Additionally, brains of children with ADHD are smaller, on average, relative to peers (Krain & Castellanos, 2006) and delays in cortical maturation throughout childhood have been shown (Shaw et al., 2007).

In concert with the neuroimaging data, a sizable literature indicates that, relative to controls, children with ADHD perform poorly on a wide array of neuropsychological measures
of executive functions (EFs) (Wilcutt et al., 2005). As a result, several investigators have posited that ADHD is largely characterized, if not caused, by deficits in executive functions (EFs) (Alderson et al., 2010; Barkley, 1997, 2006; Pennington & Ozonoff, 1996). However, children with ADHD perform poorly on measures of more basic, lower-order, non-executive processes as well (Marks et al., 2005; Rommelse et al., 2007) and most studies assessing EF deficits do not control for basic cognitive performance (Rommelse et al., 2007). Thus, observed deficient performance on EF tests may be caused by EF deficits, but may also be caused by deficits in lower-order cognitive processes. Without intact lower-order cognitive functions, performance on measures of higher-order functioning will likewise be impaired.

While there is compelling evidence for inhibitory control and working memory (WM) deficits in ADHD, the data are far from universal and neither can be said to be evident in all cases of ADHD (Wilcutt et al., 2005; Nigg et al. 2005). Furthermore, EF deficits are not unique to ADHD, rather they are found in many neurodevelopmental disorders (Geurts, Verté, Oosterlaan, Roeyers, & Sergeant, 2004; Pennington & Ozonoff, 1996). Lastly, the notion that EFs play an etiological role in the emergence of ADHD does not take into account what is known about brain development and the PFC-related circuitry, which largely mediates EFs. These brain regions do not fully develop until young adulthood, whereas ADHD typically arises in early childhood.

As indicated above, ADHD is highly heterogeneous with regard to developmental course, such that symptoms and impairment persist and even escalate for some while diminishing in others. Given the protracted maturation of the human brain throughout childhood and adolescence (Giedd & Rapoport, 2010; Gogtay et al., 2004), it has been hypothesized that differential brain development might contribute to the vast differences in trajectory of the
disorder over the course of the lifespan (Giedd & Rapoport, 2010; Halperin & Schulz, 2006; Halperin & Healey, 2011). Specifically, Halperin and Schulz (2006) have proposed that the neural and cognitive mechanisms involved in the cause of ADHD are distinct from the mechanisms involved in the recovery seen in many individuals with the disorder. According to this model, the PFC, and the EFs it mediates, is not involved in the etiology of the disorder but is associated with the remission of symptoms that typically occurs over development. In other words, the degree to which the PFC and its related neural systems are able to compensate for early non-cortical deficits through regulatory, “top-down” control is posited to account for the diminution of symptoms often seen in adolescents and adults.

In support of this model, studies of preschoolers with ADHD found nonexecutive deficits relative to controls, rather than selective executive deficits (Berwid et al., 2005; Marks et al., 2005). Additionally, Rommelse and colleagues (2007) reported that after controlling for “lower-order” cognitive processes, there was little evidence for primary EF deficits in children with ADHD. Further, recent studies report that symptom diminution over time in ADHD is associated with neuropsychological improvements, generally, (Rajendran et al., 2013a; Rajendran et al., 2013b) and EF improvements, specifically (Miller, Loya, & Hinshaw, 2013), whereas symptom persistence is associated with greater EF deficits (Halperin, Trampush, Miller, Marks & Newcorn, 2008). Additionally, recent structural neuroimaging studies have shown reduced cortical thickness (Shaw et al., 2013) and reduced brainstem white matter (Johnston et al., 2014) in ADHD. Similarly, functional neuroimaging studies have found decreased subcortical – thalamic connectivity in ADHD overall, with reduced thalamic – prefrontal connectivity distinguishing between ADHD persisters and remitters over development (Clerkin et al., 2013), as well as greater frontal connectivity in remitters relative to healthy controls (Francx et al.,
However, support for the model has not been universal with some finding no evidence that performance on lower and higher-order neurocognitive functions differentiates between ADHD persistence and remittance (van Lieshout, Luman, Buitelaar, Rommelse, & Oosterlaan, 2013; Cheung et al., 2015).

The present study aimed to test this model of recovery in a longitudinal sample of children with and without ADHD. Participants were assessed annually from ages 8 to 12 on a range of EF (higher-order processing) and non-EF measures (lower-order processing) and their symptom severity was assessed through parent interviews and parent and teacher behavioral ratings. Thus, we were able to track the association between neuropsychological function and symptom severity over time.

To provide a clear separation between EF (higher-order processing) and non-EF measures (lower-order processing), we used the Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan, & Kramer, 2001), which is based on the conceptual grounding that use of a single-score, as generated by many neuropsychological tests, masks the wide array of cognitive functions required for successful performance on a given task. The premise of the D-KEFS is that successful performance requires a combination of fundamental cognitive skills (e.g., attention, perception, language) and higher-level abilities (e.g., shifting, inhibition, planning, cognitive flexibility) and that a breakdown can occur at any stage of cognitive processing. We selected two tests from the D-KEFS that assess constructs related to ADHD and have multiple conditions to facilitate the isolation of EFs from more basic cognitive skills.

The following Specific Aims were tested:
Aim 1: To track ADHD symptom severity in a sample of children (n=160) from age 8 to age 12. 96 of the children were labeled as at-risk for ADHD at preschool and 64 were labeled as typically developing.

Hypothesis 1a: ADHD symptom severity will decrease from age 8 to age 12 for all children.

Aim 2: To investigate the predictive value of neuropsychological performance (higher- and lower-order processing) at age 8 on ADHD symptom severity and change in ADHD symptom severity from 8-12 for all children and, separately, those labeled as at risk at preschool baseline.

Hypothesis 2a: Performance at age 8 on lower-order measures would predict ADHD symptom severity at age 12 for those labeled as at risk at preschool baseline but not in the whole sample. Specifically, poorer lower-order performance at age 8 would predict higher ADHD symptom severity at age 12.

Hypothesis 2b: Performance at age 8 on higher-order measures would predict ADHD symptom severity at age 12 for those labeled as at risk as preschoolers, but not in the whole sample. Specifically, we posited that poorer higher-order performance at age 8 would predict higher ADHD symptom severity at age 12.

Hypothesis 2c: There would be no relationship between neuropsychological performance at age 8 and rate of change in ADHD symptom severity from ages 8-12 years in the whole sample or in the at risk only children.

Aim 3: To investigate the predictive value of change in neuropsychological performance (higher- and lower-order processing) from 8 to 12 years on ADHD symptom severity at age 12 and on change in ADHD symptom severity from ages 8-12 for all children and those labeled as at risk as preschoolers.
Hypothesis 3a: Greater improvement in higher-order processing will significantly predict lower ADHD symptom severity at age 12 for those labeled as at risk.

Hypothesis 3b: Greater improvement in higher-order processing will significantly predict greater rate of change in ADHD symptom severity from ages 8-12 in both the at risk children as well as the whole sample.

Hypothesis 3c: Rate of change in lower-order processing from ages 8-12 will be unrelated to ADHD symptom severity at 12 and in rate of change in ADHD symptom severity from ages 8-12.

Aim 4: To investigate performance on lower-order (non-EF) measures from ages 8 to 12 years in those labeled as at risk and those labeled as typically developing during the preschool years.

Hypothesis 4a: Both at risk and typically developing children will improve significantly on lower-order measures from age 8 to age 12 years.

Hypothesis 4b: Children labeled as at risk at preschool will perform significantly more poorly than their typically developing peers on lower-order measures across the age range.

Aim 5: To investigate performance on higher-order (EF) measures from ages 8 to 12 in those labeled as at risk and those labeled as typically developing as preschoolers.

Hypothesis 5a: Both at risk and typically developing children will improve significantly on higher-order measures from age 8 to age 12.

Hypothesis 5b: Children labeled as at risk at baseline will perform more poorly than their typically developing peers on higher-order measures across the age range.
ADHD: phenomenology and development

Attention Deficit/Hyperactivity Disorder (ADHD) is a highly prevalent neurodevelopmental disorder characterized by developmentally inappropriate levels of inattention, impulsivity and overactivity that impair daily functioning in multiple settings. The worldwide prevalence rate for ADHD is estimated to be about 5%, with boys affected three times more often than girls (Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007). The most current diagnostic classification system (Diagnostic and Statistical Manual – Fifth edition (DSM-V); American Psychological Association, 2013) specifies that a formal diagnosis is made when a child shows a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning and development. More specifically, a child must exhibit six or more symptoms in either the inattention or hyperactive/impulsive domain that are inconsistent with developmental level. Symptoms must be present for at least six months, be present from a young age, be present in at least two settings (e.g., home and school) and negatively impact social, academic and/or occupational functioning (APA, 2013).

ADHD puts children at a higher risk for poor outcomes later in life. Children with ADHD are at increased risk for academic underachievement, grade repetition, not completing high school, as well as unemployment and poor workplace performance (Barkley, Fischer, Smallish, & Fletcher, 2006; Currie & Stabile, 2006; Daley & Birchwood, 2010; Fischer & Barkley, 2006; Massetti et al., 2008; Spira & Fischel, 2005). Additionally, children with ADHD are frequently diagnosed with comorbid disruptive behavior, anxiety, mood and learning disorders, and often grow up, relative to peers, to be more truant in school, have substance abuse problems and engage in criminal misconduct (Kollins, 2008; T. W. Miller, Nigg, & Faraone, 2007; Wilens,
Biederman, Mick, Faraone, & Spencer, 1997). Accordingly, it is clear that ADHD has substantial negative impact on both the afflicted individual and society at large.

**Developmental Trajectory**

The developmental course of ADHD is highly variable among individuals. ADHD typically emerges during the preschool years, with some symptoms usually arising by three to five years of age (Barkley, Fischer, Edelbrock, & Smallish, 1990; Berwid et al., 2005; Campbell, 1995). During this time and into early childhood, hyperactive behaviors tend to be most prominent. The clinical picture changes in elementary school with a reduction in hyperactive symptoms for most individuals (Hart, Lahey, Loeber, Applegate, & Frick, 1995) whereas inattentive symptoms become more prominent (Biederman, Mick & Faraone, 2000). Furthermore, as children grow into adolescence, ADHD tends to remit in a minority of cases but continues to persist in the majority of adolescents and for some, even into adulthood (APA, 2013; Biederman et al., 1996; Biederman, Petty, Evans, Small, & Faraone, 2010; Faraone, Biederman, & Mick, 2006). Such variability in trajectory has confounded the search to identify causal factors of the disorder.

It is clear that genetic factors play an important role in increasing risk of developing the disorder. Family and twin studies of ADHD show a high heritability, estimated to be around 70 to 80% (Faraone et al., 2005). Furthermore, longitudinal twin studies suggest that genes may play a substantial role in the persistence of symptoms through to adolescence (Chang, Lichtenstein, Asherson, & Larsson, 2013; Faraone et al., 2005), with partially distinct sets of genes related to ADHD onset versus its trajectory (Pingault et al., 2015). Candidate gene studies have identified several genes related to dopaminergic, noradrenergic, and serotonergic function that might be linked to ADHD (e.g., Dopamine Receptor D4 (DRD4), Dopamine Transporter 1 (DAT1)). Yet
all are of small effect size, suggesting a polygenic inheritance model (Durston, 2008, 2010; Faraone et al., 2005).

However, genetic factors alone do not account for the variability in trajectory among individuals with ADHD (Pingault et al., 2015). Environmental factors also play an important role in increasing risk for the disorder. Broadly, dysfunctional family environments appear to be nonspecific risk factors for psychological distress and adaptive functioning and likely serve as moderators for ADHD severity (Biederman et al., 1995; Faraone & Biederman, 2002). More recently, emphasis has been placed on the role of prenatal environmental risk factors in the development of ADHD, including maternal smoking, drug and alcohol abuse, deficient diet and maternal stress during pregnancy (Sonuga-Barke & Halperin, 2010). Thus a unique interplay between genetic, prenatal and postnatal environmental risk factors contribute in varying degrees to the development and trajectory of ADHD. Such heterogeneity further complicates the ability to identify specific factors that differentiate those who persist in having the disorder from those who remit. However, the evidence strongly suggests that environmental factors (see Sonuga-Barke & Halperin, 2010 for review) and distinct genetic factors (Pingault et al., 2015) during development may alter the trajectory of ADHD as individuals grow into adulthood.

**Structural Brain Development**

Understanding normal brain development is crucial to understanding neurodevelopmental disorders such as ADHD (Gogtay et al., 2004). In normal development, over 90% of a young adult's total brain volume is attained by age 5 (Giedd et al., 1999; Gogtay et al., 2004) and total cerebral volume reaches its maximum volume by early adolescence (Giedd & Rapoport, 2010; Giedd et al., 1999). The human brain undergoes protracted maturation such that different tissue types, brain structures and neural circuits have distinct developmental trajectories (Romine &
Reynolds, 2005; Stiles & Jernigan, 2010). More specifically, cortical brain development occurs in a nonlinear, parietal to frontal (back to front) fashion (Giedd & Rapoport, 2010; Gogtay et al., 2004). The prefrontal cortex (PFC) undergoes one of the longest periods of development of any brain region, reaching full maturity after the age of 20.

**ADHD and Brain Development**

At this point, ADHD is understood as a brain disorder reflective of subtle abnormalities in neural functioning (Krain & Castellanos, 2006). Among the most robust neuroimaging findings is that ADHD is associated with globally decreased brain volumes relative to age- and sex-matched typically developing controls. This volumetric difference appears to represent a non-progressive deficit presumably resulting from early genetic and/or environmental factors (Krain & Castellanos, 2006). Additionally, cortical development is delayed in ADHD. A seminal magnetic resonance imaging (MRI) study conducted by Shaw and colleagues (2007) demonstrated that peak cortical thickness in 50% of cortical points occurred at a median age of 10.5 years for those with ADHD, compared to 7.5 years in a matched group of typically developing controls. Circuitry in the frontal and temporal areas showed the greatest maturational delay in children with ADHD. The middle PFC, one of the last areas to mature, lagged by as much as five years in those with the disorder. While most pronounced in frontal regions, delays were noted across the cortex. Additionally, others have highlighted delays in development of the cerebellum (Castellanos et al., 2002).

**Neuroanatomical Correlates of ADHD**

Aside from overall smaller brains and delayed developmental trajectory in the cortex, structural and functional neuroimaging studies have identified key brain regions and neural circuits that appear deficient in groups with ADHD relative to controls.
**Prefrontal Cortex**

The prefrontal cortex (PFC) has been shown to be significantly smaller in children with ADHD compared to controls (Castellanos et al., 1996; Durston et al., 2004; Mostofsky, Cooper, Kates, Denckla, & Kaufmann, 2002) and their unaffected siblings (Durston et al., 2004). Functional brain abnormalities, mainly described in adults with ADHD, have also consistently implicated the PFC (Bush, Valera, & Seidman, 2005). Deficits in the PFC may result in difficulties with executive functioning, including cognitive flexibility, planning, organization and problem-solving.

**Projections to PFC: Basal Ganglia and Cerebellum**

Brain regions that project to the PFC have also been implicated in ADHD pathology. While findings have been inconsistent, there appears to be some support for structural abnormalities in areas of the basal ganglia that may contribute to the motoric symptoms of ADHD (Castellanos et al., 1996; Teicher et al., 2000). Furthermore, studies looking at the effects of trauma or damage to the basal ganglia in individuals who subsequently developed secondary ADHD found that the development of ADHD corresponded with severity of injury to the basal ganglia (Max et al., 1998).

Dysfunction in the frontostriatal circuit, which comprises reciprocal connections among the striatum, thalamus, and prefrontal areas, has also been suggested as playing an important role in ADHD (Durston, van Belle, & de Zeeuw, 2011). Functional imaging studies have shown differences in dorsal frontostriatal activity during cognitive control tasks (Durston, de Zeeuw, & Staal, 2009).

**Cerebellum**
The cerebellum is associated with coordination of motor movements as well as involvement in non-motor functions such as timing and attentional shifting through connections with frontal and striatal regions (Durston, van Belle, & de Zeeuw, 2011; Tracy et al., 2000). Accordingly, it too has been investigated for possible implication in ADHD. MRI studies of the cerebellum in ADHD have detected smaller cerebellar hemispheric volumes (by up to 6%) which are sustained throughout adolescence (Durston et al., 2004; Hill et al., 2003) and remain significant even after adjusting for total cerebral volume (Castellanos et al., 2002). Functional MRI studies have reported decreased cerebellar activation in ADHD during a range of tasks of cognitive control, working memory and temporal processing (Bush et al., 2005; Rubia, Smith, Brammer, Toone, & Taylor, 2005; Schulz et al., 2004; Smith, Taylor, Rogers, Newman, & Rubia, 2002). Additionally, it has been shown that there is reduced connectivity between the cerebellum and the PFC in adults with ADHD relative to healthy controls (Wolf et al., 2009).

Taken together, there is compelling evidence for a strong role for both the frontostriatal and frontocerebellar circuits, which are both involved in cognitive control, in ADHD pathophysiology (Durston et al., 2011b). Furthermore, candidate genes for ADHD that affect dopamine systems, such as DRD4 and DAT1, influence the function of these circuits (Durston, 2010). Dysfunction in any of these circuits might cause symptoms of ADHD. For instance, dysfunction of the PFC is likely to result in a reduced ability to exert control. Dysfunction in the ventral striatum is more likely to lead to deficits in motivation and reward processing. Dysfunction of the cerebellum is likely associated with problems in the ability to predict when events are going to occur and other problems with timing. Accordingly, it has been suggested that the different neural circuits may reflect distinct neurobiological pathways to ADHD, each with its own unique cognitive profile and behavioral patterns (Durston et al., 2011). In other words, diverse behaviors that
are clinically labeled as ADHD may, in fact, be broken down by the distinct neural mechanisms involved. As will be shown below, a similar finding has begun to emerge regarding the heterogeneity of neuropsychological profiles in ADHD and the likelihood that there are, in fact, distinct neuropsychological subtypes. At this point, these ideas are largely speculative and greater research, specifically with fMRI, will help to establish dissociable cognitive functions and neural circuits involved in ADHD.

**Neuropsychological Evidence**

Consistent with neuroimaging data, there is a considerable amount of neuropsychological evidence of distinct cognitive deficits in ADHD. Studies of neuropsychological functions in ADHD have focused largely on executive functions (EFs). EFs refer to prefrontally-mediated “top-down” control functions required for proper organization of cognitive activity (Gioia, Isquith, Kenworthy, & Barton, 2003), execution of goal-directed behavior (Pennington & Ozonoff, 1996) and emotional self-control (Lezak, 1995). While specific definitions vary, commonly agreed-upon EFs include inhibitory control (e.g., the ability to inhibit an over-learned response), interference control (e.g., the ability to inhibit a competing response), the abilities to initiate and sustain behavior, set shifting/cognitive flexibility (e.g., the ability to switch between thinking about two concepts), working memory (the ability to temporarily store and manipulate information), planning and organizing problem-solving strategies, and self-regulation (Gioia et al., 2003; Packwood, Hodgetts, & Tremblay, 2011; Pennington & Ozonoff, 1996; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). In contrast, nonexecutive cognitive functions, often referred to as “bottom up” processes, are involved in more basic information processing. These are typically less complex and often, but not always, subcortically-mediated and form many of the necessary components for performing higher-order cognitive tasks (Rommelse et al., 2007).
These include learning, memory, processing speed, language, temporal processing, and motor coordination, among others.

Indeed there is a sizable literature demonstrating that, as a group, those with ADHD perform worse than their peers on a variety of neuropsychological measures of EFs. Specifically, poorer performance in ADHD has been shown on measures of inhibitory control (Barkley, 1997; Pennington & Ozonoff, 1996; Willcutt et al., 2005), set shifting (Pennington & Ozonoff, 1996; Shallice et al., 2002; Willcutt et al., 2005), working memory (Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005; Rapport et al., 2009; Willcutt et al., 2005), and planning (Barkley, 1997; Pennington & Ozonoff, 1996; Wilcutt et al., 2005). A comprehensive meta-analysis by Wilcutt and colleagues (2005) examining the role of EF deficits in ADHD found significant differences between groups with and without ADHD in 65% of the comparisons. However, the magnitude of the effect size for EF deficits was moderate, ranging from 0.4 to 0.7. Additionally, a substantial number of children with ADHD do not perform poorly on neuropsychological tests of EFs (Nigg et al., 2005).

There is also strong evidence for deficits in ADHD on an array of lower-order cognitive processes including encoding, perception, language, visuomotor integration, motor functioning, temporal processing, learning/memory and reading (Banaschewski et al., 2005; Boonstra, Oosterlaan, Sergeant, & Buitelaar, 2005; Marks et al., 2005; Purvis & Tannock, 2000; Rucklidge & Tannock, 2002; Sergeant, 2000).

Subgroups of ADHD

The heterogeneity of neuropsychological findings combined with the well-known behavioral heterogeneity characteristic of children with ADHD has led some investigators to suggest that different children with the disorder have distinct patterns of deficits, raising the possibility of
separable neuropsychological subtypes of ADHD (Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005; Sonuga-Barke, Dalen, & Remington, 2003; Sonuga-Barke & Halperin, 2010). Sonuga-Barke et al. (2010) used principal component analysis (PCA) to show that three separable components contributed to the variance in their neuropsychological task battery. Specifically, these components corresponded to timing, inhibition, and delay aversion. Of the 77 children with ADHD included in the study, 55 could be identified as having a deficit on one of these components, and the overlap between components was no greater than would be expected by chance. This suggests that these components may indeed reflect separable subtypes. De Zeeuw and colleagues (2012) report similar findings using a different neuropsychological test battery in a sample of 140 individuals (57 with ADHD) using PCA. They found that cognitive control, reward processing, and timing characterized distinct subgroups. 30 subjects with ADHD (52.6%) had a detectable deficit on at least one of the three factors and 80% of those had a deficit on only one component; there were no individuals with deficits on more than two components. In both studies, a substantial portion of children with ADHD showed no deficits on any of the components, further complicating the attempt to identify distinct subtypes of the disorder.

**Chicken or the Egg**

The relationship between executive and non-executive deficits also complicates the current literature on ADHD. As previously discussed, lower-order, non-executive processes are generally thought of as less complex than EFs, but form necessary components for higher-order cognitive operations. Accordingly, successful performance on EF tasks does not solely depend on the higher-order cognitive ability of interest, but also on many lower-order (non-executive) processes. Poor performance on an EF task can theoretically result not only from deficits in higher-order cognitive processes (a primary/direct EF deficit) but also secondarily from deficits
in lower-order cognitive processes (a secondary/indirect EF deficit). Thus far, studies investigating EFs have largely not controlled for more basic cognitive performance, making it difficult, if not impossible, to discern what cognitive domain(s) is/are truly responsible for poor performance in ADHD (Rommelse et al., 2007). This distinction is particularly important given the many causal theories of ADHD that place a central role on EFs.

**Theoretical Perspectives of ADHD**

Putting together a unitary theory of ADHD is fraught with challenges, some of which have been referenced above. Firstly, there is considerable heterogeneity in presenting symptoms and the symptoms vary considerably over the course of development (Faraone et al., 2006; Hart et al., 1995). Secondly, ADHD is highly comorbid with many other psychiatric disorders (Barkley et al., 2006; Currie & Stabile, 2006; Daley & Birchwood, 2010; Fischer & Barkley, 2006; Massetti et al., 2008; Spira & Fischel, 2005) and a theory of ADHD must account for these. Thirdly, given the neuroimaging data, a theory of ADHD must encompass the various brain regions that are purportedly involved in some way in the disorder and account for the developmental trajectory of the brain in ADHD. Fourthly, the developmental time course of ADHD is highly variable – how it changes over time, the sizable drop-off in symptoms for some as they get older while others persist with the disorder (Biederman et al., 2010; Faraone et al., 2006). Lastly, the neuropsychological findings are varied and not entirely consistent with one another – with poorer performance found in a variety of cognitive domains (Berwid et al., 2005; Chhabildas, Pennington, & Willcutt, 2001; Marks et al., 2005; Pennington & Ozonoff, 1996; Willcutt et al., 2005).

Relatedly, there are several factors to consider when weighing the importance of neuropsychological findings. There is considerable variability in the age ranges, sample sizes, recruit-
ment source (clinical vs. community samples), definition of ADHD (dimensional vs. categorical), ratings used to make the diagnosis (parent ratings vs. teacher ratings vs. clinician vs. pre-existing diagnosis) and effect sizes of findings. No single study shows poorer performance on any measure by all participants with ADHD. All of the above pose serious challenges to creating a unifying theory of the disorder. Below, I will review some of the prominent theories in the literature.

**ADHD as a Disorder of Executive Functioning**

Given the neuroimaging findings of a strong role for the PFC and its related projections in ADHD, it is not surprising that neuropsychological theories have tended to emphasize putative dysfunctions of PFC and related executive dysfunctions (Barkley, 1997; Pennington & Ozonoff, 1996; Rapport et al., 2009).

Barkley (Barkley & Murphy, 2006; Barkley, 1997) proposed that ADHD is primarily caused by a deficit in inhibitory control which then cascades to impair other EFs, specifically working memory, self-regulation of affect/motivation/arousal, internalization of speech and reconstitution. According to this theory, behavioral inhibition is required for successful execution of these other EFs and without it, as in ADHD, there is impairment in these other crucial EFs and the motor control they allow.

In contrast to behavioral inhibition models, Rapport and colleagues (2009) consider dysfunctional working memory to be the core deficit in ADHD. According to their functional working memory model of ADHD, behavioral disinhibition is a product of working memory (WM) deficits rather than a cause thereof (Kofler et al., 2011; Kofler, Rapport, Bolden, Sarver, & Raiker, 2010; Rapport et al., 2009). Behavioral inhibition is a reaction to external stimuli which must first gain access to, and be evaluated within, WM (Alderson, Rapport, Hudec, Sarver, &
Accordingly, WM deficits, rather than behavioral disinhibition, are the core of the disorder.

Moving away from isolating a single core deficit to encompass the highly variable landscape of ADHD, Sonuga-Barke (2003) also views deficits in inhibition as central to ADHD, but proposes a dual pathway model, with poor inhibitory control and a more motivationally-based delay aversion as independent contributing factors that are of equal importance to ADHD. EF dysfunction may thus play a role in only a portion of ADHD. A strength of this model is that the multiple pathways provide a plausible explanation for the many inconsistencies in the research on neuropsychological profiles of ADHD and account for the behavioral and cognitive heterogeneity.

Similarly, the cognitive energetic model (Sergeant, Geurts, & Oosterlaan, 2002; Sergeant, 2000) is a bottom-up model that combines factors from EF theories and the dual pathway model. According to this model, ADHD is associated with deficits on three levels: 1) cognitive response output (encoding, search, decision, and motor organization), 2) energetic activation, effort and arousal, and 3) EF control (planning, monitoring, detection of errors, and error correction). ADHD thus results from the inability of an individual to modulate physiological state to meet task demands, with problems occurring at one or more of the three levels. Rather than a deficit in inhibitory control itself, the failure to inhibit is caused by a reduced energetic state of the child (effort, activation, arousal).

**Problems with EF-based Models**

EF models have strong support in the neuropsychological and, to some extent, the neuroimaging literature on ADHD. As discussed above, there is a substantial literature highlighting EF deficits in ADHD relative to controls in children, adolescents and adults. However, such
models are limited by the fact that deficits in EFs are common to many psychiatric disorders and are not specific to ADHD (Banaschewski et al., 2005; Sergeant et al., 2002). Additionally, the literature on EF deficits in ADHD, while compelling, is far from conclusive. If EF dysfunction is the primary cause of the disorder, it would be observable in most children with ADHD which does not appear to be the case. As previously indicated, effect sizes for EF studies have ranged widely and often been only moderate in magnitude (Pennington & Ozonoff, 1996; Wilcutt et al, 2005). The authors of one meta-analysis (Wilcutt et al. 2005) thus concluded that, while EFs are clearly important in ADHD etiology, “EF weaknesses are neither necessary nor sufficient to cause all cases of ADHD” (p. 1343). Additionally, as pointed out above, one must be cautious when interpreting significant EF results as they fail to control for more basic, nonexecutive cognitive functions (Banaschewski et al., 2005; Marks et al., 2005). Furthermore, several studies investigating EFs have found no difference in performance between those with ADHD and controls (Wilcutt et al., 2005) and some studies have reported the presence of basic cognitive impairments in the absence of observed EF deficits (Loge, Staton, & Beatty, 1990; Marks et al., 2005; Rommelse et al., 2007; Takács, Kóbor, Tárnok, & Csépe, 2013).

Another challenge to EF-based models relates to what is known about brain development. The brain develops in a back-to-front fashion such that the PFC, and thus the EFs it mediates, takes the longest to develop (through adolescence and into young adulthood). Accordingly, if EF dysfunction is the core deficit of ADHD, the disorder should only emerge later in childhood when the PFC is maturing. The actual emergence of ADHD is typically in the preschool years, when the PFC is far from developed. Additionally, the aforementioned models do not properly account for the fact that ADHD persists for many but remits in a proportion of cases as the individuals get older.
A Neurodevelopmental Model of Recovery

Halperin and Schulz (2006) proposed that the neural and cognitive mechanisms involved in the cause of ADHD are distinct from the mechanisms involved in the recovery from the disorder. According to this model, the core pathophysiology of childhood ADHD is due to non-executive, subcortical neural dysfunction. Such defects are purported to be present early in development and remain static throughout the lifetime; they form the “core” of the disorder. The development/connectivity of the PFC, and its relationship with more caudal neural structures, is then responsible for the diminishing symptomatology over development. According to this model, the PFC is not involved in the cause of the disorder but is associated with the remission of symptoms that typically occurs over development. The degree to which the PFC and its related neural systems are able to compensate for those early non-cortical deficits through regulatory, “top-down” control will account for the diminution of symptoms typically seen in adolescents and adults.

Support for this model comes from what is known about brain development. As outlined above, prefrontal circuits are not fully developed until adolescence when higher-order cognitive functions become more pronounced. Accordingly, if executive dysfunction was a primary cause of ADHD, the behavioral manifestations of the disorder should emerge only after the PFC is fully developed, in adolescence or young adulthood, and not, as is the case, in the preschool years. Studies of preschoolers with ADHD identified nonexecutive cognitive deficits in ADHD relative to controls but no executive deficits (Berwid et al., 2005; Marks et al., 2005). Thus the behavioral manifestations of the disorder clearly emerged before executive deficits, further challenging the notion that EF dysfunction plays a causal role in the disorder. Additionally, in an fMRI study of adults who had childhood ADHD, Clerkin et al. (2013) found decreased thalamo-
cortical activation and reduced thalamic – brainstem connectivity in response to a “bottom-up” cueing task in both persisters and remitters relative to controls who never had ADHD. The authors concluded that, regardless of symptom remission, there may be less functional coordination between the brainstem and the thalamus in individuals with ADHD, even if the ADHD later remits. Additionally, Johnston et al. (2014) found that children and adolescents with ADHD “have a significantly decreased white matter volume” in the brainstem.

Furthermore, some data suggest that prefrontal cortical development does parallel the trajectory of symptom diminution over the course of adolescence and adulthood (Miller, Loya, & Hinshaw, 2013; Shaw et al., 2013). This supports the hypothesis that the PFC is involved in recovery from ADHD and not its etiology. According to the model, the degree of symptom diminution (e.g., persistence vs. remittance) over development may depend on the extent to which an individual’s executive control can compensate for the core ADHD symptoms. One study of EFs in persisters versus remitters of ADHD into adolescence found that only persisters showed deficits in EFs (Halperin, Trampush, Miller, Marks, & Newcorn, 2008). Additionally, Clerkin et al. (2013) found decreased functional connectivity between the thalamus and bilateral PFC in a sample of adult ADHD persisters relative to remitters, suggesting that improved thalamo-cortical connectivity may be involved in recovery from ADHD. Even in early childhood, improved neuropsychological functioning over development appears to attenuate ADHD symptoms and associated impairment during the early school years (Rajendran et al., 2013a). Miller, Loya, and Hinshaw (2013) followed a sample of girls with ADHD and matched controls from childhood through young adulthood. They found that improvements on some EFs but not others predicted symptom diminution over time. Similarly, using resting-state fMRI, Francx and colleagues (2015) found increased connectivity in frontal regions associated with the
executive control network was significantly associated with a developmental decrease in hyperactive-impulsive symptoms in a group of 11-17 year-olds with remitted ADHD. However, the same study did not find that subcortical deficits identified children with ADHD (persisters and remitters) relative to controls.

Nonetheless, support for this model has not been universal. Van Lieshout and colleagues (2013) conducted a systematic review of the predictive value of neurocognitive functioning on ADHD persistence or remittance. They examined whether “higher level” neurocognitive functions showed normalization in ADHD remitters whereas “lower level” functions would not differentiate between the two, as the Halperin and Schulz model would predict. They found no evidence to suggest that ADHD remitters improve on higher-level neurocognitive abilities and both persisters and remitters showed weaker performance relative to controls. In other words, both remitters and persisters performed comparably in terms of both higher and lower level functions. Thus, they reported no one-to-one relation between neurocognitive and symptomatic development. Similarly, Coghill, Hayward, Rhodes, Grimmer, & Matthews (2014) found no association between symptom reduction and executive functioning from ages 9 to 14 in 17 boys with ADHD compared to 17 controls. However, as the authors note, the sample was extremely small and thus results must be examined with caution. Cheung and colleagues (2015) examined cognitive differences in a longitudinal sample of 110 individuals with childhood ADHD (87 persisters and 23 remitters at follow-up) and 169 controls from ages 4 to 9. Not surprisingly, those with ADHD differed significantly from controls on all measures. Importantly, contrary to the model, executive control measures were not sensitive to ADHD persistence or remission. Rather, “preparation-vigilance” measures, such as reaction time variability and omission errors, were markers of
remission. That is, they improved concurrently with the diminution of ADHD symptoms whereas executive control measures did not.

**Present Study**

Documenting the developmental changes in EF abilities and how those changes are related to symptom changes over time will help to properly evaluate the Halperin and Schulz model. Further, elucidation of the neurocognitive correlates of remission in youth with ADHD has the potential to facilitate the development of interventions designed to promote recovery. The present study aimed to test the veracity of the Halperin and Schulz (2006) model in a sample of children with and without ADHD from ages 8 to 12. As discussed above, the brain, and the PFC specifically, as well as the neuropsychological functions they support, develop in a nonlinear, protracted fashion (Halperin & Schulz, 2006; Romine & Reynolds, 2005; Stiles & Jernigan, 2010). Additionally, Shaw et al. (2007, 2010) showed that cortical maturation is delayed during the middle childhood years in children with ADHD. It would be useful to examine whether EF differences between children with ADHD and typically developing peers decrease as cortical maturation “catches up” with age. A meta-analysis of developmental EF studies in typically-developing children from age 5 to adulthood (Romine & Reynolds, 2005) found the greatest advancements in one key EF, inhibition of prepotent responses, from age 5 to 8 years. Accordingly, the present study focused on a narrow age range, 8 to 12 years-old, a time where ADHD-related delays might be most evident, to compare executive and nonexecutive functioning and symptom severity in children with ADHD relative to their typically-developing peers. While this approach may limit generalizability across the lifespan, it provides a clearer picture of executive (higher-order/top-down) and nonexecutive (lower-order/bottom-up) functioning at a particular time in development and assures that we are examining children at the
same developmental stage. A major advantage of this longitudinal approach is the ability to track both neuropsychological changes as well as symptom changes during this time.

The present study aimed to address the question of whether improvement in top-down functioning is associated with symptom improvement as distinct from bottom-up cognitive deficits that remain irrespective of symptom change. As indicated above, properly parsing the higher- and lower-level cognitive processes requires looking at performance on both bottom-up and top-down executive tasks. Applying the “additive factor model” (Sternberg, 1969), one can more precisely ascertain where the cognitive deficit lies by utilizing multiple levels of a task. As the demands of the task increase, one can identify the specific manipulation(s) that result(s) in differential deterioration in performance by one group relative to the other. In other words, when task demands increase, if the degree of change in performance is greater in the clinical group than in the control group, it would suggest a selective impairment in the patients (Sergeant & van der Meere, 1990). On the other hand, if the clinical group performs more poorly across conditions, the higher-order processing deficit should not be inferred.

The Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan, & Kramer, 2001) is a well-standardized test battery that was designed to use such an approach to dissociate the role of lower level cognitive functions from EFs. The D-KEFS is comprised of nine individually administered subtests based on well-established EF tasks. The D-KEFS is intended to evaluate such EFs as cognitive flexibility, inhibition, problem solving, planning, impulse control, concept formation, abstract thinking, and creativity (Delis, Kaplan, & Kramer, 2001). By including multiple conditions for each task that get progressively more difficult, the D-KEFS assesses both fundamental skills as well as higher-order EFs, and allows for their differentiation.
The present study utilized two tests from the D-KEFS to examine performance change over time in relation to ADHD symptom change. These tests were specifically chosen because they focus on cognitive control, as measured by manipulations involving inhibition and switching/shifting sets. The traditional Trail Making Test (TMT) is a visual-motor sequencing task that requires cognitive flexibility and has been used extensively in different forms since the 1950’s to assess EF (Reitan, 1958). The basic condition (TMT A) requires the individual to draw lines connecting numbers arranged on a page in order as quickly as possible (1-2-3-4 etc.). The shift condition (TMT B) requires the individual to draw lines by switching between connecting numbers and letters as quickly as possible (1-A-2-B-3-C etc). Wilcutt et al. (2005) found that 57% of the 14 studies that compared performance of ADHD vs. Controls on TMT B yielded significant results. However, as noted above, comparing groups on TMT B performance, without considering TMT A performance tells us little about the specificity of the apparent executive deficit. By adding four basic conditions (e.g., visual scanning, motor speed, ability to sequence numbers and letters) and incorporating them into the analysis, the D-KEFS TMT better isolates the fundamental cognitive components necessary for completion of this visual-motor sequencing and flexibility task.

Secondly, we used the Color-Word Interference subtest (CWIT), which is a variant of the Stroop task (Stroop, 1935), a classic interference task that requires inhibition of a prepotent response. First, one is asked to name patches of colors, then to read color words (e.g., red, blue) as quickly as possible; these are the basic cognitive conditions. In the third condition, the interference condition, the examinee is shown color words written in different colored ink and is asked to inhibit reading the word and instead name the color of ink. Considerable data exist on the Stroop task in a variety of neuropsychological disorders. Two recent meta analyses
(Homack, 2004; van Mourik, Oosterlaan, & Sergeant, 2005) examined the Stroop paradigm in over 40 studies comparing individuals with ADHD and controls. Both found that individuals with ADHD performed significantly worse than their typically developing peers across all conditions and not exclusively on the interference condition. These results suggest that deficits among youth with ADHD are not uniquely executive, but may exist at a more basic cognitive level. Beyond the three established CWIT conditions (i.e., word reading, color naming, color-word interference), the D-KEFS version of the CWIT includes a fourth condition that requires not only inhibition but also set-shifting between conflicting rules (reading the word and naming the ink color).

The present study aimed to extend previous EF findings relating to these tasks by taking into account the more basic, bottom-up, cognitive processes and examining the relationship between top-down and bottom-up processing over a five year period. Specifically, per the Halperin and Schulz (2006) model, we aimed to assess whether bottom-up processing remains weaker in ADHD regardless of symptom improvement and whether top-down improvements are associated with ADHD symptom reduction over the age range. A key limitation of previous findings related EFs, or top-down processing, is that there is little way to be sure that observed differences are uniquely executive. Using the D-KEFS versions of these measures will allow for examination of both top-down and bottom-up processing. According to the Halperin and Schulz (2006) model, if ADHD is caused by lower-order cognitive deficits, then we would expect bottom-up performance to be poorer regardless of symptom reduction over time. On the other hand, if ADHD is primarily an EF disorder as others have suggested (e.g., Barkley, Rapport), then we would expect top-down performance to be differentially worse for the ADHD group regardless of bottom-up performance. Furthermore, if top-down improvement accounts for symptom improvement, we
would expect that, for those children with ADHD whose top-down performance improves, they will also have a corresponding reduction in symptoms over the five-year period. Using trajectory analysis with hierarchical linear modeling, we will be able to examine whether bottom-up and/or top-down processing can account for diminution of symptoms between age 8 and 12.

**Hypotheses**

Given the Halperin and Schulz (2006) model, the following Specific Aims were tested:

**Aim 1:** To track ADHD symptom severity in a sample of children (n=160, 96 at risk for ADHD at preschool, 64 typically developing) from age 8 to age 12.

Hypothesis 1a: ADHD symptom severity will decrease from age 8 to age 12 for all children.

**Aim 2:** To investigate the predictive value of neuropsychological performance (higher- and lower-order processing) at age 8 on ADHD symptom severity and change in ADHD symptom severity from 8-12 for all children and, separately, those labeled as at risk for ADHD at preschool baseline (“at risk”).

Hypothesis 2a: Performance at age 8 on lower-order measures would predict ADHD symptom severity at age 12 for the at risk children but not in the whole sample. Specifically, poorer lower-order performance at age 8 would predict higher ADHD symptom severity at age 12.

Hypothesis 2b: Performance at age 8 on higher-order measures would predict ADHD symptom severity at age 12 for at risk children, but not in the whole sample. Specifically, we posited that poorer higher-order performance at age 8 would predict higher ADHD symptom severity at age 12.
Hypothesis 2c: There would be no relationship between neuropsychological performance at age 8 and rate of change in ADHD symptom severity from ages 8-12 years in the whole sample or in the at risk only children.

Aim 3: To investigate the predictive value of change in neuropsychological performance (higher- and lower-order processing) from 8 to 12 years on ADHD symptom severity at age 12 and on change in ADHD symptom severity from ages 8-12 for all children and at risk children.

Hypothesis 3a: Greater improvement in higher-order processing will significantly predict lower ADHD symptom severity at age 12 for the at risk children.

Hypothesis 3b: Greater improvement in higher-order processing will significantly predict greater rate of change in ADHD symptom severity from ages 8-12 in both the at risk children as well as the whole sample.

Hypothesis 3c: Rate of change in lower-order processing from ages 8-12 will be unrelated to ADHD symptom severity at 12 and in rate of change in ADHD symptom severity from ages 8-12.

Aim 4: To investigate performance on lower-order (non-EF) measures from ages 8 to 12 years in those labeled as at risk and those labeled as typically developing as preschoolers.

Hypothesis 4a: Both at risk and typically developing children will improve significantly on lower-order measures from age 8 to age 12 years.

Hypothesis 4b: Children labeled as at risk at preschool baseline will perform significantly more poorly than their typically developing peers on lower-order measures across the age range.

Aim 5: To investigate performance on higher-order (EF) measures from ages 8 to 12 in those labeled as at risk and those labeled as typically developing as preschoolers.
Hypothesis 5a: Both at risk and typically developing children will improve significantly on higher-order measures from age 8 to age 12.

Hypothesis 5b: Children labeled as at risk at preschool baseline will perform more poorly than their typically developing peers on higher-order measures across the age range.
Method

Participants

Participants for this study (n = 216) were part of a larger longitudinal investigation of the development of ADHD in preschoolers (NIH Grant #R01MH068286). Briefly, 3- and 4-year-old children were recruited and classified as either “at risk” for ADHD or “typically developing” on the basis of parent and teacher reports on the Attention Deficit Hyperactivity Disorder Rating Scale, Fourth Edition (ADHD-RS-IV; DuPaul, Power, Anastopolous & Reid, 1998). Typically developing participants (n = 76) had three or fewer items on the ADHD-RS-IV rated as “often” or “very often” by both parents and teachers. At risk participants (n = 140) had six or more items within a domain rated as “often” or “very often” by either parent or teacher.

Preschoolers were excluded from the initial study if they or their parents were non-English speaking; did not attend preschool or childcare; had a neurological or pervasive developmental disorder; were taking systemic medication, including for ADHD; and/or had a Full Scale IQ less than 80 as measured by the Wechsler Preschool and Primary Scale of Intelligence-Third Edition (WPPSI-III; Wechsler, 2002).

Follow-up evaluations occurred yearly and consisted of a neuropsychological assessment of the child, collection of parent and teacher ratings of ADHD, as well as a semi-structured interview conducted with the parent(s) (see Diagnostic Measures). Each year, based on the ratings and interview, children were given an ADHD severity score (from Kiddie-Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (K-SADS-PL); Kaufman et al., 1997) and classified as either meeting or not meeting DSM-IV-Text Revision diagnostic criteria for ADHD and other psychiatric disorders regardless of baseline status. The sample for this study consisted of 160 at-risk (n = 96) and typically-developing (n = 64) children who were
evaluated annually from age eight years [mean (SD; range) age = 8.61 (0.31; 8.0 – 9.4) years] through age 12 years [12.67 (0.31; 11.98-13.38) years; n = 109].

Table 1. Mean (SD) age for the 8 year-old to 12 year-old evaluations across the whole sample and as a function of preschool baseline clinical status

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Whole Sample</th>
<th>At Risk</th>
<th>Typically Developing</th>
<th>t-value</th>
<th>df^</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>8</td>
<td>n</td>
<td>160</td>
<td>96</td>
<td>64</td>
<td>-0.91</td>
<td>158</td>
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<tr>
<td></td>
<td>Mean Age (SD)</td>
<td>8.61 (0.31)</td>
<td>8.63 (0.31)</td>
<td>8.58 (0.30)</td>
<td></td>
<td></td>
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<tr>
<td>9</td>
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<td>86</td>
<td>62</td>
<td>-1.70</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>Mean Age (SD)</td>
<td>9.63 (0.31)</td>
<td>9.67 (0.32)</td>
<td>9.58 (0.29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
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<td>137</td>
</tr>
<tr>
<td></td>
<td>Mean Age (SD)</td>
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<td>10.69 (0.33)</td>
<td>10.60 (0.32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>n</td>
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<td>-0.90</td>
<td>131</td>
</tr>
<tr>
<td></td>
<td>Mean Age (SD)</td>
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<td>11.71 (0.35)</td>
<td>11.65 (0.33)</td>
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<td></td>
</tr>
<tr>
<td>12*</td>
<td>n</td>
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<td>59</td>
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<td>-0.37</td>
<td>107</td>
</tr>
<tr>
<td></td>
<td>Mean Age (SD)</td>
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<td>12.68 (0.31)</td>
<td>12.66 (0.33)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*12-yo assessments were ongoing as of the date of data analyses, accordingly, fewer participants included

^Degrees of Freedom

At the eight-year-old starting point of this study, participants were mostly male (n = 121, 75.6%) and the sample was racially and ethnically diverse, reflective of the NYC community from which it was recruited; 94 children were Caucasian (58.75%), 17 were African-American (10.63%), 20 were Asian (12.5%), and 29 were of mixed descent (18.13%); 48 participants were Hispanic (30%). There were more African Americans in the at risk group than the typically developing group (13.5% vs. 6.25%) and more Asians in the typically developing group than the at risk group (23.4% vs. 5.21%). Mean socioeconomic status (SES) was 63.9 (17.94) as measured by the Nakao and Treas (1994) scale of Occupational Prestige, representing, on
average, a middle class sample. Table 2 describes the characteristics of the at risk and typically developing groups at preschool baseline.

Table 2. Mean (SD) preschool baseline demographics as a function of preschool baseline clinical status (At Risk vs. Typically Developing).

<table>
<thead>
<tr>
<th></th>
<th>At Risk (n = 96)</th>
<th>Typically Developing (n = 64)</th>
<th>t-value</th>
<th>df</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (at baseline)</td>
<td>4.32 (0.47)</td>
<td>4.16 (0.49)</td>
<td>-2.06</td>
<td>158</td>
<td>0.04</td>
</tr>
<tr>
<td>SES</td>
<td>60.20 (18.15)</td>
<td>69.47 (16.22)</td>
<td>3.30</td>
<td>158</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FSIQ</td>
<td>103.91 (13.03)</td>
<td>112.52 (12.37)</td>
<td>4.18</td>
<td>158</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Parent ADHD Severity</td>
<td>27.72 (10.53)</td>
<td>8.52 (4.54)</td>
<td>-13.75</td>
<td>158</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Teacher ADHD Severity</td>
<td>28.77 (13.41)</td>
<td>4.38 (4.40)</td>
<td>-14.05</td>
<td>157</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>N (%)</th>
<th>χ²*</th>
<th>df</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: (Male)</td>
<td>77 (80.2)</td>
<td>44 (68.75)</td>
<td>2.74</td>
<td>1</td>
<td>0.10</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td>13.09</td>
<td>3</td>
<td>0.004</td>
</tr>
<tr>
<td>Caucasian</td>
<td>61 (63.5)</td>
<td>33 (51.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African</td>
<td>13 (13.5)</td>
<td>4 (6.25)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>5 (5.21)</td>
<td>15 (23.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other/Mixed</td>
<td>17 (17.7)</td>
<td>12 (18.75)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity (Hispanic/Latino)</td>
<td>32 (33.33)</td>
<td>16 (25)</td>
<td>1.27</td>
<td>1</td>
<td>0.26</td>
</tr>
</tbody>
</table>

Socioeconomic status (SES) measured using Nakao-Treas Socioeconomic Prestige Index (Nakao & Treas, 1989); Full-scale IQ (FSIQ) measured using Wechsler Preschool and Primary Scale of Intelligence, Third Edition (WPPSI-III, Wechsler, 2002); Parent and Teacher ADHD Severity measured using Attention Deficit Hyperactivity Disorder Rating Scale, Fourth Edition (ADHD-RS-IV) home and school versions respectively, range is 0-36 (DuPaul et al., 1998).

*Chi Square
As can be seen, the groups, by design, did not differ significantly in gender ($\chi^2 = 2.74$, df = 1, $p = 0.10$). As expected, those with ADHD had significantly higher scores on the ADHD-RS-IV, and significantly lower FSIQ scores and SES at preschool baseline. Unexpectedly, the two groups differed significantly in age at preschool baseline ($p = .04$), although notably, the mean difference was only about 1.9 months, as well as in race, with the at-risk group containing a higher proportion of African Americans and a lower proportion of Asians.

Of the original sample, 160 children completed the eight-year-old evaluation (25.9% attrition from preschool recruitment sample). At each year, there were participants who did not complete the evaluation because they had either discontinued involvement in the longitudinal study, were not able to be contacted, or declined to participate that year.

Table 3. *Demographics of participants in current sample vs. those lost to attrition*

<table>
<thead>
<tr>
<th></th>
<th>Current Sample (n=160)</th>
<th>Lost to Attrition (n = 56)</th>
<th>t-value</th>
<th>df</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SES (baseline)</td>
<td>63.9 (17.94)</td>
<td>60.84 (17.37)</td>
<td>1.11</td>
<td>214</td>
<td>0.27</td>
</tr>
<tr>
<td>FSIQ (baseline)</td>
<td>107.35 (13.41)</td>
<td>101.05 (12.90)</td>
<td>3.05</td>
<td>214</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>N (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Status (At Risk)</td>
<td>96 (60)</td>
<td>44 (78.6)</td>
<td>6.27</td>
<td>1</td>
<td>0.01</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>121 (76)</td>
<td>36 (64)</td>
<td>2.69</td>
<td>1</td>
<td>0.10</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>94 (58.75)</td>
<td>32 (57)</td>
<td>3.79</td>
<td>3</td>
<td>0.29</td>
</tr>
<tr>
<td>African American</td>
<td>17 (10.63)</td>
<td>10 (18)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>20 (12.5)</td>
<td>3 (5)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Other/Mixed 29 (18.13) 11 (20)
Ethnicity (Hispanic/Latino) 48 (30) 20 (36) 0.63 1 0.43

SES measured using Nakao-Treas Socioeconomic Prestige Index (Nakao & Treas, 1989); Full-scale IQ (FSIQ) measured using Wechsler Preschool and Primary Scale of Intelligence, Third Edition (WPPSI-III, Wechsler, 2002); Preschool baseline status was determined by scores on the Kiddie-Sads – Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997) combined with ADHD-RS-IV scores (DuPaul et al., 1998).

As can be seen in Table 3, the participants who stayed (n = 160) did not differ significantly from those who dropped out (n = 56) on gender, race, ethnicity, or baseline SES; those who dropped out did have a significantly lower Full Scale IQ and a significantly greater proportion labeled as at risk at preschool baseline.

The university’s Institutional Review Board (IRB) approved all research procedures. After a full description of the study, parents signed IRB-approved informed consent forms at each yearly evaluation. Children’s assent was obtained prior to participation in the each of the evaluations included in the study.

**Diagnostic Measures**

*Attention Deficit/Hyperactivity Disorder Rating Scale, Fourth Edition (DuPaul, Power, Anastopolous & Reid, 1998)*

The ADHD-RS-IV, which was completed by parents and teachers at each time point, consists of the 18 DSM-IV ADHD symptoms rated on a four-point scale (0 = never/rarely; 1 = sometimes; 2 = often; 3 = very often). Individual item scores were summed to provide a dimensionalized measure of ADHD severity. This measure has been shown to have good reliability and validity in preschoolers (McGoey, DuPaul, Haley, & Shelton, 2007) and school-age children (DuPaul et al., 1998). Within the current sample, Cronbach’s alpha for parent and
teacher versions were both 0.97 at 8 years of age.

**Kiddie-Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997)**

The K-SADS-PL is a reliable, commonly-used, semi-structured child psychiatric interview based on DSM-IV criteria that was administered to parents. Each behavioral symptom is scored as 1 (not present), 2 (sub-threshold) or 3 (at threshold, present with impairment). Like others (e.g., Lahey et al., 1996; MTA Cooperative Group, 1999), we annually determined children’s diagnoses by combining parent reports from the interview with teacher ratings of symptoms on the ADHD-RS-IV to arrive at a score for each symptom. Beyond diagnosis, a dimensional ADHD severity score was derived from the K-SADS-PL by recoding the 1 to 3 scoring to a 0 to 2 scoring range and then summing the score for each item across the 18 ADHD items so that the range of scores for ADHD symptom severity on the K-SADS-PL is 0-36. By looking at the dimensional score, we can better assess incremental changes even in children who continue to meet criteria for ADHD diagnosis. As shown in Table 4, the at risk group had significantly higher ADHD symptom levels at all age-points.

**Table 4. Mean (SD) KSADS-PL (0-36) symptom severity score for the whole sample and as a function of preschool baseline clinical status from age 8 through 12 years.**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Whole Sample</th>
<th>At Risk</th>
<th>Typically Developing</th>
<th>t-value</th>
<th>df</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>n 160</td>
<td>96</td>
<td>64</td>
<td>17.62 (11.85)</td>
<td>23.83 (9.6)</td>
<td>8.3 (8.26)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>n 148</td>
<td>86</td>
<td>62</td>
<td>16.65 (12.15)</td>
<td>23 (10.3)</td>
<td>7.84 (8.51)</td>
</tr>
<tr>
<td>10</td>
<td>n 139</td>
<td>84</td>
<td>55</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

35
Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan, & Kramer, 2001)

The D-KEFS is a battery of nine, nationally-normed, “stand-alone” tests designed to comprehensively assess EFs in individuals aged 8 – 89 years. The D-KEFS is based on the conceptual grounding that use of a single score, as generated by many neuropsychological tests, masks the wide array of cognitive functions required for successful performance on a given task. As such, the premise of the D-KEFS is that successful performance requires a combination of fundamental cognitive skills (e.g., attention, perception, language) and higher level abilities (e.g., shifting, inhibition, planning, cognitive flexibility) and that a breakdown can occur at any stage of cognitive processing. The goal is to determine whether poor performance is due to deficits in lower-order cognitive skills vs. higher-order EFs (e.g., bottom-up vs. top-down processing). The D-KEFS has been used effectively to assess higher- and lower-order functioning in children with ADHD relative to controls (Holmes et al., 2009; Wodke et al., 2008). To meet the aims of this study, we selected two tests (see below) from the D-KEFS that assess constructs related to ADHD and have multiple conditions to facilitate the isolation of EFs from more basic cognitive skills. Test-retest reliability over 25 +/- 12.8 days was moderate to high for the tests used in this study, ranging from 0.57 (Trail Making Test condition 3) to 0.90 (Color Word Interference Test Condition 3); an exception was Trail Making Test Condition 4 which was 0.20 (D-KEFS...
Trail Making Test (TMT)

This version of the TMT is a visual-motor sequencing task that measures cognitive flexibility through the administration of five conditions designed to systematically assess basic as well as higher-order processes. For each of the five conditions, participants are presented with two pages on which different numbers and letters are printed and are asked to complete the tasks as quickly as possible. Condition 1 is a Visual Scanning task that requires the examinee to find all the 3s on the pages. Condition 2 is a Number Sequencing task that requires the examinee to connect numbers in sequential order. Condition 3, a Letter Sequencing task, requires the examinee to connect letters in alphabetical order. Condition 4, Letter-Number Switching, requires the examinee to switch between connecting numbers and letters in sequential and alphabetical order (e.g., 1-A-2-B, etc.). Finally, during Condition 5, a Motor Speed task, the examinee traces a line connecting dots as quickly as possible. Conditions 1 and 5 measure the most basic processes; visual scanning and motor speed. Conditions 2 and 3 increase demands somewhat by requiring the sequencing of automatized stimuli (numbers and letters). Condition 4 is the key EF measure in the series requiring cognitive control in the form of shifting, inhibition and cognitive flexibility. The dependent measure is time to completion (measured in seconds).

It should be noted that on the TMT, if the participant made an error, the examiner would correct the mistake, which would increase time to completion. Accordingly, longer completion time may reflect slower performance speed (favoring accuracy >speed) or may reflect impulsivity if many errors were made and corrected.

Color Word Interference Test (CWIT)

The CWIT is an expansion of the classic Stroop (1935) procedure for studying verbal
interference effects by requiring the inhibition of more automatic verbal responses (reading) in order to generate a conflicting response (naming dissonant ink colors). The first two conditions of the CWIT serve as baselines for evaluating performance on the higher-level tasks. Condition 1, Naming, requires basic naming of color patches on a page. Condition 2, Word Reading, requires basic reading of words that denote colors printed in black ink. Condition 3, Inhibition, is the traditional interference task where the examinee is required to inhibit reading the words on the page in order to name the dissonant ink colors in which the word is printed. Condition 4, Inhibition/Switching, requires the examinee to switch back and forth between naming the dissonant ink colors and reading the words. This latter condition is a measure of both inhibition and cognitive flexibility. Participants are asked to complete each condition as quickly as possible; the dependent measure is time to completion (measured in seconds).

**Procedure**

At 8, 9, 10, 11, and 12 years of age, participants returned for their annual evaluation. During each evaluation, parents were interviewed using the K-SADS-PL (Kaufman, et al., 1997) to determine the presence and severity of ADHD behaviors exhibited by their children. Interviews were carried out by trained graduate students who were blind to children’s initial preschool clinical status. Additionally, parents and teachers completed the ADHD-RS-IV (DuPaul et al., 1998). While parents were being interviewed, children were administered a battery of neuropsychological tasks, which included the two D-KEFS subtests, by a different evaluator who was blind to the clinical data. Following completion of the evaluation, parents were compensated for their time and children received a small prize.

Interviewers reviewed all cases with their doctoral-level supervisors and preliminary diagnoses were formulated by integrating the parent and teacher ratings on the ADHD-RS-IV
with parent reports on the K-SADS-PL interview. Subsequently, all clinical diagnostic data (blind to D-KEFS results) were presented at a weekly case conference to members of QCPP, including doctoral level supervisors and trained graduate students, where preliminary diagnostic determinations were reviewed and final diagnostic determinations were made.
Data Analyses

Exploratory factor analyses of the TMT and CWIT conditions were conducted at each age using Maximum Likelihood and direct oblimin rotation to determine whether our measures loaded onto unobserved, underlying factors (i.e., “bottom up” and “top down” factors). At ages 9 and 10 years, initial analyses yielded 2 factors for the “bottom up” conditions, with conditions 1 and 5 of the TMT (Visual Scanning and Motor Speed) loading onto a separate factor. Additionally, TMT conditions 1 and 5 were highly skewed (range: 2.41 (age 11) - 4.28 (age 8)) and kurtotic (range: 7.86 (age 11) - 25.89 (age 8)); accordingly, these two conditions were excluded from analyses. This left two conditions from TMT (Number Sequencing and Letter Sequencing) and two conditions from CWIT (Color Naming and Word Reading), which loaded onto one factor, accounting for between 43.89 (age 10) and 54.28 (age 12)% of the variance. This factor was considered to represent “bottom up” performance. One condition from TMT (Number-Letter Switch) and two conditions from CWIT (Inhibition and Inhibition/Switch) loaded onto a separate factor which accounted for between 43.54 (age 8) and 65.34 (age 12)% of the variance and was considered to reflect “top down” performance.

Factor scores were not used in subsequent analyses because factor loadings are standardized coefficients with a mean (SD) of 0 (1) which, when entered into Hierarchical Linear Modeling (HLM) at each time point would fail to show change over time. Instead, because all of the tests included in the factor analysis were timed, we used mean completion time (in seconds) of the four bottom-up tests (Number Sequencing, Letter Sequencing, Color Naming, Word Reading) as the “bottom up” performance score at each year and mean completion time (in seconds) of the three top-down tests (Letter-Number Switch, Inhibition, Inhibition/Switch) as the “top
down” performance score at each year. The K-SADS ADHD symptom severity score (0-36) was used as the indicator of ADHD symptom severity at each time point.

HLM was used to examine individual growth trajectories from age 8 through age 12 years, and predictors of this growth. HLM is a flexible statistical technique that allows for analysis of nested data, including individual change in longitudinal data sets, where repeated observations for each individual over time are considered to be nested within a person (Raudenbush & Bryk, 2002). The major advantage of this approach is that it is able to adequately handle situations where individuals may have been evaluated a different number of times (i.e., some participants completed all yearly assessments, whereas others may have missed some assessments but returned for later ones), or the delay between observations varies among individual (e.g., if time between assessments varies from 9 months to 13 months; Raudenbush & Bryk, 2002).

For the present study, HLM was used to examine the individual growth trajectories of ADHD symptom severity from age 8 through age 12 years. Then, predictors of ADHD symptom severity at age 12 years, and of rate of change of ADHD symptom severity in the entire sample, were assessed. Specifically, we investigated whether: (a) “bottom up” and “top down” performance at age 8 years was associated with ADHD symptom severity at age 12 years; (b) “bottom up” and “top down” performance at age 8 years was associated with rate of change in ADHD symptom severity from 8 to 12 years; (c) the rate of change of “bottom up” and “top down” performance over age 8 to 12 years was associated with ADHD symptom severity at age 12 years; (d) the rate of change of “bottom up” and “top down” performance over age 8 to 12 years was associated with rate of change in ADHD symptom severity from age 8 to 12 years.

**Model 1: investigate trajectories of change in ADHD symptom severity from age 8 to age 12.** Using the whole sample, a random-coefficient regression model was tested. The level-1
model examined ADHD symptom severity from age 8 to age 12. This is an important step to assess whether there is sufficient individual variability around ADHD symptom severity either at age 12 years (intercept) or in the rate of change from 8 to 12 years (slope) to warrant examining predictors of variability. For this model, age was centered at 12 years because when dealing with constructs such as cognitive functioning as predictor variables, it is not ecologically sound to center at an age before the end point.

Level 1 Model:

$$ADHD_{ij} = \pi_{0j} + \pi_{1j} \text{Age}_{ij} + e_{ij}$$

Level 2 Model:

$$\pi_{0j} = \gamma_{00} + r_{0j}$$

$$\pi_{1j} = \gamma_{10} + r_{1j}$$

where $$ADHD_{ij}$$ is the symptom severity of ADHD for time i for participant j; $$\pi_{0j}$$ is the intercept, which represents the degree of severity for participant j at age 12 years; and $$\pi_{ij}$$ is the growth rate for participant j over age 8-12 years; $$\text{Age}_{ij}$$ is the age at time i for participant j and $$e_{ij}$$ is the level 1 regression residual for each participant at time i. In the level 2 equations, $$\gamma_{00}$$ and $$\gamma_{10}$$ indicate the fixed effects, mean intercept and mean growth rate, respectively. The level 2 random effects, $$r_{0j}$$ and $$r_{ij}$$, signify differences between the individual and the sample average on the intercept and slope, respectively.

We then obtained the slopes of “bottom up” and “top down” performance from 8 to 12 (centered at 12):

1) Level 1 Model:

“bottom up” Score$_{ij} = \pi_{0j} + \pi_{1j} \text{Age}_{ij} + e_{ij}$

Level 2 Model:
\[ \pi_{0j} = \gamma_{00} + r_{0j} \]
\[ \pi_{1j} = \gamma_{10} + r_{1j} \]

2) Level 1 Model:

“top down” _Score\textsubscript{ij} = \pi_{0j} + \pi_{1j} Age\textsubscript{ij} + e_{ij}

Level 2 Model:

\[ \pi_{0j} = \gamma_{00} + r_{0j} \]
\[ \pi_{1j} = \gamma_{10} + r_{1j} \]

From these analyses, Empirical Bayes estimates were saved for use in subsequent models that looked at predictors of ADHD symptom severity change over time.

Model 2: Investigate predictive ability of “bottom up” performance at age 8 on ADHD symptom severity at age 12 and on change in symptom severity from 8-12: 1) Does “bottom up” performance at age 8 predict ADHD symptom severity at age 12 (intercept); 2) Does “bottom up” performance at age 8 predict rate of change (slope) of ADHD severity from 8-12?

Level 1 Model:

ADHD\textsubscript{ij} = \pi_{0j} + \pi_{1j} Age\textsubscript{ij} + e_{ij}

Level 2 Model:

\[ \pi_{0j} = \gamma_{00} + \gamma_{01} “bottom up” _{Score_{j}} + r_{0j} \]
\[ \pi_{1j} = \gamma_{10} + \gamma_{11} “bottom up” _{Score_{j}} + r_{1j} \]

Model 3: Investigate predictive ability of rate of change of “bottom up” performance from 8-12 on ADHD symptom severity at age 12 and on rate of change in ADHD symptom severity from 8-12: 1) Does rate of change (slope) in “bottom up” performance from 8 to 12 predict ADHD symptom severity at age 12 (intercept); 2) Does rate of
change (slope) in “bottom up” performance from 8 to 12 predict rate of change (slope) in ADHD symptom severity from 8 to 12?

Level 1 Model:
\[ \text{ADHD}_{ij} = \pi_0 + \pi_1 \text{Age}_{ij} + e_{ij} \]

Level 2 Model:
\[ \pi_0 = \gamma_{00} + \gamma_{01} \text{“bottom up”}_\text{Slope}_j + r_{0j} \]
\[ \pi_1 = \gamma_{10} + \gamma_{11} \text{“bottom up”}_\text{Slope}_j + r_{1j} \]

Model 4: Investigate predictive ability of “top down” performance at age 8 on ADHD symptom severity at age 12 and on change in symptom severity from 8-12: 1) Does “top down” performance at age 8 predict ADHD symptom severity at age 12 (intercept)?; 2) Does “top down” performance at age 8 predict the rate of change (slope) in ADHD symptom severity from age 8 to 12?

Level 1 Model:
\[ \text{ADHD}_{ij} = \pi_0 + \pi_1 \text{Age}_{ij} + e_{ij} \]

Level 2 Model:
\[ \pi_0 = \gamma_{00} + \gamma_{01} \text{“top down”}_\text{Score}_j + r_{0j} \]
\[ \pi_1 = \gamma_{10} + \gamma_{11} \text{“top down”}_\text{Score}_j + r_{1j} \]

Model 5: Investigate predictive ability of rate of change of “top down” performance from 8-12 on ADHD symptom severity at age 12 and on rate of change in ADHD symptom severity from 8-12: 1) Does rate of change (slope) in “top down” performance from 8 to 12 predict ADHD symptom severity at age 12 (intercept)?; 2) Does rate of change (slope) in “top down” performance from 8 to 12 predict rate of change (slope) in ADHD symptom severity from 8 to 12?
Level 1 Model:
\[ \text{ADHD}_{ij} = \pi_{0j} + \pi_{1j} \text{Age}_{ij} + e_{ij} \]

Level 2 Model:
\[ \pi_{0j} = \gamma_{00} + \gamma_{01} \text{“top down” Slope}_j + r_{0j} \]
\[ \pi_{1j} = \gamma_{10} + \gamma_{11} \text{“top down” Slope}_j + r_{1j} \]

In cases where both “bottom up” and “top down” performance were found to be significant predictors in their respective models, we ran an additional analysis with both “bottom up” and top down performance in the same model to ascertain which of the two remained significantly predictive when both were examined together.

Level 1 Model:
\[ \text{ADHD}_{ij} = \pi_{0j} + \pi_{1j} \text{Age}_{ij} + e_{ij} \]

Level 2 Model:
\[ \pi_{0j} = \gamma_{00} + \gamma_{01} \text{“bottom up” Slope} + \gamma_{02} \text{“top down” Slope}_j + r_{0j} \]
\[ \pi_{1j} = \gamma_{10} + \gamma_{11} \text{“bottom up” Slope} + \gamma_{12} \text{“top down” Slope}_j + r_{1j} \]

As outlined above, fitted models were carried out in order to explain significant variability among individuals in both ADHD symptom severity at age 12 years and rate of change of ADHD symptom severity from age 8 through age 12 years. When significant predictors of intercept or slope were identified, we calculated the proportion of variance they explained using the following equations:

Intercept, proportion of variance explained:
\[
\left( \frac{r_{0j} \text{(unconditional model)} - r_{0j} \text{(fitted model)}}{r_{0j} \text{(unconditional model)}} \right) \times 100
\]

Slope, proportion of variance explained:
We then restricted the above set of analyses to the participants who were labeled as at risk at preschool baseline (e.g., had a diagnostically significant number of ADHD symptoms) to examine whether the effects of “bottom up” and “top down” performance on ADHD symptom severity are different for those with high levels of ADHD symptoms in preschool.

**Mixed Model Analysis: Comparing At Risk vs. Typically Developing.** In addition to the HLM analyses, we conducted a mixed model analysis of the mean “bottom up” and “top down” performance scores across the five years for those labeled as at risk for ADHD in preschool compared to those labeled as typically developing in preschool. A mixed model was chosen because of its ability to deal with missing values in a longitudinal data set.
Results

Hierarchical Linear Modeling

Whole sample

**ADHD Symptom Severity over time.** The estimate of average ADHD symptom severity (range: 0-36) at age 12 years was 14.67 (SE = 0.93, df = 159, T ratio = 15.84, p < 0.001). The average rate of change (slope) was -0.84 units per unit of time (approximately one year) (SE = 0.15, df = 159, T ratio = -5.45, p < 0.001), meaning that, on average, symptom severity scores decreased by 0.84 per year. Figure 1 depicts individual growth trajectories in ADHD symptom severity from ages 8 through 12. There was significant variation around the average intercept ($\chi^2 = 2217.19$, df = 146, p < 0.001) and the average slope ($\chi^2 = 246.16$, df = 146, p < 0.001), indicating that the children varied both in their ADHD symptom severity at 12 years and in their rate of change in symptom severity from 8 through 12 years. Accordingly, the potential of “bottom up” and “top down” performance to predict symptom severity at age 12 and rate of change over time was investigated.

*Figure 1.* Individual growth trajectories of ADHD symptom severity from age 8 through age 12 years.
“Bottom-up” performance at age 8 on ADHD symptom severity. Mean (SD) “bottom up” performance (mean completion time in seconds) at age 8 was 54.16 (15.84) seconds and at age 12 was 30.50 (8.53) seconds for the entire sample.

As can be seen in Table 5, “bottom up” performance at age 8 was marginally (p = .05) associated with ADHD symptom severity at age 12. The pattern of findings suggests that a unit increase in “bottom up” performance (i.e., slower speed) at age 8 years is associated with an increased intercept at age 12 years. The predicted increase in intercept at age 12 years with a unit increase in “bottom up” performance at age 8 years was 0.12 units. “Bottom up” performance at 8 predicted 2.34% of the variance in ADHD symptom severity at age 12. “Bottom up” performance at age 8 did not significantly predict rate of change (slope) in ADHD symptom severity from age 8 through 12.

Table 5. “Bottom up” performance at age 8 as a predictor of ADHD symptom severity at age 12 and of rate of change of ADHD symptom severity from 8 through 12 years for the whole sample.

<table>
<thead>
<tr>
<th>Fixed Effect</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>T-ratio</th>
<th>Approximate d.f.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD symptom severity at age 12 (Level 1 intercept)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>14.67</td>
<td>0.91</td>
<td>16.06</td>
<td>158</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>“Bottom up” Performance at age 8</td>
<td>0.12</td>
<td>0.06</td>
<td>1.94</td>
<td>158</td>
<td>0.05</td>
</tr>
<tr>
<td>Rate of change in ADHD symptom severity (Level 1 slope)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-0.84</td>
<td>0.15</td>
<td>-5.44</td>
<td>158</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>“Bottom up” Performance at age 8</td>
<td>-0.00</td>
<td>0.01</td>
<td>-0.15</td>
<td>158</td>
<td>0.88</td>
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</table>

<table>
<thead>
<tr>
<th>Random Effect</th>
<th>Standard Deviation</th>
<th>Variance Component</th>
<th>d.f.</th>
<th>$\chi^2$</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD symptom severity at age 12 (Level 1 intercept)</td>
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<td>121.41</td>
<td>145</td>
<td>2103.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rate of change in ADHD symptom severity (Level 1 slope)</td>
<td>1.18</td>
<td>1.40</td>
<td>145</td>
<td>245.82</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
“Top down” performance at 8 years on ADHD severity. Mean (SD) “top down” performance at age 8 was 123.75 (31.52) seconds and at age 12 was 68.20 (23.17) seconds. For the entire sample, as can be seen in Table 6, “top down” performance at age 8 significantly predicted ADHD symptom severity at age 12 (intercept). That is, a unit increase in “top down” performance (i.e., slower speed) at age 8 years is associated with an increase in ADHD symptom severity intercept at age 12 years. The predicted increase in intercept at age 12 years with a unit increase in “top down” performance at age 8 years was 0.10 units. “Top down” performance at 8 predicted 7.47% of the variance in ADHD symptom severity at age 12. “Top down” performance at age 8 did not significantly predict rate of change (slope) in ADHD symptom severity from age 8 to 12.

Table 6. “Top down” performance at age 8 as a predictor ADHD symptom severity at age 12 and of rate of change of ADHD symptom severity from 8 through 12 years for the whole sample.

<table>
<thead>
<tr>
<th>Fixed Effect</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>T-ratio</th>
<th>Approximate d.f.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD symptom severity at age 12 (Level 1 intercept)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>14.68</td>
<td>0.89</td>
<td>16.46</td>
<td>158</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>“Top down” Performance at age 8</td>
<td>0.10</td>
<td>0.03</td>
<td>3.51</td>
<td>158</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rate of change in ADHD symptom severity (Level 1 slope)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-0.83</td>
<td>0.15</td>
<td>-5.43</td>
<td>158</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>“Top down” Performance at age 8</td>
<td>-0.00</td>
<td>0.00</td>
<td>-0.30</td>
<td>158</td>
<td>0.76</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Random Effect</th>
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<th>Variance Component</th>
<th>d.f.</th>
<th>$\chi^2$</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD symptom severity at age 12 (Level 1 intercept)</td>
<td>10.73</td>
<td>115.03</td>
<td>145</td>
<td>1961.97</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rate of change in ADHD symptom severity (Level 1 slope)</td>
<td>1.18</td>
<td>1.40</td>
<td>145</td>
<td>245.60</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Level-1, R</td>
<td>4.02</td>
<td>16.15</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Rate of change in “bottom-up” and “top down” performance from 8 through 12 years on ADHD symptom severity. When rate of change (slope) in “bottom up” performance was entered, it emerged as a significant predictor of ADHD symptom severity at age 12 (intercept). The predicted decrease in ADHD symptom severity at age 12 for a unit change in “bottom up” performance was 1.23 units (SE = 0.54, df = 158, T ratio = -2.29, p = 0.02). Rate of change in “bottom up” performance was not a significant predictor of rate of change of ADHD symptom severity over time (coefficient = 0.01, SE = 0.09, df = 158, T ratio = 0.12, p = 0.90).

When rate of change (slope) in “top down” performance was entered, it also emerged as a significant predictor of ADHD symptom severity at age 12 (intercept). The predicted decrease in ADHD symptom severity at age 12 for a unit change in “top down” performance slope was 1.18 units (SE = 0.31, df = 158, T ratio = -3.79, p < .0001). Rate of change in “top down” performance was not a significant predictor of rate of change of ADHD symptom severity over time (coefficient = 0.02, SE = 0.05, df = 158, T ratio = 0.43, p = 0.67).

Accordingly, the model was run with both rate of change in “bottom up” performance and rate of change in “top down” performance entered into the model to see which predictor remained significant. When run together, rate of change in “bottom up” performance was no longer significant and only rate of change in “top down” processing remained a significant predictor of ADHD severity at 12 (see Table 7). That is, a unit increase in “top down” performance slope from 8-12 years is associated with a decrease in ADHD symptom severity (intercept) at age 12 years. The predicted decrease in intercept at age 12 years with a unit increase in “top down” rate of change from 8-12 was -1.27 units. “Top down” rate of change from 8 through 12 years predicted 8.06% of the variance in ADHD symptom severity at age 12.
Table 7. Rate of change of “bottom up” performance and rate of change in “top down” performance from 8 through 12 years as predictors of ADHD symptom severity at age 12 and of rate of change of ADHD symptom severity from 8 through 12 years for the whole sample.

<table>
<thead>
<tr>
<th>Fixed Effect</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>T-ratio</th>
<th>Approximate d.f.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD symptom severity at age 12 (Level 1 intercept)</td>
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</tr>
<tr>
<td>Intercept</td>
<td>14.68</td>
<td>0.89</td>
<td>16.56</td>
<td>157</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>“Bottom up” Rate of Change (8-12)</td>
<td>0.22</td>
<td>0.70</td>
<td>0.31</td>
<td>157</td>
<td>0.76</td>
</tr>
<tr>
<td>“Top down” Rate of Change (8-12)</td>
<td>-1.27</td>
<td>0.43</td>
<td>-2.99</td>
<td>157</td>
<td>0.004</td>
</tr>
<tr>
<td>Rate of change in ADHD symptom severity (Level 1 slope)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-0.834</td>
<td>0.15</td>
<td>-5.43</td>
<td>157</td>
<td>&lt;0.001</td>
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<tr>
<td>“Bottom up” Rate of Change (8-12)</td>
<td>-0.03</td>
<td>0.10</td>
<td>-0.26</td>
<td>157</td>
<td>0.79</td>
</tr>
<tr>
<td>“Top down” Rate of Change (8-12)</td>
<td>0.03</td>
<td>0.07</td>
<td>0.52</td>
<td>157</td>
<td>0.61</td>
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<th>d.f.</th>
<th>$\chi^2$</th>
<th>p-value</th>
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</thead>
<tbody>
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<td>144</td>
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<td>&lt;0.001</td>
</tr>
<tr>
<td>Rate of change in ADHD Severity (Level 1 slope)</td>
<td>1.19</td>
<td>1.43</td>
<td>144</td>
<td>245.48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Level-1, $R$</td>
<td>4.02</td>
<td>16.15</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**At Risk Sample**

**ADHD symptom severity over time.** The estimate of average ADHD symptom severity in the at risk group at age 12 years was 20.18 (SE = 1.11, df = 95, T ratio = 18.21, p < 0.001).

The average rate of change (slope) was −1.10 units per unit of time (approximately one year) (SE = 0.20, df = 95, T ratio = -5.58, p < 0.001), meaning that, on average, symptom severity scores decreased by 1.10 per year. Figure 2 depicts individual growth trajectories in ADHD symptom...
severity from ages 8 through 12 for the at risk sample. There was significant variation around the average intercept ($\chi^2 = 1008.34, \text{df} = 86, p < 0.001$) and the average slope ($\chi^2 = 117.84, \text{df} = 86, p = 0.01$), indicating that the children varied both in their ADHD symptom severity at 12 years and in their rate of change in ADHD symptom severity from 8 through 12 years. Accordingly, the potential of “bottom up” performance and “top down” performance to predict ADHD symptom severity at age 12 and rate of change over time was investigated.

![Graph showing individual growth trajectories of ADHD symptom severity from age 8 through age 12 years for children identified as at risk for ADHD at preschool.](image)

**Figure 2.** Individual growth trajectories of ADHD symptom severity from age 8 through age 12 years for children identified as at risk for ADHD at preschool.

“Bottom-up” performance at age 8 years and ADHD symptom severity. Mean (SD) “bottom up” performance (mean completion time in seconds) at age 8 was 54.92 (16.10) seconds and at age 12 was 31.72 (10.31) seconds for the at risk group. As can be seen in Table 8, “bottom up” performance at age 8 significantly predicted a decrease in ADHD symptom severity at age 12. In other words, a unit increase in “bottom up” performance (i.e., slower speed) is significantly associated with an increase in ADHD symptom severity intercept at age 12 years. The predicted increase in intercept at age 12 years with a unit increase in “bottom up” processing
at age 8 years was 0.13 units. “Bottom up” performance at 8 predicted 3.68% of the variance in ADHD symptom severity at age 12. “Bottom up” performance at age 8 did not significantly predict rate of change (slope) in ADHD symptom severity from age 8 through 12.

Table 8. “Bottom up” performance at age 8 as a predictor of ADHD symptom severity at age 12 and of rate of change of ADHD symptom severity from 8 through 12 years for the at risk sample.

<table>
<thead>
<tr>
<th>Fixed Effect</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>T-ratio</th>
<th>Approximate d.f.</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>ADHD symptom severity at age 12 (Level 1 intercept)</td>
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<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>20.17</td>
<td>1.08</td>
<td>18.60</td>
<td>94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>“Bottom up” Performance at age 8</td>
<td>0.13</td>
<td>0.057</td>
<td>2.31</td>
<td>94</td>
<td>0.02</td>
</tr>
<tr>
<td>Rate of change in ADHD symptom severity (Level 1 slope)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-1.10</td>
<td>0.20</td>
<td>-5.60</td>
<td>94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>“Bottom up” Performance at age 8</td>
<td>0.01</td>
<td>0.01</td>
<td>0.76</td>
<td>94</td>
<td>0.45</td>
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<tr>
<td></td>
<td>9.99</td>
<td>99.72</td>
<td>85</td>
<td>943.39</td>
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<tr>
<td>Rate of change in ADHD symptom severity (Level 1 slope)</td>
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<tr>
<td></td>
<td>0.98</td>
<td>0.97</td>
<td>85</td>
<td>116.73</td>
<td>0.01</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.23</td>
<td>17.91</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

“Top down” performance at 8 years on ADHD symptom severity. Mean (SD) “top down” performance (mean completion time in seconds) at age 8 was 129.72 (32.06) seconds and at age 12 was 73.62 (26.88) seconds for the at risk group. “Top down” performance at age 8 did not significantly predict ADHD symptom severity at age 12 (intercept) (coefficient = 0.05, SE = 0.04, df = 94, T ratio = 1.56, p = 0.12) or the rate of change (slope) in ADHD symptom severity from age 8 to 12 (coefficient = -0.00, SE = 0.00, df = 94, T ratio = -0.08, p = 0.94).
Rate of change in “bottom-up” and “top down” performance from 8 through 12 years on ADHD symptom severity. The rate of change (slope) in “bottom up” performance did not significantly predict ADHD symptom severity at age 12 (intercept) (coefficient = -0.97, SE = 0.60, df = 94, T ratio = -1.63, p = 0.11) or the rate of change in ADHD symptom severity (slope) (coefficient = -0.05, SE = 0.10, df = 94, T ratio = -0.53, p = 0.599) from 8 to 12.

Furthermore, the rate of change in “top down” performance (slope) did not significantly predict ADHD symptom severity at age 12 (intercept) (coefficient = -0.49, SE = 0.39, df = 94, T ratio = -1.25, p = 0.21) or the rate of change in ADHD symptom severity from 8 to 12 (slope) (coefficient = 0.01, SE = 0.06, df = 94, T ratio = 0.22, p = 0.82).

Mixed Model Analysis: Comparing At Risk vs. Typically Developing

In addition to HLM to assess the respective roles of “bottom up” and “top down” performance on trajectory of ADHD severity from age 8 to 12, we compared the at risk and typically developing groups’ “bottom up” and “top down” performance across the age range. A mixed model, with preschool baseline status as a fixed effect, was used to compare the at risk and typically developing groups’ performance on mean “bottom up” and “top down” scores. Figure 3 shows the mean “bottom up” performance for the at risk and typically developing groups from ages 8-12 (see Table 9 for breakdown of mean “bottom up” performance at each year). Overall mean (SD) “bottom up” performance across the age range was 42.76 (15.22) seconds for the at risk group and 39.48 (13.89) seconds for the typically developing group; the mixed model analysis of at risk vs. typically developing group approached significance (Estimate = -2.97, St. Error = 1.52, df = 266.21, t = -1.95, p = 0.052). Figure 4 shows mean “top down” performance for the at risk and typically developing groups from ages 8-12 (see Table 10 for breakdown of mean “top down” performance at each year). Overall mean (SD) “top down”
performance was 99.32 (35.69) for the at risk group and 84.63 (28.85) for the typically developing group. The mixed model analysis showed a significant difference between the at risk and typically developing groups (Estimate = -11.50, St Error = 3.44, df = 152.57, t = -3.34, p = 0.001).

Figure 3. “Bottom up” performance# as a function of preschool baseline clinical status.

# “Bottom up” performance calculated from the mean of D-KEFS TMT- Number Sequencing and Letter Sequencing, D-KEFS CWIT – Color Naming and Word Reading
Table 9. Mean (SD) “bottom up” performance\(^\#\) across the whole sample and as a function of preschool baseline clinical status.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Whole Sample</th>
<th>At Risk</th>
<th>Typically Developing</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>n 160</td>
<td>54.16 (15.84)(^4)</td>
<td>54.92 (16.10)(^3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>96</td>
<td>64</td>
</tr>
<tr>
<td>9</td>
<td>n 148</td>
<td>44.79 (13.90)(^5)</td>
<td>46.04 (15.20)(^2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>86</td>
<td>62</td>
</tr>
<tr>
<td>10</td>
<td>n 139</td>
<td>38.78 (10.25)(^4)</td>
<td>40.34 (10.44)(^2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>84</td>
<td>55</td>
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<tr>
<td>11</td>
<td>n 133</td>
<td>33.83 (8.54)(^2)</td>
<td>34.93 (8.80)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>76</td>
<td>57</td>
</tr>
<tr>
<td>12(^*)</td>
<td>n 109</td>
<td>30.50 (8.53)(^3)</td>
<td>31.74 (10.31)(^2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>59</td>
<td>50</td>
</tr>
</tbody>
</table>

\(^\#\) “Bottom up” performance calculated from the mean of D-KEFS TMT- Number Sequencing and Letter Sequencing, D-KEFS CWIT – Color Naming and Word Reading.

\(^\wedge\) Number of scores changed to 3 Standard Deviations from the mean

Figure 4. “Top Down” performance\(^\#\) as a function of preschool baseline clinical status.

\(^\#\) “Top Down” performance calculated from the mean of D-KEFS TMT-Number Letter Switch subtest, D-KEFS CWIT – Inhibition and Inhibition/Switch subtests.
Table 10. *Mean (SD) “top down” performance*\(^#\) across the whole sample and as a function of preschool baseline clinical status.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Whole Sample</th>
<th>At Risk</th>
<th>Typically Developing</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>n 160</td>
<td>96</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>123.75 (31.52)</td>
<td>129.72 (32.06)(^1)</td>
<td>114.89 (29.04)(^1)</td>
</tr>
<tr>
<td>9</td>
<td>n 148</td>
<td>86</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>101.82 (31.33)</td>
<td>108.92 (34.88)</td>
<td>92.04 (22.67)</td>
</tr>
<tr>
<td>10</td>
<td>n 139</td>
<td>84</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>85.31 (23.71)(^3)</td>
<td>90.68 (25.59)(^1)</td>
<td>77.39 (19.10)</td>
</tr>
<tr>
<td>11</td>
<td>n 133</td>
<td>76</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>75.33 (21.90)(^3)</td>
<td>79.56 (23.32)</td>
<td>69.48 (17.91)(^1)</td>
</tr>
<tr>
<td>12(^*)</td>
<td>n 109</td>
<td>59</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>68.20 (23.17)(^4)</td>
<td>73.62 (26.88)(^1)</td>
<td>61.95 (16.32)</td>
</tr>
</tbody>
</table>

\(^#\) “Top down” performance calculated from the mean of D-KEFS TMT-Number Letter Switch subtest, D-KEFS CWIT – Inhibition and Inhibition/Switch subtests.

\(^*\)Number of scores changed to 3 Standard Deviations from the mean
Discussion

The present study sought to examine whether improvements in specific neuropsychological functions, namely bottom-up and top-down processing, account for the diminution of ADHD symptom severity over the course of development. The Halperin and Schulz (2006) model of ADHD posits that ADHD is associated with subcortical deficits that remain throughout the lifespan while recovery over time is associated with prefrontal development and the degree to which improvements in top-down processing can compensate for those deficits.

Participants were assessed annually from ages 8 to 12 years using measures of ADHD symptom severity and neuropsychological performance. Based on the above model, it was predicted that “bottom up” performance would be poorer for at risk children despite a reduction in symptom severity over time. It was also expected that improvements in top-down processing would be associated with symptomatic improvement over time.

With regard to neuropsychological functioning across the age range studied, the at risk group performed significantly worse than the typically developing group on “top down” performance, with a marginal difference on “bottom up” performance. On average, across the whole sample, ADHD symptom severity decreased significantly between ages 8 and 12 years, although there was significant variability in trajectories across participants. Importantly, the rate of change of “top down” performance from ages 8-12 was significantly associated with ADHD symptom severity at age 12. In other words, greater improvement in “top down” performance was associated with lower ADHD symptom severity at age 12. To a lesser extent, “bottom up” performance at age eight was associated with ADHD symptom severity at age 12. That is, poorer “bottom up” performance at age 8 was associated with higher ADHD symptom severity scores at
age 12. Additionally, when the at risk sample was examined separately, only “bottom up” performance at age 8 was significantly associated with ADHD symptom severity at age 12.

The present findings offer some support for the Halperin and Schulz developmental model of ADHD pathology and recovery. While, on average, at risk participants performed more poorly than typically-developing peers on “top down” performance, nonetheless improvement in “top down” performance was associated with later ADHD symptom severity. This association is consistent with the hypothesis that improvement in cortical, and perhaps more specifically prefrontal, functioning plays a role in the diminution of symptoms seen across childhood. Also, somewhat consistent with the model are the results that the at risk group tended to have poorer “bottom up” performance across the entire age range and that poorer “bottom up” processing at age 8 years was marginally associated with greater ADHD symptom severity at age 12. These findings are consistent with the view that ADHD is associated with subcortical deficits that remain despite a reduction of symptoms over development.

Nevertheless, the data were not fully consistent with what would be predicted by the Halperin and Schulz model. Specifically, we did not find that rate of change in “top down” performance from 8-12 was significantly associated with rate of change in ADHD symptom severity during that same age range. In other words, improvements in “top down” performance did not predict reduction in ADHD symptom severity in either the at risk group, as would be expected, or in the entire sample.

Albeit less robust, these results are consistent with other studies of neuropsychological function and ADHD severity over development. In two separate studies looking at at risk participants from the current sample at a younger age using different neuropsychological measures, Rajendran et al. (2013a, 2013b) found improved neuropsychological functioning was
associated with subsequent diminution of ADHD symptom severity. Again, the results are consistent with the notion that more optimal neural development is associated with greater symptom reduction whereas less favorable development may lead to less symptom reduction. Similarly, Miller, Loya and Hinshaw (2014) used latent growth curve estimations to examine the development of specific EFs and the relationship between trajectories of EFs and ADHD symptoms from childhood to young adulthood in a sample of girls with and without childhood ADHD. They found that greater improvement on a “global EF measure” was associated with greater reduction in both inattentive and hyperactive/impulsive symptoms. Moreover, those with childhood ADHD, who had poorer EF performance at baseline, showed greater improvements on the global EF measure, but not other specific EF measures, as compared to typically developing peers. The authors posit that this may be because the ADHD group, which had greater EF impairment in childhood, had “more room to improve in their global EF” scores. Alternatively, they suggest that their findings “reflect the heterogeneity inherent to ADHD” and the different trajectories of EF and symptom reduction over development.

Using neuroimaging to test aspects of the Halperin and Schulz model, Francx and colleagues (2015) conducted a longitudinal follow-up study of 129 children with ADHD-combined type and 100 healthy controls. The sample was slightly older than the present sample – average age at baseline was 11.8 years and 17.5 at follow-up. The study examined brain structure and activity (resting state functional connectivity) in the executive control network. In support of the model, they found that a developmental decrease in hyperactive/impulsive symptoms was associated with “stronger functional connectivity in the frontal regions of the executive control network.” Additionally, those who no longer met criteria for ADHD (remitters) had higher frontal connectivity than healthy controls, lending support to the model’s view that
frontal compensatory mechanisms are at play in ADHD recovery. However, they did not find subcortical dysfunction to be associated with ADHD pathology, as the model suggests. To that end, Clerkin et al. (2013) found decreased subcortical connectivity on “bottom up” tasks in both persister and remitter adults as compared to healthy controls suggesting that subcortical dysfunction is present in ADHD regardless of symptom reduction over time.

Interestingly, in the current study, the greatest support for the model came from evaluation of the entire sample and not when the at risk sample was examined alone. This may simply be a function of having a larger sample size with the entire sample allowing for greater power to detect differences. However, it also may reflect the fact that attention exists on a continuum with ADHD representing the extreme end and frontal development is generally responsible for improvements in attention and behavior. To that end, Lubke and colleagues (2011) used factor mixture models on maternal ratings of attention problems in a large sample and concluded that ADHD is the “extreme end of a continuous trait rather than as a disorder category.” Symptoms of ADHD reflect behaviors and processes that exist in all children and more optimal frontal development, even in typically developing children, yields greater behavioral development. Shaw and colleagues (2011) examined cortical development in a sample of typically developing children with hyperactive/impulsive symptoms. They found that typically developing children with hyperactive/impulsive symptoms demonstrate neurodevelopmental changes similar to those with ADHD (e.g., slower cortical thinning in predominantly frontal areas). Accordingly, the authors conclude that the results give “neurobiological support to the dimensional view of ADHD.” It is, therefore, not surprising that we found “top down” improvement associated with reduced symptom levels at 12 years-old in the entire sample.
As reviewed earlier, there is a sizable literature showing poorer performance on neuropsychological measures in children with ADHD relative to typically developing peers (Alderson et al., 2010; Berwid et al., 2005; Halperin et al., 2008; Rajendran, Rindskopf, et al., 2013; Rajendran, Trampush, et al., 2013; Willcutt et al., 2005) but identification of specific cognitive domains is less consistent. Coghill and colleagues (2014) directly compared six cognitive domains that have been posited to be associated with ADHD. They found that children with ADHD performed more poorly in each domain, though, notably, each deficit was associated with a distinct subset of the individuals with ADHD. These results highlight the diversity of cognitive deficits that may underlie, or are associated with, ADHD. Further complicating the picture, there was a significant minority for whom no cognitive deficits were identified.

Indeed, Durston et al. (2011) have suggested that ADHD likely reflects a relatively broad spectrum of distinct neurobiological pathways, cognitive profiles and behavioral patterns. Similarly, some suggest separable neuropsychological subtypes of ADHD (Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005; Sonuga-Barke, Dalen, & Remington, 2003; Sonuga-Barke & Halperin, 2010). The heterogeneity of cognitive, behavioral, and developmental profiles in ADHD raises important issues regarding the etiology of ADHD as well as effective treatments. The present results show considerable variability in neuropsychological functioning and in rate of change of symptomatology over time. As reviewed earlier, there are several models of ADHD that focus on executive dysfunction (Barkley, 1997; Barkley & Murphy, 2006; Pennington & Ozonoff, 1996; Rapport et al., 2009) but, as the present results suggest, it is unlikely that frontal/executive deficits, alone, are responsible for ADHD symptomatology and impairment. Rather, a greater appreciation of the role of bottom-up functioning is warranted (Rommelse et al., 2007). The degree to which poor bottom-up functioning may affect performance on tests of top-
down functioning is still unknown but the data suggest that the relationship is more complex than most models have acknowledged.

Coghill and others (2014) and others have raised the important issue that ADHD is far too heterogeneous to neatly fit into any “cognitive deficit X causes ADHD” model. Rather, they propose that cognitive deficits in ADHD are independent of symptoms such that, both cognitive deficits and behavioral symptoms are caused by an interplay of genes, environment and brain structure/function, and that both independently cause functional impairment. More simply, the relationship between cognitive deficits and behavioral symptoms in ADHD is more complex than a straight “cause and effect.”

While it is true that there should be a more nuanced understanding of the role of cognitive deficits in the clinical presentation of ADHD, the data do not support a complete divide in the relationship between cognitive deficits and behavioral symptoms. The present results and others (Halperin et al., 2008; Miller et al., 2013; Rajendran et al., 2013a; Rajendran et al., 2013b) offer compelling data that improvement in neuropsychological functioning is linked to symptom reduction over time. However, neuropsychological data have not consistently supported the Halperin and Schulz model. In a literature review of 18 studies examining neurocognitive abilities and ADHD symptoms over time, van Lieshout and colleagues (2013) found no evidence to suggest that, for those with childhood ADHD, a reduction of ADHD symptoms is associated with improvements on higher-level neurocognitive abilities. Similarly, Coghill and colleagues (2014) found no association between symptom reduction and executive functioning from ages 9 to 14 in a small (n=34) sample of boys with and without ADHD. In a longitudinal examination of 279 individuals, Cheung and colleagues (2015) found that executive control measures were not sensitive to ADHD persistence or remission.
The inconsistent neuropsychological results may reflect a general problem with the sensitivity of neuropsychological tests to effectively detect the subtle differences in neurodevelopmental disorders, especially when there are likely several brain regions and functional circuits involved (Krain & Castellanos, 2006). As opposed to brain lesions where a cognitive deficit is likely to be focal, neurodevelopmental disorders are likely the result of functional abnormalities across brain regions (namely subcortical/frontal connectivity). Accordingly, neuropsychological research in ADHD is hindered by an inconsistent ability to truly assess relative effects of different yet closely-linked cognitive functions. The combination of heterogeneity in ADHD and the limited specificity of neuropsychological tests may partially account for inconsistent findings linking cognitive performance to ADHD symptom severity. In general, studies that have failed to link neuropsychological performance to ADHD symptom change have focused on individual neuropsychological tests (e.g., van Lieshout et al., 2013; Coghill et al., 2014; Cheung et al., 2015). In contrast, studies providing support for the model tended to use latent factor scores, combinations of multiple tests (as done here) and/or more global measures of neuropsychological functioning (e.g., Miller, Loya, & Hinshaw, 2014; Rajendran et al., 2013a; 2013b).

In recent years, the literature highlighting executive and working memory deficits in ADHD has led to a push to create cognitive (in particular working memory) training programs aimed at improving cognitive functioning and, by extension, behavioral symptoms. Given what is known about the relationship between improvements in higher-order functioning and symptom reduction, as seen in the present results as well, they offered a promising and novel approach to effective, long-term treatment. However, such training programs have had only limited success at reducing behavioral symptoms. While some show evidence of improved performance on the
cognitive measures, only minimal improvement in ADHD symptoms have been reported (Chacko et al., 2014; Gray et al., 2012; Klingberg, Forssberg, & Westerberg, 2002). A meta-analytic review of 23 studies with 30 group comparisons found that cognitive training programs produced “reliable short-term improvements in working memory skills” but that “there was no convincing evidence of the generalization of working memory training to other skills” (Melby-Lervåg & Hulme, 2013).

The lack of support for cognitive training programs as a successful treatment for ADHD is disappointing and begs the question of “why?” Perhaps, as Coghill (2014) suggests there is no cause-effect relationship between neuropsychological functioning and ADHD symptoms. It is therefore, not surprising that cognitive training does not successfully reduce ADHD symptoms. Alternatively, as the Rajendran (2013b) findings in 4-5 year olds suggest, such training may be most beneficial at a young age (e.g., Halperin et al., 2012) but less so as the child enters school age. Once the school years start, the relationship between ADHD symptoms and neuropsychological functioning becomes more complex. For instance, as opposed to just neuropsychological functioning influencing ADHD severity, it could be that greater ADHD symptom severity also leads to poorer neuropsychological functioning. If so, cognitive intervention before school age may be most beneficial—when improved neuropsychological functioning might have a stronger impact on symptom severity.

Additionally, it may be useful to focus on more basic cognitive training, such as processing speed or learning/memory training, which is crucial to higher-order functioning and may be more closely linked to ADHD pathology. As the present results and others (Marks et al., 2005) suggest, bottom-up processing is an important area of deficiency in ADHD that has been overlooked in most cognitive training treatments and may be a valuable target. Alternatively,
given the heterogeneity of cognitive and behavioral symptoms, perhaps a single treatment modality is unlikely to be universally effective for the varied cognitive and behavioral landscape of ADHD. Moving forward, an important task may be identifying different treatment targets for different children based on presentation and etiology.

**Strengths of the current study**

A major strength of the current study is the inclusion of neuropsychological data, including “bottom up” and “top down” performance, as well as clinical assessments, across a five year period. Specifically, the school-age years, 8 to 12, is an important time when the demands of school increase and the relative role of top-down compensatory mechanisms likely becomes more pronounced. Longitudinal data in general are important for properly understanding dynamic neurodevelopmental disorders such as ADHD. Examining the trajectories of both clinical presentation and cognitive functioning allows us to better understand what drives more optimal development. More specifically, examining a sample of children from 8 to 12, a period when there are cortical delays in ADHD (Shaw et al., 2007) and when the educational demands on the child increase, offers valuable information about the role of cognitive functioning on ADHD symptom severity during this childhood transition. Specifically, by looking at both bottom-up and top-down processing, we were able to more clearly evaluate the distinctiveness of executive deficits in ADHD and the oft-overlooked role of more basic cognitive functions. Accordingly, by using HLM trajectory analysis, we were able to evaluate relations between the different neuropsychological functions and changes in symptom severity. Additionally, by using a dimensional approach to ADHD severity, as opposed to a categorical (ADHD vs. control) approach, we were able to evaluate change in ADHD severity even in children who remained symptomatic or continued to meet diagnostic criteria. This allowed us to
capture clinical information that would not be possible had we focused on diagnostic status.

Furthermore, given imaging data that suggest a cortical maturation delay in ADHD (Shaw et al., 2007; 2010), the age range of 8 to 12 is a critical time to assess differences and see whether there is normalization over the pre-adolescence childhood years (Drechsler et al., 2005).

**Study Limitations**

There are a number of limitations that need to be addressed as well. As referenced above, a common critique of neuropsychological tests in general is that it is difficult to get a “pure” measure of any single cognitive domain because there are several different cognitive functions at play on any given task.

To that end, our goal was to evaluate both bottom-up and top-down processing to properly parse out the relative contributions of both. However, it is possible that the specific measures we chose, and the way they were combined, do not properly capture true bottom-up versus top-down functioning. Similarly, while we examined “bottom up” and “top down” performance on the same neuropsychological measures (TMT and CWIT), we did not specifically examine “top down” performance controlling for “bottom up” performance which may have allowed us to better assess the relative contribution of bottom-up functioning to “top down” performance.

In terms of sample composition, the attrition rate disproportionately affected individuals in the at risk group, which may have affected our results. However, this is a commonly observed phenomenon (Campbell, Ewing, Breaux, & Szumowski, 1986) and Wolke and colleagues (2009) have shown that while selective attrition likely results in lower rates of diagnoses at outcome, it is unlikely to affect the relations observed among modeled variables. Accordingly, it is unlikely that the association identified in the present study were substantially influenced by attrition.
Additionally, it is possible that the present study focused on too-narrow an age range. Given what is known about prefrontal development and delays in ADHD, this study would be stronger if we had a wider age range and were able to continue observations of the children into adolescence.

Also not unique to this study, is the role of medication or other treatment on parents’ and teachers’ reports of symptom severity. For a child who is medicated, teachers only see him/her while medicated which leads to a lower rating of symptoms severity. For the parents, they are asked to try and rate the child when they are off medication; however this can often be difficult. Accordingly, ratings of symptom severity may be lower than is truly appropriate for that child.

Lastly, while there was a year between each assessment, there is the possibility of practice effects, which affect scores on neuropsychological measures, leading to the appearance of greater improvement on neuropsychological tests.

**Future Directions**

Results suggest that a variety of neuropsychological functions, specifically both bottom-up and top-down processing, are important to ADHD pathology and trajectory over development. Models of ADHD that focus on a single cognitive function as the source of the disorder are likely too narrow. ADHD symptoms do diminish over the years in most individuals and neuropsychological improvements appear to be correlated with that diminution. However, there are likely other biological and environmental factors at play. If cognitive deficits are solely responsible for behavioral symptoms, it would be expected that “improve the cognitive function to improve the ADHD symptoms” would be fruitful. And yet, cognitive training programs have not been hugely successful. Thus, it is possible that cognitive functions, per se, are not the appropriate treatment target, but rather the underlying neural substrates that affect both cognition
and ADHD severity. Additionally, there needs to be a greater appreciation of the heterogeneity of presentation within and between individuals across the age range and a wider range of treatment options should be available perhaps based on the key deficit/symptom for the individual child. We may not find a single treatment that works for all children. Moving forward, greater integration of structural and functional neuroimaging data, combined with neuropsychological data, especially in large longitudinal data sets spanning a wide age-range from early childhood through young adulthood, will be critical to gaining a broader understanding of the untidy picture of ADHD pathology over the course of development.
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