Executive Function in Attention Deficit Hyperactivity Disorder (ADHD): Examining the Role of Subtypes and Comorbid Disorders

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Author Contribution

Both Manuscripts included in this dissertation are co-authored. This dissertation is part of a larger study, which began in September 1999. Dr. Grizenko and Dr. Joober are the principal investigators (PI) and have been involved in all aspects of the study, including study design, obtaining funding, psychiatric assessment of the children, data analysis and interpretation, and providing feedback on the manuscripts. Dr. Joober is also my co-supervisor.

Dr. Victoria Talwar is my supervisor. She has been involved in data analysis and interpretation, and in revisions of this dissertation. Dr. Kim Cornish was my supervisor during my Masters degree at McGill University and the first two years of my Doctoral degree. She was involved in conceptualisation of this dissertation, and revisions. Dr. Norbert Schmitz, is the statistical consultant on the team and Dr. Valentin Mbekou was involved in setting up neurocognitive and executive function aspect of the project.

I have been part of the research team since the beginning of the project, first in a capacity of a project coordinator and later as a Master's student and Doctoral student. I have contributed in the design of the project, and have been responsible for ethics submissions. I have collected the data during the first years, have trained research assistants to collect data, and supervised the students. I have analysed and interpreted the data, wrote both manuscripts and the dissertation, incorporated the revisions and feedback.

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Abstract

The relationship between Attention Deficit Hyperactivity Disorder (ADHD) and Executive Function (EF) continues to be at the forefront of research. An improved understanding of this relationship will advance the assessment and treatment of individuals with ADHD. The purpose of this dissertation is to examine how the clinical presentation of ADHD relates to performance on EF tasks in children age 6 to 12, diagnosed with ADHD. The first manuscript examines the relationship between ADHD symptoms and EF performance. Three hundred and sixty three children were included in the study. Children performed a battery of neuropsychological tests, commonly used to assess EF. The three DSM-IV ADHD subtypes and the Sluggish Cognitive Tempo (SCT) subtype were examined. The results indicate that children's performance differed depending on the DSM-IV subtype diagnosis and on SCT. However, when age was controlled, the results were no longer significant. This finding suggests that age plays a significant role in children's performance on EF tasks. The second manuscript further examines EF, but takes into consideration the presence of comorbid disorders. This study included 355 children, ages 6-12. Children completed a neurocognitive battery, which included measures of working memory, set-shifting, planning, and attention. The comorbid disorders examined were Oppositional Defiant Disorder (ODD), Conduct Disorder (CD) and anxiety disorders. Significant differences were found between children with anxiety disorders and without anxiety disorders on measures of attention and working memory. A significant difference was found between children with CD and without CD on set-shifting measure, and a significant sex by CD interaction was observed on this measure. The results stress the importance of considering comorbid disorders when assessing and treating children with ADHD.

Aberégé

La relation entre le trouble du déficit de l'attention avec hyperactivité (TDAH) et les fonctions exécutives demeure au centre des recherches actuelles. Une meilleure compréhension de cette relation influera sur l'évaluation et le traitement des personnes présentant un TDAH. L'objectif de cette étude est d'examiner le lien entre la présentation clinique du TDAH et la performance de tâches faisant appel aux fonctions exécutives d'enfants de 6 à 12 ans présentant un TDAH. La premier étude examine la relation entre les symptômes du TDAH et les fonctions exécutives. Trois cent soixante-trois enfants ont été inclus dans cette étude. Les enfants ont fait l'objet d'une série de tests neuropsychologiques couramment utilisés dans l'évaluation des fonctions exécutives. Les trois sous-types de TDAH du DSM-IV et le sous-type de rythme cognitif lent (RCL) ont été examinés. Les résultats indiquent que les performances des enfants différaient en fonction du diagnostic du sous-type DSM-IV et RCL. Cependant, lorsque l'âge était contrôlé, les résultats cessaient d'être significatifs. Ces résultats suggèrent que l'âge joue un rôle important dans la performance de tâches faisant appel aux fonctions exécutives chez les enfants. La deuxième étude pousse l'examen des fonctions exécutives, mais en tenant compte de la présence de troubles comorbides. Dans cette étude, trois cent cinquante-cinq enfants de 6 à 12 ans ont été inclus. Les enfants ont fait l'objet d'une série de tests neurocognitifs incluant des mesures de la mémoire de travail, de la souplesse cognitive, de la planification et de l'attention. Les troubles comorbides examinés étaient le trouble oppositionnel avec provocation (TOP), le trouble des conduites et les troubles anxieux.

D'importantes différences ont été relevées entre les enfants présentant ou non des troubles anxieux dans le cadre des mesures de l'attention et de la mémoire de travail. Une différence importante a été relevée dans le cadre des mesures de souplesse cognitive entre les enfants ayant un trouble des conduites; de plus, une interaction significative a également été notée entre le sexe et le trouble des conduites pour cette mesure. Ces résultats soulignent l'importance de tenir compte des troubles comorbides lors de l'évaluation et du traitement d'enfants présentant un TDAH.

CHAPTER 1

Introduction and Review of the Literature

Attention Deficit Hyperactivity Disorder (ADHD) continues to be the most common psychiatric disorder among school-age children. In the past several decades an important body of research has been devoted to understanding the nature of this disorder and its impact on individual functioning throughout development, from pre-school years to adulthood. As new research emerges, the current diagnostic classification of ADHD is being questioned and new light is being shed on the pathophysiology of the disorder and comorbid disorders. The purpose of the current dissertation is to examine Executive Function (EF) in children with ADHD. The following *General Introduction* presents a brief review of current literature on ADHD, beginning with a discussion of diagnostic considerations and the current views on ADHD subtypes and comorbid disorders. This is followed by an introduction of theories of EF and ADHD formulated on the basis of EF deficits often observed in children with ADHD. Lastly, current literature examining the association between EF and ADHD subtypes will be discussed followed by a review of EF and comorbid disorders.

Attention Deficit Hyperactivity Disorder: An Overview

ADHD has a 6-9% prevalence rate (Dopheide & Pliszka, 2009) and is a major risk factor for educational failure, later antisocial and high risk behaviour, and other psychopathology (Biederman et al., 2006; Biederman, Petty, Fried, et al., 2008; Pagani, Derevensky, & Japel, 2009). This is particularly true if ADHD is left undiagnosed (Mannuzza, Klein, & Moulton, 2008) or untreated (Shaw et al., 2012). At the core of this disorder is a pervasive difficulty in attention allocation that can be mapped at both behavioural and cognitive levels.

From an aetiological perspective, and similar to most psychiatric disorders, genetic and environmental factors have been identified as contributors to the development of ADHD, with a more recent emphasis on gene-environment interactions. A flurry of studies has aimed at bringing to light the cognitive phenotype of ADHD. More recently researchers have been focusing on identifying a possible useful endophenotype of ADHD. Endophenotypes, heritable traits that indicate an individual's liability to develop the disorder (Castellanos & Tannock, 2002), are considered important when examining and understanding the aetiology of complex disorders, such as ADHD, in which environmental and genetic factors, as well as their interactions, contribute to phenotypic expression (Cannon & Keller, 2006; Doyle et al., 2005). EF has been proposed as a useful endophenotype for genetic studies of ADHD (Crosbie, Perusse, Barr, & Schachar, 2008).

Diagnostic Challenges

Historically, ADHD has been viewed as a categorical disorder of childhood, with attention and hyperactivity/impulsivity symptoms as core deficits. Recently clinicians and researchers have moved away from defining ADHD as a disorder of childhood, instead, ADHD is viewed as a neurodevelopmental disorder with a continuation, albeit with a more subtle expression into adulthood (Biederman, 2005; Greydanus, Pratt, & Patel, 2007; American Psychiatric Association, 2013). These findings are reflected in part in the new Diagnostic and

Statistical Manual, Fifth Edition (DSM-5: American Psychiatric Association, 2013), where particular attention has been paid to the adolescent and adult ADHD diagnosis. The changes in DSM-5 ADHD diagnostic criteria may affect the selection of participants in future research projects. For example the DSM-IV requires for the ADHD symptoms to be present before age seven. Based on several studies this requirement was removed from manual and is not present in the DSM-5. The required number of symptoms for the diagnosis of ADHD in adolescents has also changed. According to the current manual the adolescents can be diagnosed with ADHD if presented with five symptoms and not six as required by DSM-IV.

DSM-IV subtypes. The Diagnostic and Statistical Manual, Fourth Edition (DSM-IV: American Psychiatric Association, 1994) identifies three ADHD subtypes: ADHD predominantly inattentive type (ADHD-I), ADHD predominantly hyperactive/impulsive type (ADHD-H) and ADHD combined type (ADHD-C), a differentiation that is not present in the International Classification of Diseases (Woo & Rey, 2005), but has been retained in DSM-5.

The ADHD-C subtype requires six or more symptoms of hyperactivity/impulsivity and six or more symptoms of inattention. This type is more common then other subtypes and has a higher prevalence in the clinical population (Baeyens, Roeyers, & Walle, 2006). The ADHD-I subtype is diagnosed if the child presents with six or more inattentive symptoms and less than six hyperactive/impulsive symptoms. It is most common in the community sample (Baeyens et al., 2006) and children with this subtype are more likely to be girls or to be older (Woo & Rey, 2005). The ADHD-H subtype requires six or more hyperactive/impulsive symptoms and less than six inattentive symptoms; it is relatively rare and is associated with younger age (Woo & Rey, 2005).

The reliability and validity of the three DSM-IV ADHD subtypes are continually being questioned, particularly in light of emerging research in this domain (Hinshaw, 2001; Milich, Balentine, & Lynam, 2001; Nigg, Tannock, & Rohde, 2010; Woo & Rey, 2005). The subtypes have been found to be unstable across time, especially ADHD-H, as children with this diagnosis are often reported to shift to ADHD-C subtype over time (Lahey, Pelham, Loney, Lee, & Willcutt, 2005; Willcutt et al., 2012). Subtype diagnoses have been found to be highly affected by the informant, suggesting cross-situational differences of behaviour (Valo & Tannock, 2010; Woo & Rey, 2005). However, distinct differences have been found between inattentive and hyperactive symptoms (Lahey & Willcutt, 2010). Milich et al. (2001) found that children with the ADHD-C subtype are more distractible, while children with the ADHD-I subtype present with sluggish cognitive tempo. Several studies indicate that children diagnosed with the ADHD-I subtype may have impairment in different forms of attention as compared to children with the ADHD-C subtype (Adams, Derefinko, Milich, & Fillmore, 2008; Barkley, 1997; Derefinko et al., 2008). Moreover, Diamond (2005) suggests the two subtypes may be two different disorders.

Sluggish Cognitive Tempo. Recently, a different cluster of behaviours associated with ADHD has been gaining attention. These behaviours are characterised as sluggish, hypoactive and drowsy and are referred to as the sluggish cognitive tempo (SCT) subtype. SCT is estimated to be present in approximately 30% of children diagnosed with the ADHD-I subtype (Carlson & Mann, 2002). The methods used to measure this construct vary from study to study (Lee, Burns, Snell, & McBurnett, 2013), and to date the validity and utility of the SCT subtype warrants further investigation (Garner, Marceaux, Mrug, Patterson, & Hodgens, 2010; Harrington & Waldman, 2010; Todd, Rasmussen, Wood, Levy, & Hay, 2004). Nevertheless, several recent studies have underlined the significance of SCT as either a subtype of ADHD or as a distinct disorder that is highly associated with ADHD (Barkley, 2013; Capdevila-Brophy et al., 2012; Lee et al., 2013). The emerging interest in SCT and the recent findings add to the current debate around ADHD subtype diagnosis, calling for further research in this area to achieve a more refined classification of the disorder. This is particularly relevant given the recent re-evaluation of the ADHD diagnosis, although the time there was not enough research to substantiate the inclusion of SCT in the diagnostic criteria in the DSM-5.

ADHD and Comorbid Disorders

ADHD rarely occurs in isolation and there is now a well-established literature identifying a range of comorbid psychiatric disorders that frequently present along with ADHD. These include, but are not limited to, oppositional defiant disorder (ODD), conduct disorder (CD), anxiety disorders, depressive disorders and learning disabilities (Biederman, Petty, Dolan, et al., 2008; Daviss, 2008; Fischer et al., 2007; Schatz & Rostain, 2006). This dissertation examined the three most common psychiatric comorbidities observed in children with ADHD: ODD, CD and anxiety disorders.

Reported rates of comorbid disorders range from 24% to 71% and vary across studies and across disorders (Jensen, 2001; Kadesjo & Gillberg, 2001; Kraut et al., 2013; Robison, Sclar, Skaer, & Galin, 1999). The National Institute of Mental Health (NIMH) Multimodal Treatment Study of ADHD (MTA), one of the largest studies conducted to evaluate the effectiveness of different treatment modalities, found that only 31.8% of children with ADHD had no other psychiatric comorbidity and, more importantly, that as many as 24.7% of children received a diagnosis of two other psychiatric disorders in addition to ADHD (Jensen et al., 2001). Disruptive behaviours, as seen in ODD and CD, for example, are easily observed and relatively well documented. Internalizing disorders, on the other hand, such as anxiety, are less evident, attract less attention and are largely underreported (Barbosa, Tannock, & Manassis, 2002; Klein, 2009; Vance et al., 2002). About 50% of children with ADHD meet the criteria for ODD or CD, and between 25% and 33% meet the criteria for anxiety disorders (Jarrett & Ollendick, 2008; Pliszka, 2000).

The presence of comorbid disorders undoubtedly adds to the complexity of the clinical presentation, heightens the degree of impairment, affects the outcome of ADHD, and poses challenges for therapeutic intervention (Biederman, Petty, Dolan, et al., 2008; Lee, Falk, & Aguirre, 2012; Ollendick, Jarrett, Grills-Taquechel, Hovey, & Wolff, 2008; Spencer, Biederman, & Mick, 2007). Given the frequency of comorbid disorders, a new dimension of ADHD subtype categorisation has been suggested, one that takes into account the specific comorbid disorders in the diagnosis (Jensen et al., 2001; Ostrander, Herman, Sikorski, Mascendaro, & Lambert, 2008).

Executive Function and ADHD

The constellation of behavioural and cognitive difficulties observed in children with ADHD has led researchers to infer that ADHD is associated with a primary EF deficit. As a result, while searching for the cognitive phenotype of ADHD, particular attention has been devoted to identifying EF deficits in children, adolescents and adults with ADHD. EF relates to a cognitive process that integrates information from working memory with information about the context in order to select optimal action (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). All too frequently the term has been used as an umbrella term, yet the importance of differentiating the subcomponents that comprise this cognitive domain is becoming increasingly evident. The models and theories that attempt to explain EF from a developmental perspective focus on the domains of working memory, set-shifting and inhibition (Garon, Bryson, & Smith, 2008). The sub-domains of EF most often differentiated in research are that of *planning*, a cognitive process that guides response for successful, goal directed behaviour (Asato, Sweeney, & Luna, 2006), *cognitive flexibility*, a process that allows for selection and coordination of processes for monitoring and adjusting action as needed (Crone, Ridderinkhof, Worm, Somsen, & van der Molen, 2004), *working memory*, a cognitive system that allows individuals to hold and manipulate information for short periods of time for task completion (Leffard et al., 2006), and *inhibition*, which refers to the ability to suppress a response to stimuli (Arnsten, 2006).

Structural and functional brain imaging studies have advanced considerably in the past few years and have shed new light on EF and ADHD. The prefrontal cortex and the fronto-parietal-occipital network have been implicated in skills that require *planning* (Boghi et al., 2006), the dorsolateral region of the prefrontal cortex in *working memory* (Dowker, 2006) and in *task shifting* (Ortuno, Moreno-Iniguez, Millan, Soutullo, & Bonelli, 2006), while the right prefrontal cortex and basal ganglia in skills that require *response inhibition* (Casey et al., 1997).

The brain regions associated with EF task performance have also been found to be implicated in ADHD. Anatomical differences in the prefrontal cortex, caudate nucleus, and cerebellum have been reported in patients with ADHD when compared to those without ADHD (Krain & Castellanos, 2006). Functional neuroimaging studies involving patients with ADHD have shown frontostriatal, mesolimbic, motor-executive, and parietal-temporal circuitries to be associated with such functions as working memory, response inhibition and interference control (Vaidya & Stollstorff, 2008). In children with ADHD, an association was found between performance on attention tasks and prefrontal cortex and basal ganglia, and performance on set-shifting tasks and reversed normal asymmetry. This is consistent with findings that indicate these children demonstrate weakness in EF (Krain & Castellanos, 2006). Hypoactivation of the frontoparietal system was also found in adults with ADHD (Cortese et al., 2012).

Research examining EF and ADHD is extensive and continues to grow. Performance on EF tasks has been compared in affected children and their typically developing peers, and among children with different ADHD subtype diagnoses. Children with ADHD have been found to perform more poorly on EF tasks, and EF impairment appears to be more common in children with ADHD than in typically developing children (Sjowall, Roth, Lindqvist, & Thorell, 2013). However, the strength of the association is unclear. An earlier meta-analytical study of neuropsychological test performance in ADHD reported effect sizes ranging from small to large for tests commonly used to assess EF (Frazier, Demaree, & Youngstrom, 2004). EF deficits were found in the domains of response inhibition and execution, vigilance, working memory, set and task-switching/cognitive flexibility, and planning (Toplak, Bucciarelli, Jain, & Tannock, 2009; Willcutt et al., 2005).

Given the association between EF and ADHD, EF has been proposed as a useful endophenotype for genetic studies of ADHD (Crosbie, Perusse, Barr, & Schachar, 2008; Rommelse, 2008). The search for endophenotypes began when traditional genetic linkage strategies failed to identify genes that are responsible for common but complex psychiatric disorders (Cannon & Keller, 2006). As ADHD is one such disorder, identifying endophenotypes of ADHD is considered important in understanding its aetiology (Doyle et al., 2005). Since the brain areas most affected by EF are now well documented, as is evidence for areas implicated in ADHD, the possibility of using EF deficits as an endophenotype for ADHD is gaining support (Doyle et al., 2005).

Twin studies have yielded further support for EF as a potential endophenotype. Unaffected twin siblings of children with ADHD were found o performe more poorly on a cognitive flexibility task than did typically developing children, a difference which remained significant after controlling for sub-threshold ADHD symptoms (Bidwell, Willcutt, Defries, & Pennington, 2007).

Executive Function Theories of ADHD

Documented deficits in EF performance are a driving force behind the development of many ADHD theories that seek to explain the pathophysiology of the disorder (Castellanos & Tannock, 2002). A number of ADHD models have emerged that incorporate both the disorder's behavioural manifestation and its observed EF deficit. The most recognised model by far is Barkley's (1997) Behavioural Inhibition Model of ADHD, a top down model, in which behavioural inhibition is identified as the central deficiency of ADHD. Barkley argues that weak behavioural inhibition affects the ability to suppress irrelevant responses, to resist interference and to perform complex sequences of responses, resulting in a range of executive impairments (Nigg, 2006). Barkley's model has recently been revised in his newly published book (Barkley, 2012), in which Barkley describes EF as self-regulation and proposes an extended phenotype of EF with multiple levels.

In the Cognitive-Energetic Model, Sergeant (2000) argues that the deficiency in inhibition depends on the energetic state and the efficacy of information processing across three levels: *the process level*, which includes processes such as encoding, search, decision making and motor organization, *the state level*, which includes arousal and activation, and *the management/evaluation level*, which is associated with planning, monitoring error detection and error correction (Livesey, Keen, Rouse, & White, 2006).

Sonuga-Barke (2002) proposed the Dual-Pathway Model, that explains the heterogeneous nature of ADHD by two distinct pathways and an expression of motivational style—specifically, the motivation to either escape or avoid delay (Antrop et al., 2006). According to the Dual-Pathway Model, the two distinct pathways implicated in the disorder are the executive pathway (dysregulation of thought and action) and the reward pathway (Sonuga-Barke, 2002, 2003).

To examine the validity of the EF theory of ADHD, Willcutt et al. (2005) conducted a meta-analysis of EF and ADHD literature. The authors found significant differences between children with and without ADHD on all examined EF tasks with an effect size falling in the medium range. However, the results were not consistent across studies, as most of the studies reviewed found significant differences on inhibition tasks, while group differences in other EF areas were less frequent. Lambek et al. (2011) found that children with ADHD display EF deficits at the group level. At an individual level, however, only a proportion of children in the ADHD group were classified as having EF deficits. Thus, the search for common deficit continues, as researchers attempt to address previous methodological shortcomings that may account for the inconsistencies in the findings. One of the areas that has been examined is the DSM-IV diagnostic classification of ADHD, with expectation that children's performance on EF tasks will differ depending on the diagnostic subtype. Another, possible significant factor is the presence of comorbid disorders.

Executive Function and ADHD Subtypes

Given the observed behavioural differences between the three DSM-IV ADHD subtypes, many investigators have attempted to identify differences in EF performance, not only between typically developing children and children with ADHD, but also between children with different subtype diagnoses. Most studies that address the different subtypes focus on ADHD-C and ADHD-I. A number of studies report no significant difference between ADHD-C and ADHD-I subtypes on most EF tasks (Chhabildas, Pennington, & Willcutt, 2001; Houghton et al., 1999; Nigg, Blaskey, Huang-Pollock, & Rappley, 2002; Riccio, Homack, Jarratt, & Wolfe, 2006), while others have found significant differences between these subtypes (Klorman et al., 1999; Lockwood, Marcotte, & Stern, 2001; O'Driscoll et al., 2005; Schmitz et al., 2002).

Very few studies examine the ADHD-H subtype, possibly because it is relatively rare, compared to the ADHD-C or ADHD-I. There is indication that children with ADHD-H may be less impaired on EF than children with ADHD-C or ADHD-I. Schmitz et al. (2002) compared EF performance across all three ADHD subtypes using measures of cognitive flexibility, inhibition and working memory. Along with finding significant differences between the ADHD-C and ADHD-I subtypes and the control group, the authors also reported significant differences between the ADHD-H and ADHD-I groups on an interference control task and a set-shifting task. The ADHD-H and ADHD-C groups also differed significantly on Digit Span, a verbal working memory task. In all cases, children in the ADHD-H group performed better than children in the other two ADHD groups and did not perform significantly differently from children in the control group. Similarly, Chhabildas et al. (2001) found that children diagnosed with the ADHD-H subtype, as compared to typically developing children, did not show impairment on inhibition or processing speed tasks when symptoms of inattention were controlled, while children with ADHD-C and ADHD-I both performed worse than children with the ADHD-H subtype.

Response Inhibition. Some areas of EF have received more attention while others remain less examined. Not surprisingly, the most studied EF area in ADHD is response inhibition. It is now well established that children with ADHD have response inhibition deficits when compared to their typically developing peers (Alderson, Rapport, & Kofler, 2007; Kieling, Goncalves, Tannock, & Castellanos, 2008; Vaidya & Stollstorff, 2008). Impaired inhibition appears to remain stable throughout development, as hyperactive children were found to perform worse than the control group when tested as adults in follow-up (Fischer, Barkley, Smallish, & Fletcher, 2005). Crosbie et al. (2013) conducted a large population study and found support for validity of response inhibition as an endophenotype for ADHD.

While both children with ADHD-I and ADHD-C have been shown to have a deficit in response inhibition, children with ADHD-I may have a unique deficit in processing environmental cues (Adams et al., 2008). Fillmore, Milich, and

Lorch (2009) also hypothesized that children with ADHD-I have impairment on a different type of inhibition than children with ADHD-C. The authors compared children with ADHD-I, ADHD-C and ADHD-C plus ODD with typically developing children in order to examine reflexive inhibition (which occurs automatically) and intentionally controlled inhibition (which is under the person's control). Reflexive inhibition was found to be substantially impaired in children with ADHD-C and ADHD-C plus ODD, and significantly less impaired in children with ADHD-I with less than four hyperactive symptoms. The three ADHD groups were slower than typically developing children on intentionally controlled inhibition, but no difference was found between the subtypes. As with many studies, it was not specified whether any internalising disorders were present. Furthermore, while children receiving treatment with stimulant medication were asked to not take their medication on the day of assessment, no indication was given as to the number of hours since the last dose was taken or types of medication. The authors conclude that their findings support Barkley's (1997) theory of ADHD (Fillmore et al., 2009). Their findings also suggest that different pathways may entail different degrees of impairment in the two subtypes: the executive function pathway may be a central impairment in children with ADHD-C (substantially delayed, or even absent), while the deficient motivational pathway may be central to those with ADHD-I (impaired, but not absent), thus providing possible support for the Dual Pathway Model (Sonuga-Barke, 2005).

Working Memory. Working memory is another area that has received considerable attention. Martinussen, Hayden, Hogg-Johnson and Tannock (2005) conducted a meta-analysis of studies examining working memory in children with ADHD. The authors found moderate to large working memory impairment in ADHD, particularly in spatial storage and spatial central executive domains. A working memory deficit has also been reported in adults with ADHD (Finke et al., 2011; Marchetta, Hurks, Krabbendam, & Jolles, 2008) and in non-affected twin siblings of children with ADHD (Bidwell et al., 2007). Teacher rated ADHD symptoms were found to be associated with spatial working memory (Oosterlaan, Scheres, & Sergeant, 2005). Girls with ADHD have been found to perform more poorly than the control group on both digit span forward and digit span backward tasks. However when comorbidities and other variables were controlled, only the digit span forward task remained significant (Hinshaw, Carte, Fan, Jassy, & Owens, 2007). In boys with ADHD, a significant difference was found between ADHD-I and typically developing boys on the digit span backward task, but no similar difference was found between ADHD-C boys and typically developing boys, or between ADHD-C and ADHD-I boys (Pasini, Paloscia, Alessandrelli, Porfirio, & Curatolo, 2007). In a recent study, both children with ADHD-I and ADHD-C were found to perform significantly worse than healthy controls on a working memory task (Skogli, Egeland, Andersen, Hovik, & Oie, 2013).

On a visual working memory task, Geurts et al. (2005) found no differences between non-ADHD boys and boys with ADHD, irrespective of subtype, but the authors did report significant group differences on a visuo-spatial short term memory task; boys with ADHD-C were more impaired than boys with ADHD-I. Wahlstedt, Thorell, and Bohlin (2009) found that inattentive symptoms and not hyperactive symptoms were associated with the spatial working memory deficit. In contrast, a longitudinal study by Brocki, Nyberg, Thorell and Bohlin, (2007) found no significant relationship between working memory and symptoms of ADHD. This study differed from others in that the children included in the study were much younger (five years of age at the first assessment and seven at the second) than those in other studies. An earlier study conducted with preschoolers also reported no association between ADHD and working memory, but did report a strong association between inhibition and ADHD, and between working memory and inhibition prior to controlling for age and IQ (Sonuga-Barke, Dalen, Daley, & Remington, 2002). Brocki et al. (2007) suggest that their findings support Barkley's theory, and that inhibition is a central deficit in ADHD that triggers other, more complex EF deficits that emerge at an older age.

A study of EF performance in adolescents with and without ADHD found that adolescents with ADHD performed worse on all EF tasks, including working memory, compared to their non affected peers, and irrespective of gender (Toplak et al., 2009). The differences found between findings among adolescents and preschoolers could be explained by delays in working memory occurring during the elementary school age years. As working memory continues to develop rapidly during the preschool years (Garon et al., 2008), it is possible that in children with ADHD a maturation delay in working memory is occurring during this critical time, resulting in greater differences in working memory between individuals with ADHD and their typically developing peers later in childhood, subsequently also in adolescence and adulthood. Differences in findings between age groups highlight the need for further longitudinal investigations to map the development of working memory and its relation to attention and inhibition in children.

Cognitive flexibility. The relationship between set-shifting or cognitive flexibility and ADHD is particularly unclear, and meta-analytical reviews have reported lower effect sizes (Frazier et al., 2004; Willcutt et al., 2005). For example, Bidwell et al. (2007) found that children with ADHD performed significantly worse than typically developing children on cognitive flexibility/set-shifting as measured by the Trail Making Test, but not by the Wisconsin Card Sorting Test (WCST). Pasini et al. (2007) compared boys with ADHD with non-ADHD boys on WCST and also found no significant differences in performance, while Solanto et al. (2007) reported worse performance on WCST with regard to the number of solved categories and number of total errors for the ADHD-C subtype as compared to the ADHD-I subtype and the control group. The two studies however had different designs. The population in the first study consisted of boys only, while the second study included both boys and girls. An additional limitation was the gender distribution between the ADHD and comparison groups in the later, with 65% of the ADHD-C group being boys, while only 40% of the comparison group were boys. Furthermore, the first study excluded children with comorbid disorders other than ODD, while in the second study, 19% of the

ADHD-I group and 6% of the ADHD-C group had comorbid anxiety, another possible confounding factor.

In contrast to Bidwell et al, Wodka et al. (2008) found no significant group differences on Trail Making test, but found that children with ADHD performed more poorly on the Color-Word Switching task, and when subtypes were compared, children with ADHD-I performed significantly worse than those with ADHD-C. Nigg et al. (2002) also did not find significant difference between ADHD and typical controls or between ADHD-C and ADHD-I on the set-shifting aspect of the Trail Making test (part B). However, they did find that when IQ was covaried, ADHD-I children were more impaired than ADHD-C children on a simple output aspect of the test (Trail Making A). Children with ADHD-I were also reported to have performed more poorly than healthy controls on the Trail Making test in a more recent study, and this finding did not change after the authors covaried for IQ (Skogli et al., 2013). This study found no significant difference between children with ADHD-C and healthy controls.

Planning. A deficits in planning ability have also been documented in children with ADHD (Barnett, Maruff, & Vance, 2009; Oosterlaan et al., 2005; Wodka et al., 2008). Nig et al. (2002) found that children in the ADHD-C group were significantly impaired on the planning task, as opposed to those in the ADHD-I group. However, ADHD-C and ADHD-I groups did not significantly differ from each other. Geurts et al. (2005) examined the neuropsychological profiles of the ADHD subtypes as compared with typically developing children. The participants were children 6-13 years of age, 16 children diagnosed with

ADHD-I, 16 with the ADHD-C subtypes and control group of 16 children without ADHD diagnosis, all matched for age, IQ and comorbid profile. Both the ADHD and the typically developing groups underwent careful selection, including ADHD, disruptive behaviour and autism diagnostic measures. The authors found no group differences on most EF measures used, including the planning task. Similarly, Skogli et al. (2013) found no differences between ADHD-C, ADHD-I and healthy control groups.

Executive Function and Sluggish Cognitive Tempo

While very few studies have examined SCT and EF, due to a growing interest in SCT several studies have been published in the past few years. Wahlstedt and Bohlin (Wahlstedt & Bohlin, 2010) found ADHD-I to be associated with EF deficits while finding SCT to be associated with sustained attention. In contrast, Hinshaw (2007) found no difference between the two subtypes. Using only a parent ratings of EF, Barkley (2013) compared three clinical groups of children against a typically developing group—children with SCT, children with ADHD and those with a combination of SCT and ADHD—and found all three clinical groups to be impaired, but children with SCT to be the least impaired. Again, using a rating form to assess EF, Capdevila-Brophy et al. (2012) compared two groups of children, one group with SCT and primarily inattentive symptoms and another group with low SCT symptoms, but both inattentive and hyperactive symptoms. Children in the high SCT group obtained scores in the clinical range on Working Memory, Plan/Organisation, Self-Monitoring and Metacognition scales of the EF rating inventory, while children in the low SCT group showed clinical impairment only on the Working Memory scale. Bauermeister, Barkley, Bauermeister, Martinez, & McBurnett (2012) used the four items from CBCL to construct the SCT scale, and a neuropsychological battery to assess EF. The authors found no association between working memory and SCT or hyperactivity, and inattention symptoms explained most of the variance in working memory scale. Similarly, no association was found between interference control and SCT or hyperactivity, nor was one found between planning/problem solving and SCT or hyperactivity. In both cases inattention symptoms were associated with interference control and planning/problem solving in this study. Wahlstedt and Bohlin (2010), also using a neuropsychological battery, found SCT to be independently related to sustained attention while inattention was related to working memory, reaction time variability and inhibitory control.

Executive Function and ADHD with Comorbid Disorders

EF deficits are not specific to ADHD, but are also found in other psychiatric conditions. The presence of comorbid psychiatric disorders often amplifies the clinical presentation of ADHD, and thus may also play a role in the severity or type of EF deficit. Surprisingly, studies examining and taking into consideration comorbid disorders in EF and ADHD are limited in number and report inconsistent findings (Biederman et al., 2004; Doyle, 2006).

Anxiety disorders. Several studies have reported an association between EF and internalising symptoms (Chang, McCracken, & Piacentini, 2007; Emerson, Mollet, & Harrison, 2005; Spitznagel & Suhr, 2002). Deficits in attention and reaction time have been reported in adults and children with anxiety disorders or depression (Dozois & Dobson, 2001). Obsessive Compulsive Disorder (OCD) has been found to be associated with deficits in set-shifting/cognitive flexibility and impulsivity (Chamberlain et al., 2007; Shin et al., 2008). From a neurobiological perspective, a frontal lobe function deficit has been reported for boys who are anxious or depressed, as assessed by sequencing and problem solving tasks (Emerson et al., 2005). These findings suggest that children with ADHD and anxiety may have a different EF profile than do children with ADHD only.

Using parent and teacher rating scales of the Behavioural Assessment System for Children, but without subdividing children into specific comorbid groups, Jonsdottir, Bouma, Sergeant and Scherder (2006) investigated EF performance in clinical and non-clinical groups. In this study, 43 clinic-referred, elementary school-age children, diagnosed with ADHD, were compared to 115 control participants using measures of planning and verbal working memory. An ADHD diagnosis was determined by a clinical interview conducted prior to referral to the study, while comorbid symptoms were assessed using parent and teacher questionnaires. The authors reported poorer performance in the clinical group on working memory, planning task and visual attention tasks, and found a significant relationship between teacher rated inattention symptoms and planning test performance. With respect to comorbidities, a negative relationship was found between teacher rated atypical and depression symptoms and planning test performance, and teacher rated anxiety symptoms and visual attention test

(Jonsdottir et al., 2006). In a different study, performance on working memory tasks was compared between children with anxiety, children with ADHD, children with ADHD plus anxiety and a control group (Manassis, Tannock, Young, & Francis-John, 2007). Contrary to what the authors had predicted, children with the dual diagnosis displayed a similar impairment to children with ADHD only. It is important to note that in this study children with OCD or Post Traumatic Stress Disorder (PTSD) were excluded from the anxiety group.

In a study of inhibition in children with anxiety and ADHD, Korenblum, Chen, Manassis and Schachar (2007) compared children with generalised anxiety disorder and separation anxiety disorder, ADHD, ADHD with anxiety, and a comparison group on a stop signal inhibition task. All three clinical groups were found to perform worse than the comparison group on the inhibition task. However, when ADHD symptoms were controlled by identifying sub-threshold ADHD symptoms in the anxiety group, the significant difference was no longer present, leading the authors to conclude that the significant difference was driven by the sub-threshold ADHD symptoms. While this explanation may be valid, one should consider symptom overlaps between generalized anxiety disorder and ADHD, such as restlessness and difficulty concentrating. If children with these symptoms were considered as having sub-threshold ADHD, then it is possible that the anxiety subgroup without these symptoms represented a subgroup with a milder form of generalized anxiety. Manassis et al. (2007) suggested that even when no differences found, anxiety may still have a negative effect on working memory; however, that effect could be dependent on context (i.e. an anxiety inducing setting).

ODD/CD. Studies comparing children with CD with typically developing peers suggest that CD may have an effect on EF (Toupin, Dery, Pauze, Mercier, & Fortin, 2000). In the ADHD literature, however, the presence of comorbid ODD or CD does not seem to affect EF performance, as several studies found no differences between children with ADHD plus comorbid ODD or CD and children with ODD or CD alone, nor did they find any differences between children with ADHD plus comorbid CD or ODD and ADHD alone (Kalff et al., 2002).

Oosterlaan, Scheres and Sergeant (2005) found that EF deficits, as measured by working memory and planning tasks, were associated with ADHD but not with ODD or CD, as teacher ratings of ADHD predicted performance on working memory tasks, and parent and teacher ratings of ADHD predicted performance on planning tasks. In this study children who met the diagnostic criteria for ADHD obtained lower scores on these tasks than those without ADHD. Moreover, high parent ODD/CD ratings were associated with fewer errors on the planning task. These findings should be interpreted with caution as the study has several limitations. The authors used parent and teacher questionnaires to identify ADHD, ODD and CD, and did not report the presence of any other comorbid disorders. Also, the control group differed from the clinical group as it included a significantly higher number of girls and children with significantly higher IQ. In contrast, Rhodes et al. (2012) found that children with ADHD or ODD, and children with both ADHD and ODD, performed worse on working memory tasks than typically developing children. In teens with disruptive behavioural disorders, the presence of comorbid ADHD determined worse performance on EF tasks (Hummer et al., 2011).

Fischer et al. (2005) found that adults with ADHD and CD made more perseverative errors on a set-shifting task than adults with ADHD only. Similarly, Pajer et al. (2008) compared adolescent girls with CD to peers without CD on a number of EF tasks, such as working memory, interference control and set-shifting. Girls with CD performed worse on the set-shifting task only. Such findings support the notion that EF deficits may be more pronounced in adolescence and adulthood, underlining the role of development and brain maturation in EF, particularly in the clinical population.

Comorbid disorders have also been considered in the attempt to identify ADHD endophenotypes. In a recent study Rommelse et al. (2009) examined comorbid disorders and inhibition, cognitive flexibility, visuo-spatial working memory and verbal working memory in children diagnosed with ADHD and their non-affected siblings. The authors identified an EF endophenotype by deriving one major component through factor analysis of all EF measures used in the study. The EF endophenotype accounted for 59% of task variance, and was found to be associated with comorbid autistic traits, motor problems and reading problems, but not with ODD or anxiety disorders. While they do recognise the limitations of their study, particularly the use of questionnaires to identify comorbid disorders, the authors suggest that there is no need to define new

ADHD subtypes based on the presence of comorbid disorders (Rommelse et al., 2009).

Sex differences

As mentioned earlier, ADHD is more common in boys than girls (Cuffe, Moore, & McKeown, 2005). Sex differences have been reported in the phenotypic expression of the disorder, for instance, in lower levels of disruptive behaviour and higher levels of inattentive symptoms in girls (Stefanatos & Baron, 2007). In a recent meta-analytical study, Willcutt (2012) reported that females were more likely than males to meet the criteria for ADHD-I, and that males were more likely to meet the criteria for ADHD-C. These findings were true throughout development (Willcutt, 2012). One study that examined children with ADHD found that girls were more than twice as likely to be diagnosed with ADHD-I than boys (Biederman et al., 2002).

Patterns of comorbid disorders have also been found to differ between boys and girls. For example, girls with ADHD were found to be at a lower risk for major depression and behavioural disorders, but at a higher risk for substance use (Biederman et al., 2002). Anxiety disorders have been found to be more likely in girls with ADHD-I than boys with ADHD-I (Bauermeister et al., 2007). Overall, girls with ADHD have been found to have more internalising problems than do boys with ADHD (Gershon, 2002) and boys have more externalizing symptoms than do girls (Levy, 2004).

On attention measures such as CPT, girls were reported to be significantly less impulsive than boys (Newcorn et al., 2001). Girls with ADHD generally show less impairment compared with girls without ADHD, than do boys with ADHD when compared with boys without ADHD (Hasson & Fine, 2012). Others have found girls to have slower reaction times, and to make more omission errors on CPT (Brocki & Bohlin, 2004).

Sex differences have also been observed in neurocognitive performance, however, the findings are inconsistent and many studies suggest that girls and boys develop EF in a similar manner (Anderson, 2002). Nevertheless, females have been found to perform better on certain memory tasks and attention tasks (Gur et al., 2012), yet boys have been found to outperform females on short-term memory task and working memory tasks (De Luca et al., 2003). Among children with ADHD, no gender differences have been found and both girls and boys have been found to be more impaired than typically developing children (Seidman et al., 2005).

Conclusion

Thus, the role of EF in ADHD continues to be unclear. What are the areas of deficit? What clinical, environmental and genetic factors contribute to EF deficits? Does EF performance differentiate between children with ADHD subtypes, or children with comorbid disorders? Driven by findings from neurobiological and genetic studies, the heterogeneous nature of ADHD is receiving more and more attention and the advances in the field are promising. Clinicians and researchers are recognizing the multiple factors that may play a role in the development and expression of the disorder and that may affect the course of the disorder and treatment outcomes.

To date, research findings are insufficient to identify a specific profile of EF in children with ADHD, with or without comorbid disorders. While it appears that CD and ODD in conjunction with ADHD do not affect EF performance, the role of internalizing disorders is largely understudied. Similarly, the relationship between ADHD subtypes and EF also remains unclear.

Methodological differences between studies pose a considerable challenge when reviewing ADHD literature, including those examining EF. Studies differ with respect to the measures used to assess different areas of EF, to diagnose ADHD and comorbid disorders and to categorize and define ADHD subtypes. Studies vary with regard to the length of time prior to assessment that they require participants to discontinue taking psychostimulants or other medications commonly used to treat ADHD symptoms and which have the potential to affect EF task performance. Potential effects of confounding factors such as gender and age are often neglected.

Current Research Objectives

This dissertation aims to indentify a clinical sub-profile of ADHD based on subtypes, comorbid disorders and EF performance in order to better understand the deficits associated with ADHD and help to guide future interventions with children with ADHD. To do so a large sample of children clinically diagnosed with ADHD was examined. The first manuscript examines ADHD subtypes and EF. First, the three DSM-IV subtypes are examined, then an additional subtype, SCT, is derived. The goal is to examine the ADHD subtypes that have been identified in the literature as clinically pertinent in a relatively large sample of children who have undergone a thorough diagnosis for ADHD.

The second manuscript examines the role of comorbid disorders on EF task performance. Given the impact comorbid disorders have on clinical presentation of ADHD, the goal of the second manuscript was to understand whether their presence also affects the EF performance, adding to the impairment. One of the overall goals of the dissertation is to address some of the methodological concerns frequently encountered in the literature such as small sample size, unclear inclusion criteria with respect to diagnosis. Thus this study included a relatively large sample size, children who have undergone thorough diagnostic assessment prior to referral to the study and thorough assessment of comorbid disorders, and a standardised EF assessment procedure that included a multi-day medication wash-out period for children previously receiving pharmacological treatment.

CHAPTER 2

MANUSCRIPT 1

Attention Deficit Hyperactivity Disorder and Executive Function: Beyond the DSM-IV Subtypes

Running title: Executive function and ADHD subtypes

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Abstract

Background: Understanding the relationship between ADHD and executive function (EF) continues to be pertinent for both research and clinical practice. The objective of this study was to examine the profile of EF performance in children diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) as a function of their DSM-IV and Sluggish Cognitive Tempo (SCT) subtypes. **Methods**: Three hundred and sixty three 6-12 year old children clinically diagnosed with ADHD were characterised according to their clinical profile. The EF domains were assessed using the Conners' Continuous Performance Test (CPT), Wisconsin Card Sorting Test (WCST), Tower of London (ToL), and Self Ordered Pointing Test (SOPT). **Results**: The majority (52.6%) of children were diagnosed with the combined subtype, 16.3% with SCT, 18.2% with inattentive subtype/sub-threshold hyperactivity, and 12.9% with the hyperactive subtype. The CPT, SOPT and WCST were correlated with ADHD symptoms. A significant difference was found between the DSM-IV subtypes on measures of attention, reaction time and set shifting and between the SCT and other subtypes on the CPT. However, the results were no longer significant after controlling for age. **Conclusion**: These results indicate that age plays a key role in EF performance in children diagnosed with ADHD. Further investigation of other cognitive domains from a developmental perspective is needed to better understand the clinical profile associated with ADHD. **Keywords**: Attention Deficit Hyperactivity Disorder, ADHD subtypes, Executive Function, Sluggish Cognitive Tempo, Wisconsin Card Sorting Test, Conners' Continuous Performance Test, Tower of London, Self Ordered Pointing Test.

Introduction

Attention Deficit Hyperactivity Disorder (ADHD), the most common psychiatric disorder of childhood, is characterised by persistent and pervasive inattention, overactivity and impulsiveness and is a major risk factor for educational failure, delinquency, drug abuse and several other negative psycho-social outcomes (Dopheide & Pliszka, 2009). Currently, DSM-IV (American Psychiatric Association, 1994) identifies three distinct ADHD subtypes: predominantly inattentive (ADHD-I), predominantly hyperactive/impulsive (ADHD-H) and ADHD combined (ADHD-C) subtypes. The ADHD-H subtype is relatively rare and is associated with younger age at the time of the diagnosis. The ADHD-C subtype is more common in the clinical population, while the ADHD-I subtype is more common in the community sample and children with this subtype diagnosis are more likely to be girls or to be older then children with ADHD-H or ADHD-C (Baeyens et al., 2006; Woo & Rey, 2005).

From a diagnostic perspective there is much debate as to the reliability and validity of ADHD subtypes (Hinshaw, 2001; Woo & Rey, 2005). The diagnosis of subtypes has been found to be unstable across time, particularly the ADHD-H subtype, and is frequently dependant on the informant, possibly due to cross-situational differences of behaviour (Lahey et al., 2005; Valo & Tannock, 2010; Woo & Rey, 2005).

A new different ADHD subtype has recently been gaining attention: the sluggish cognitive tempo (SCT) subtype (Capdevila-Brophy et al., 2012; S. Lee et al., 2013; Watabe, Owens, Evans, & Brandt, 2013). SCT represents a cluster of behaviours characterized as sluggish, hypoactive and drowsy, symptoms that are estimated to be present in about 30% of children diagnosed with the ADHD inattentive subtype. It has therefore been suggested that these symptoms be included in the diagnostic criteria for ADHD (Carlson & Mann, 2002). To date, the validity and utility of the SCT construct is still being investigated (Garner et al., 2010; Garner, Mrug, Hodgens, & Patterson, 2013; Harrington & Waldman, 2010; Todd et al., 2004). More evidence is emerging that suggests SCT is a distinct subtype. It has been associated with lower academic and social functioning independent of inattentive or hyperactive symptoms, and with a higher prevalence of internalising symptoms (Lee et al., 2013). In the psychiatric clinical population SCT has been found to be statistically distinct from other psychopathology (Becker, Luebbe, Fite, Stoppelbein, & Greening, 2014). Further research is needed to understand this construct.

Over the last decade, many studies have begun to dissect the cognitive phenotypes associated with ADHD and its subtypes (Geurts et al., 2005). One of the most consistently reported cognitive deficits in ADHD is that of Executive Function (EF). EF embodies cognitive processes (working memory, planning, inhibition) that allow the integration of contextual information in order to select optimal action (Willcutt et al., 2005). EF in children diagnosed with ADHD has been widely studied, yet the relationship between ADHD subtypes and EF performance continues to be unclear, largely due to inconsistent results across studies (Willcutt et al., 2005). While a number of studies report no significant difference between ADHD-C and ADHD-I subtypes on most EF tasks (Chhabildas et al., 2001; Houghton et al., 1999; Nigg et al., 2002; Riccio et al., 2006), several report significant differences between these subtypes (Klorman et al., 1999; Lockwood et al., 2001; O'Driscoll et al., 2005; Schmitz et al., 2002). It is noteworthy that there are very few studies comparing all three ADHD subtypes. Even less is known about the EF profile of the SCT subtype.

Lockwood, Marcotte and Stern (2001) attempted to differentiate ADHD-I and ADHD-C subtypes according to their neuropsychological profiles and found that the neuropsychological tasks chosen in their study discriminated between the two subtypes with 80% accuracy. O'Brien, Dowell, Mostofsky, Denckla, and Mahone (2010) reported no significant differences between ADHD-I and ADHD-H subtypes on EF task performance. Geurts, Verte, Oosterlaan, Roeyers, and Sergeant (2005) found no significant differences between the ADHD-I and ADHD-C subtypes on any of the EF measures. However, they found that children with ADHD-C made more mistakes on a visual short term memory task compared to children with ADHD-I. This study, however, included only 16 participants in each group and, as is often the case, no children with ADHD-H were included. In a similar study, Nigg et al. (2002) found that ADHD-C and ADHD-I subtypes shared a deficit in response speed and vigilance, but not in planning. Both the ADHD-C and ADHD-I groups showed deficits on behavioural inhibition measures as compared to typically developing children, and when subtypes were compared, ADHD-C boys were slower than ADHD-I boys. In addition, on a set-shifting task the ADHD-I group showed a deficit as compared to typically developing children, and differed significantly from the ADHD-C group when IQ was co-varied (Nigg et al., 2002). Finally, Riccio et al. (2006) examined differences in performance between the two subtypes on five EF measures and found that the only significant difference between subtypes was in interference control when boys were analysed separately. Here, ADHD-I boys again performed worse than boys with ADHD-C subtype.

Of the few published studies that examine all three DSM-IV subtypes to date, Schmitz et al. (2002) compared EF performance across ADHD subtypes using measures of cognitive flexibility, inhibition and working memory. The authors found that on a measure of cognitive flexibility, children with ADHD-C received significantly lower scores than children with either ADHD-I or ADHD-H. They reported that the ADHD-H group performed better than the other two ADHD groups, and did not differ significantly from typically developing children. Similarly, Chhabildas, Pennington and Willcutt (2001) found that children diagnosed with the ADHD-H subtype, as compared to typically developing children, did not show impairment on tasks of inhibition or processing speed when symptoms of inattention were controlled. On the other hand, children with either the ADHD-C or ADHD-I subtype performed worse on processing speed task as compared to children with the ADHD-H subtype.

The relationship between the SCT and EF is not well investigated. In one recent study Wahlstedt and Bohlin (2010) examined inhibitory control, sustained attention, reaction time variability and working memory and found that SCT was related to sustained attention independent of DSM-IV inattention. Hinshaw et al. (2002) examined girls with SCT and found that the neuropsychological battery used in the study did not classify girls with SCT well. Adults with SCT have been found to report greater EF difficulties on an EF rating scale (Barkley, 2012).

Understanding EF variability in performance will bring researchers closer to identifying a potential endophenotype or multiple endophenotypes of ADHD (Doyle et al., 2005), which in turn can help to disentangle the heterogeneity of this complex syndrome. This task could be better achieved when all three DSM-IV ADHD subtypes, as well as SCT, are examined with regard to their EF. In the present study, we first compared EF performance across all three DSM-IV ADHD subtype groups in a relatively large sample of children clinically diagnosed with ADHD. We then examined the subtypes, including the SCT subtype. It was hypothesized that children with different ADHD subtypes will present distinct deficits of EF.

Methods

Participants

Children diagnosed with ADHD and referred to the ADHD clinic or Severe Disruptive Behaviour Disorder Day Treatment program at a large urban mental health institute were recruited sequentially for the study as part of an ongoing Clinical and Pharmacogenetic Study of ADHD. Participants fulfilling the inclusion criteria were all referred to the research team by their primary treating psychiatrists, paediatricians or family physicians. Children were excluded from the study if they met DSM-IV criteria for psychosis, pervasive developmental disorder, Gilles de la Tourette's syndrome, seizure disorders, had a major medical condition or had an IQ less than 70 as measured by the Wechsler Intelligence Scale for Children, 3^{rd} or 4^{th} edition (WISC: Wechsler, 1991). Data collection for this study began in 1999, at which time only the 3^{rd} edition of the WISC was available. WISC-III continued to be used until the 4^{th} edition was published. For this study the WISC measure was used for inclusion/exclusion criteria, and as a general description of the population. The Median for WISC-III Full scale IQ was 97, while for WISC-IV was 96. Given this the results for two IQ measures were combined for descriptive purpose. The final sample for this manuscript consisted of 363 children, ranging in age from 6 to 12, with a mean age of 8.96 (SD=1.81).

Study Procedure

All children included in the study underwent clinical assessment by team psychiatrists. This step was taken in order to standardise the diagnostic procedure and insure rigorous assessment of the participants. Children entered the study once the diagnosis was confirmed. All primary caregivers were interviewed and completed questionnaires while their children completed a neuropsychological battery. Each primary caregiver (hereafter referred to as "parent") was interviewed by a trained research assistant using *The National Institutes of Mental Health Diagnostic Interview Schedule for Children, 4th edition* (DISC-IV: Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). The DISC-IV is a highly structured DSM-IV diagnostic interview that assesses the most common mental disorders in children and adolescents and takes into account the severity, frequency and clinical significance of symptoms.

The participant's diagnostic subtype was determined based on the DISC-IV interview results. The concurrent validity of the ADHD module of this structured interview has been found to be acceptable (McGrath, Handwerk, Armstrong, Lucas, & Friman, 2004). The DISC-IV interview allows for three ADHD subtype classifications: hyperactive (ADHD-H), inattentive (ADHD-I) and combined (ADHD-C). Classification into one of these three types is based on the number of reported symptoms, their occurrence in more than one setting and their significant interference with the child's functioning. Only those participants who completed the core neuropsychological tests were included in this analysis. This resulted in a final sample of 363 children, including 284 boys and 79 girls. Forty-seven children were classified as ADHD-H, 125 as ADHD-I, and 191 as ADHD-C.

SCT was defined by identifying children with ADHD-I without sub-threshold hyperactive symptoms (four or less symptoms according to DISC-IV) who "often" exhibited one of the following symptoms: day dreaming, being confused or in a fog, overtired, underactive or staring blankly, as measured by the Child Behaviour Checklist (Achenbach, 1991). As a result, out of a total of 125 children were given the ADHD-I diagnosis, 59 children were classified with the SCT subtype and 66 children were classified with sub-threshold hyperactivity (ADHD-I/subH).

Executive Function Assessment

A neuropsychological battery specially developed for use with children was administered when participants were not receiving any pharmacological treatment for ADHD symptoms. Children who were taking medication at the time underwent a five to seven day medication washout period prior to completing the neuropsychological assessment. All tests were administered in the morning by trained research assistants. The following tests were used to assess EF: Conners' Continuous Performance Test (CPT), the Wisconsin Card Sorting Test (WCST), the Tower of London (ToL), and the Self Ordered Pointing Test (SOPT).

Conners' Continuous Performance Test (CPT). The CPT is one of the most widely used computerized tests of attention (Conners, Epstein, Angold, & Klaric, 2003). It is a 14 minute, computerised task during which participants are presented with a black screen and letters that randomly appear in the middle of the screen. Participants are asked to press the space bar as soon as they see a letter, but to refrain from pressing the space bar if the letter that appears is an “X.” The letters are shown for 250 milliseconds. The task is divided into six different time blocks. The length of time between the appearance of the letters varies from block to block. CPT is used to measure attention, response inhibition and executive control (Homack & Riccio, 2006; Riccio et al., 2006). The *T* scores for the following variables were used for the analysis: the number of omissions, the number of commissions, hit reaction time (RT), hit reaction time standard error, hit RT block change and hit RT inter-stimulus interval (ISI).

Wisconsin Card Sorting Test (WCST). The WCST is a set-shifting task and is among the most widely used EF tasks in both clinical and applied research (Heaton, Chelune, Talley, Kay, & Curtiss, 1993). Participants completed a computerized version of the WCST, in which they were shown a card and asked to match it to one of four stimulus cards that differ from each other in shape, colour and number. The children were not given any rules or categories according to which they should match the card, but after matching the card, they were told if their choice was correct or incorrect. The matching rule was changed after the child successfully matched 10 consecutive cards. Standard scores for the following variables were used in the analysis: Perseverative Errors, Perseverative Responses, and Non-Perseverative Errors. A raw score for the Number of Categories Completed was also used.

Tower of London (ToL). The ToL is a planning task based on the Tower of Hanoi and consists of three poles with three different heights and three balls—one red, one blue and one green arranged on the poles in starting pattern. The participant is presented with pictures of the balls arranged on the poles in different patterns, one at a time, and is instructed to match the presented pattern by moving the balls on the poles, while following a set of rules. There are several administration versions of ToL. The ToL administration version and the normative tables used in this study were adopted from Anderson, Anderson and Lajoie (1996). For the analysis, the standard score was used that incorporates the time taken by the child to solve each problem.

Self Ordered Pointing Test (SOPT). The SOPT is primarily a measure of planning and monitoring aspects of working memory (Petrides & Milner, 1982). In this task, the participant is presented with a page that displays a set of pictures and is asked to choose a picture. The page is then turned. The same pictures are presented again, but in a different arrangement. The child is then asked to pick a different picture than before. The test consists of sets of 6, 8, 10 and 12 pictures and the selection task is repeated three times for each set. If the child points to the same picture more than once on one trial, an error is recorded. The total number of errors across all trials and sets was calculated (raw score) and used for this analysis.

Statistical Analysis

Continuous variables were expressed as means ± standard deviation (SD). Categorical variables were expressed as proportions (%). Chi Square analysis was used to compare proportions between groups. Pearson Correlation analysis was used to determine correlation between continuous variables. SPSS General Linear Model (GLM) univariate and multivariate analysis of variance (MANOVA) were used to examine the effect of multiple fixed factors and control for confounding variables, such as participant age. For Post-Hoc procedures, to control for Type I error, SPSS Bonferroni correction was employed, resulting in a conservative approach (Field, 2005). The observed power for the statistically significant results ranged from .67 to 1.0.

Results

The majority of children were classified with the ADHD-C subtype (52.6%; N = 191), 34.4% (N = 125) of children with the ADHD-I subtype and 12.9% (N = 47) with the ADHD-H subtype. Table 1 presents the gender distribution within the respective subtypes. A significant association was found between subtypes and gender (χ^2 (2, 283) = 7.69, p = .021, Cramer's V =.146), with females being more represented in the ADHD-I subtype. The mean (M) age for this sample was 8.96 years, SD =1.81. The diagnostic groups were significantly different with regard to age (F = 15.81, p = .009, η_p^2 = .07, Power = .998). Specifically, a significant difference was observed between all three ADHD subtypes, with children in the ADHD-H group being the youngest and those in the ADHD-I group being the oldest (Table 1). Groups did not differ significantly with respect to verbal, performance or full scale IQ (Table 1).

ADHD Symptoms and Executive Function

Prior to comparing children in the different ADHD subtype groups, the relationship between ADHD symptoms and EF performance was explored using Pearson correlation analysis with number of hyperactive, inattentive and total ADHD symptoms. As seen in Table 2, the number of hyperactive symptoms was positively correlated with CPT omission errors (r^2 = .033, p = .001), RT (r^2 = .019, p = .009), RT standard error (r^2 = .052, p < .001), RT block change (r^2 = .011, p = .048), RT ISI (r^2 = .03, p = .001), and number of errors on SOPT (r^2 = .012, p = .041). The number of inattentive symptoms was negatively correlated with CPT RT standard error (r^2 =.015, *p* = .021) and positively correlated with WCST Non-Perseverative errors (r^2 = .014, *p* = .036). The number of completed categories on WCST was positively correlated with the number of inattentive symptoms (r^2 = .018, *p* = .015) and negatively correlated with the number of hyperactive symptoms (r^2 = .015, *p* = .031).

ADHD Subtypes and Executive Function Performance

EF measures that assess different domains were analyzed separately (Table 3; Table 4). First, the relationship between ADHD subtypes and the CPT was examined without controlling for any potential confounding factors. A significant multivariate main effect of DSM-IV subtypes was observed (*F* = 1.85, *p* = .038, η_p^2 = .031, Power = .9). The examination of between-subject factors revealed that children with ADHD-I performed better than children with ADHD-C on omission errors (*F* = 4.82, *p* = .009, η_p^2 = .027) and RT ISI (*F* = 4.48, *p* = .012, η_p^2 = .025), and better than both children with ADHD-C and ADHD-H on RT standard error (*F* = 7.89, *p* < .001, η_p^2 = .043). However, when age was controlled, a main effect of age was observed (*F* = 12.19, *p* < .001, η_p^2 = .174, Power = 1.0) and the effect of the subtypes was no longer significant (*F* = .963, *p* = .483).

Since SOPT has not been not normed for this population, the data was analyzed using age and gender as covariates. Only age showed a significant main effect (*F* = 54.97, *p* < .001, η_p^2 = .131, Power = 1.0) the subtypes was not significant (*F* = .051, *p* = .95).

Four WCST variables were examined for this analysis. These were Perseverative Errors, Perseverative Responses, Non-Perseverative Errors and Number of Categories Completed (*F* = 1.93, *p* = .053, η_p^2 = .024, Power = .8). A significant group difference was observed in Number of Categories Completed (F = 5.07, p = .007,η_p^2 = .031), where children with ADHD-I performed better than children with ADHD-C and ADHD-H. However, this difference was no longer significant after age and gender were co-varied. A significant main effect of age was observed (F = 14.51, p < .001, η_p^2 = .160, Power = 1.0). The results of the ToL indicated no significant group differences (F = 2.16, p = .116). Again, a significant main effect of age was observed when age and gender were covaried (F = 5.93, p = .015, η_p^2 = .019, Power = .680).

The SCT Subtype

Finally, the ADHD-I subtype was subdivided into ADHD-I/subH (18.2%) and SCT (16.3%) subtypes. The data were analysed again using all four subtypes: SCT, ADHD-I/subH, ADHD-C and ADHD-H. When all four groups were compared, children in the SCT group were found to be older than children with ADHD-H or ADHD-C (F = 12.12, p < .001, η_p^2 = .031, Power = .502) and a trend was observed between SCT and ADHD-I/subH group (F = 3.92, p = .050, η_p^2 = .031, Power = .502). No significant difference was found between the SCT and ADHD-I/subH subtypes with respect to gender (χ^2 (1, 125) = .991, p = .320) overall IQ performance (F = .084, p = .772) or to previous treatment for ADHD symptoms (χ^2 (1, 116) = .058, p = .810).

The relationship between EF measures and the four subtypes was analyzed. A significant multivariate effect of the subtype was observed for the CPT (F = 1.62, p = .048, η_p^2 = .027). An examination of the univariate analysis revealed that children with SCT performed significantly better then children with ADHD-C with respect to the number of omission errors (F = 3.39, p = .018, η_p^2 = .028) and RT ISI change (F = 3.75, *p* = .011, η_p^2 = .031). On RT standard error, children with SCT performed better than children with ADHD-C and ADHD-H (*F* = 6.335, *p* < .000, η_p^2 = .051). The analysis was repeated, controlling for age and gender. The subtype no longer showed a significant effect, however a significant age effect emerged (*F* = 11.92, *p* < .001, η_p^2 = .171). Similarly, children with SCT and children with AHDH-I/subH performed better on the SOPT than children with ADHD-H (*F* = 3.240, *p* = .022, η_p^2 = .027, Power = .743). However, SOPT performance was no longer significantly different when age and gender were controlled. On the ToL, however, children with ADHD-H obtained higher scores than children with the SCT subtype (*F* = 2.799, *p* = .040, η_p^2 = .026, Power = .672), as can be seen in Table 4. Again, this significance was not observed once age and gender were included in the analysis. No significant differences were found between SCT and other subtypes on WCST performance (*F* = 1.343, *p* = .188).

Discussion

In the present study, we sought to identify an EF profile in children with different ADHD subtype diagnoses. Contrary to most studies, we examined all three DSM-IV ADHD subtypes, then did a re-examination after subdividing ADHD-I into two groups: the SCT subtype and the ADHD-I/subH group. To begin with, significant differences were found in gender distribution between the ADHD subtypes. Similar findings have been previously reported (Lahey et al., 1994). The findings show that various domains of EF are not affected by clinical subtypes when age is taken into consideration. This suggests that ADHD should be viewed in the context of development. The maturational process of brain regions implicated in EF, as well as possible compensatory mechanisms, may explain these findings, as children with

ADHD may display greater within-group variability in these processes (Halperin & Schulz, 2006). Thus, further research is needed before EF can be considered a useful endophenotype.

Several measures used in the study provided normative sample scores, which provides important information from a clinical perspective. Lambek et al. (2011) had previously found that only 50% of children with ADHD had EF deficits when compared with typically developing children. The review of mean scores from our sample, however, indicated that children performed within the average range in many domains as compared to normative samples, irrespective of subtype. This was true for tasks that assess planning, set-shifting, measures of vigilance (RT block change), overall reaction time (RT) and impulsivity (commissions) on the CPT. Mean scores for these CPT measures did not reach the clinical range for any of the groups. When the SCT was derived, children in this subgroup were shown to be significantly better performers on these measures, while children who remained in the ADHD-I/subH group due to sub-threshold hyperactive symptoms no longer differed significantly from the hyperactive or combined groups. On the CPT, children with SCT obtained lower scores (better performance) than children with other ADHD subtypes. Both groups, however, performed in the typical range.

When compared to children in the ADHD-I subtype, children with the ADHD-C subtype and the ADHD-H subtype demonstrated a tendency towards overall poorer performance in the domain of set-shifting. Since, after controlling for age, the significance was no longer present, we concluded that children in the three DSM-IV subtypes did not differ in their performance on this task. Similar findings were reported when only the ADHD-I and ADHD-C subtypes were examined (Houghton et al., 1999). Skogli, Egeland, Andersen, Hovik, and Oie (2013) also found no significant differences between the ADHD-I and ADHD-H subtypes in the domains of working memory, cognitive flexibility and planning. However, when all three subtypes were compared, children with the ADHD-C subtype were found to have more total errors than children with ADHD-I or ADHD-H subtypes (Schmitz et al., 2002). Solanto et al. (2007) reported poorer performance on WCST with respect to number of categories and total errors for children with the ADHD-C subtype as compared to the ADHD-I subtype, but, in contrast to our approach, the authors chose to control for IQ which removed the significant effect.

The debate about the relationship between EF and IQ is ongoing, as many EF domains have been found to be related to IQ (Ackerman, Beier, & Boyle, 2005; Arffa, 2007). The WISC, battery used to measure Full Scale IQ in our study, includes working memory subtests. Working memory was assessed as part of EF, as well as may play a role in other EF tasks. Also, since IQ is a widely used clinical measure, many children in our study completed the IQ assessment while being treated with medication. There is now evidence suggesting that pharmacological treatment of ADHD symptoms may affect children's performance on cognitive tasks (Jepsen, Fagerlund, & Mortensen, 2009; Zhang, Jin, & Zhang, 2011). Given this, to avoid over-controlling we did not include IQ as one of our confounding variables. However, this area requires a thorough investigation in clinical population.

It is difficult to compare Tower of London task results across studies because a wide variety of administration and scoring procedures are used in the literature. In our study children asked to work as fast as possible and were told how many moves they should make to solve each problem. The solution time was recorded. Nig et al. (2002) used a similar procedure and also found no difference in performance between Inattentive and Combined subtypes. Similar to the planning task, we found no association between working memory and ADHD subtypes. Oosterla et al. (2005) found that teacher reported ADHD symptoms predicted performance on the SOPT, but that parent reported symptoms did not. In our study, the teacher reports were not available but parent results were similar. In addition, we found many EF measures to be correlated with ADHD symptoms, stressing the pertinence of symptom severity rather than subtypes.

Strengths, Limitations and Conclusion

All children in this study had received a clinical diagnosis of ADHD by a psychiatrist and had undergone a medication washout period for at least five days prior to testing. A structured diagnostic interview accounted for the severity and frequency of symptoms included in the subtype classification. All EF tasks were administered in the morning to maximize standardization of assessments and reduce the effect of fatigue on task performance. Moreover, the same research team administered the EF measures over 12 years of data collection. The current study had a comparatively large sample size. In addition, the examination of all three DSM-IV subtypes and SCT subtype provides a better understanding of the clinical profile in relation to EF functioning.

One of the limitations of our study is that it did not include a typically developing group of children, which thus also limits the conclusions we can draw regarding overall EF deficits as compared to typically developing peers. Furthermore, while many children diagnosed with ADHD also present with comorbid disorders, the examination of comorbid disorders was beyond the scope of this manuscript and will be explored elsewhere.

The debate continues as to whether ADHD subtypes are cognitively distinct from each other. The present study implicates the dynamic role of development itself in producing ADHD cognitive phenotypes, so adding another piece of the puzzle to this intriguing but complex condition. The next step is to provide experimentally rich developmental data that can trace trajectories of performance across proposed subtypes and see how they map onto typically developing pathways. An understanding of these processes will enable clinicians to tailor interventions for each age group that address the specific needs of children in each subgroup.

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Table 1

ADHD Subtypes and Demographic Information

	ADHD Subtypes								
	DSM-IV Subtypes					DSM-IV inattentive Subtype			
	C 52.6%	I 34.4%	H 12.9%	p		SCT	I/subH	p	
Sex									
Boys [a]	54.6%	31.0%	14.4%	.021		13.7%	17.3%	.031	
Girls [b]	45.6%	46.8%	7.6%			25.3%	21.5%		
Age Mean (SD)	8.79 (1.71)	9.57 (1.87)	8.0 (1.52)	.009	I>C,H C>H	9.92 (1.8)	9.26 (1.9)	<.001	H<SCT, I, C C>SCT
Comorbidity present (%)	89.4	76.6	74.5	.003		78.0	75.4	.008	
Verbal IQ Mean (SD)	93.04 (13.13)	97.09 (14.24)	94.84 (14.16)	.055		97.71 (14.45)	96.58 (14.71)	.111	
Performance IQ Mean (SD)	102.08 (13.66)	99.67 (15.36)	101.70 (16.05)	.389		98.73 (15.56)	100.44 (15.27)	.517	
Full Scale IQ Mean (SD)	96.48 (13.24)	96.42 (14.06)	97.57 (15.12)	.883		96.00 (14.46)	96.77 (13.84)	.953	
CBCL Ext. Mean (SD)	72.32 (7.9)	64.84 (10.98)	70.0 (9.2)	001	C>I I<H	62.79 (11.6)	66.7 (10.1)	<.001	SCT<H C>I/subH, H, SCT
CBCL Int. Mean (SD)	65.7 (9.70)	64.22 (10.52)	61.02 (8.80)	.016	C>H	65.31 (10.0)	63.23 (10.9)	.022	C>H
CBCL Total Mean (SD)	71.99 (7.26)	67.30 (8.91)	67.67 (7.94)	.001	C>I,H	67.66 (8.0)	66.98 (9.7)	<.001	C>SCT,C,H,I /subH

Note. SCT and I/subH subtypes were compared to combined and hyperactive subtypes; ADHD = Attention Deficit Hyperactive Symptoms; C=Combined subtype, I=Inattentive subtype; H = Hyperactive subtype; SCT = Sluggish Cognitive Tempo; I/subH = Inattentive subtype with sub threshold Hyperactive symptoms; CBCL = Child Behaviour Checklist; Int. = Internalizing; Ext. = Externalising.

Table 2

Correlation between Executive Function Measures and ADHD Symptoms

	Inattention symptoms	Hyperactivity symptoms	Total ADHD symptoms
CPT Omission Errors Percentile	-.050	.183**	.125*
CPT Commission Errors T score	-.050	-.026	-.053
CPT RT T score	-.043	.138**	.091
CPT RT Standard Error T score	-.123*	.229**	.118*
CPT RT Block Change T score	.003	.105*	.091
CPT RT Inter-Stimuli-Interval T score	-.084	.172**	.094
WCST Persevarative Response SS	.035	-.090	-.056
WCST Perseveartive Error SS	.045	-.096	-.054
WCST Non Persevarative Error SS	.117*	-.015	.059
WCST Number of Categories Solved	.135*	-.121*	-.021
SOPT	-.086	.108*	.038
ToL	-.082	.086	.027

Note. *. Correlation is significant at the 0.05 level; **. Correlation is significant at the 0.01 level; CPT = Continuous Performance Test; RT = Reaction Time; WCST = Wisconsin Card Sorting Test; SOPT = Self Ordered Pointing Test; ToL = Tower of London;

Table 3

ADHD Subtypes and CPT Performance

	ADHD subtypes								
	DSM-IV					DSM-IV ADHD-I			
	C	I	H	p		SCT	I/subH	p	
Omission Errors Mean (SD)	74.26 (24.94)	64.79 (27.22)	70.49 (28.74)	.009	C>I	62.92 (25.19)	66.43 (28.98)	.018	SCT< C
Commission Errors Mean (SD)	52.17 (8.00)	52.31 (8.04)	53.79 (7.01)	.455		52.04 (9.07)	52.54 (7.08)	.638	
RT Mean (SD)	53.38 (12.25)	50.53 (10.53)	52.84 (12.31)	.108		49.47 (9.91)	51.46 (11.03)	.149	
RT Standard Error Mean (SD)	63.09 (11.53)	58.06 (11.99)	63.49 (10.16)	<.001	I<C,H	56.09 (9.93)	59.79 (13.38)	<.001	SCT< C,H
RT Inter-Stimuli-Interval Mean (SD)	61.63 (19.39)	55.89 (15.95)	62.47 (14.95)	.012	C>I	53.31 (14.08)	58.15 (17.22)	.011	SCT< C
RT Block Change Mean (SD)	53.34 (11.89)	52.53 (13.25)	52.19 (11.89)	.779		49.88 (10.19)	54.86 (15.14)	.143	

Notes. CPT = Continuous Performance Test; RT = Reaction Time; ADHD = Attention Deficit Hyperactive Symptoms; C = Combined subtype, I = Inattentive subtype; H = Hyperactive subtype; SCT = Sluggish Cognitive Tempo; I/subH = Inattentive subtype with sub threshold Hyperactive symptoms;

Table 4

ADHD Subtypes and WCST, SOPT and ToL Performance

	ADHD subtypes								
	DSM-IV					DSM-IV ADHD-I			
	C	I	H	p		SCT	I/subH	p	
WCST Perseverative responses SS Mean (SD)	97.87 (12.82)	100.13 (13.42)	97.43 (9.58)	.285		100.11 (13.09)	100.15 (13.81)	.474	
WCST Perseverative Errors SS, Mean (SD)	97.36 (12.98)	99.87 (13.70)	96.85 (10.03)	.221		99.76 (13.58)	99.97 (12.78)	.388	
WCST Non Perseverative Error SS, Mean (SD)	92.26 (15.07)	93.46 (14.59)	90.79 (16.05)	.603		92.52 (15.88)	94.29 (13.43)	.703	
WCST number of categories completed Mean (SD)	4.12 (1.78)	4.66 (1.54)	3.82 (1.76)	.007	I>C,H	4.56 (1.73)	4.75 (1.36)	.016	I>H
SOPT, Mean (SD)	16.13 (8.21)	14.00 (6.82)	17.68 (7.15)	.008	I<H	13.87 (6.74)	14.11 (6.95)	.022	SCT>H
ToL SS, Mean (SD)	105.67 (13.91)	105.14 (15.51)	110.74 (12.07)	.116		102.46 (15.17)	107.76 (15.52)	.040	SCT<H

Note. SS = Standard Scores; WCST = Wisconsin Card Sorting Test; SOPT = Self Ordered Pointing Test; ToL = Tower of London; ADHD = Attention Deficit Hyperactive Symptoms; C = Combined subtype, I = Inattentive subtype; H = Hyperactive subtype; SCT = Sluggish Cognitive Tempo; I/subH = Inattentive subtype with sub threshold Hyperactive symptoms

Bridging Manuscripts

This dissertation is addressing one of the clinical challenges associated with ADHD: its clinical presentation, first due to diagnostic subtypes and second, due to associated comorbid disorders. The results of the first manuscript support the research which questions the validity of ADDH subtypes. We reported that the differences in EF performance seen between the ADHD diagnostic subtypes can be explained by age differences. These results suggest that ADHD subtypes do not account for EF variability seen in the literature. We identified an important age effect associated with EF performance and with subtypes, supporting the significance of development and maturation in the course of the disorder.

The second, perhaps even more important clinical factor is the presence comorbidities. What is the impact of comorbid disorders on ADHD? How does it affect the EF performance? This aspect was not examined in the previous manuscript, leading to the next step: to closely examine if comorbid disorders play a role in EF performance in this population. If comorbid disorders play a role, which specific disorders are associated with diminished performance with which EF domain. Identifying such association may help to explain some of the variability in functioning in children and adults with ADHD.

In the next manuscript we examine the same EF measures as in the first manuscript. In addition we added a new measure, Finger Windows, to assess the visual special memory, in order to gather more in debt information about working memory. The comorbid disorders assessed in the second manuscript are those that have been found to be most impairing in elementary school age children. The two manuscripts together are believed to contribute to an in-dept understanding of clinical presentation of ADHD and EF.

CHAPTER 3

MANUSCRIPT 2

Attention and Executive Function in Children with ADHD: The Role of Comorbid Disorders

Running title: Executive function and ADHD

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Abstract

Background: Evidence continues to emerge suggesting that children with Attention Deficit Hyperactivity Disorder (ADHD) also have executive function (EF) deficit, compared to typically developing children. However, the results are inconsistent, and the role of frequently occurring comorbid disorders is unclear. **Methods**: Three hundred and fifty five, 6-12 year old children clinically diagnosed with ADHD were included in the study. Comorbid Anxiety Disorders, Oppositional Defiant Disorder and Conduct Disorder were examined. The EF domains were assessed using the Conners' Continuous Performance Test (CPT), Wisconsin Card Sorting Test (WCST), Tower of London (ToL), Finger Windows (FW) and Self Ordered Pointing Test (SOPT). **Results**: Majority (69%) of children were diagnosed with at least one comorbid disorder. Children with Anxiety performed worse on several CPT variables and on FW. Children with CD obtained lower scores (poor performance) and a significant sex by CD interaction was observed on WCST. **Conclusion**: These results indicate that comorbid disorders should be carefully examined as they play a significant role in EF performance and subsequently in day to day functioning of children with ADHD. **Keywords**: Attention Deficit Hyperactivity Disorder, Comorbid Disorders, gender differences, Executive Function, Sluggish Cognitive Tempo, Wisconsin Card Sorting Test, Conners' Continuous Performance Test, Tower of London, Self Ordered Pointing Test.

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is the most frequently diagnosed psychiatric disorders in school-age children and is a major risk factor for educational failure, later high risk behaviour, and other psychopathology (Biederman et al., 2006; Biederman, Petty, Dolan, et al., 2008; Pagani et al., 2009). The risks imparted by ADHD are even more pronounced if ADHD is left untreated (Mannuzza et al., 2008). The prevalence rate of ADHD in school-age children is 6-9% (Dopheide & Pliszka, 2009). It is more common in boys, estimated to be between 2:1 and 9:1 according to a recent meta-analysis (Rucklidge, 2010). Sex differences have been reported in the phenotypic expression of the disorder, such as lower levels of disruptive behaviour and higher levels of inattentive symptoms in girls (Stefanatos & Baron, 2007).

ADHD rarely occurs in isolation and there is now a well established literature that identifies a range of comorbid psychiatric disorders, including oppositional defiant disorder, conduct disorder (Biederman, Petty, Dolan, et al., 2008), anxiety disorders (Schatz & Rostain, 2006), depressive disorders (Daviss, 2008) and learning disabilities (Fischer et al., 2007; Schatz & Rostain, 2006). Rates of comorbid disorders range from 24% to 71%, varying across studies and across disorders (Jensen et al., 2001; Kadesjo & Gillberg, 2001; Robison et al., 1999). The National Institute of Mental Health (NIMH) Multimodal Treatment Study of ADHD (MTA), one of the larger clinical trials conducted to date, found that only 31.8% of children with ADHD had no other psychiatric disorders and, more importantly, up to 24.7% of children received a diagnosis of two other psychiatric disorders in addition to ADHD (Jensen et al., 2001). Disruptive behaviours, such as oppositional defiant disorder (ODD) and conduct disorder (CD), are easily observed and relatively well documented, while internalizing disorders, such as anxiety disorders, are less evident, attract less attention, and are likely to be underreported (Barbosa et al., 2002; Klein, 2009; Vance et al., 2002). About 50% of children with ADHD have been found to meet the criteria for ODD or CD, and between 25 to 33% meet the criteria for anxiety disorders (Jarrett & Ollendick, 2008; Pliszka, Sherman, Barrow, & Irick, 2000).

Boys and girls have been found to have different patterns of comorbid disorders, girls being at a lower risk for major depression and behavioural disorders, but at higher risk for anxiety disorders and substance use (Bauermeister et al., 2007; Biederman et al., 2002). Overall, girls with ADHD have been found to have more internalising problems than boys with ADHD (Gershon, 2002), with boys showing more externalizing symptoms than girls (Levy, 2004).

The presence of comorbidities plays a role in the degree of impairment and the course of the disorder and presents an additional challenge to the diagnosis and treatment of individuals with ADHD (Biederman, Petty, Dolan, et al., 2008; Biederman, Petty, Monuteaux, et al., 2008; Ollendick et al., 2008). For example, children with both ADHD and anxiety disorders have been found to have more attention problems, academic difficulties and social problems as compared to children with ADHD only or with anxiety only (Brown, 2008). The presence of comorbidities predicts the persistence of ADHD over time (Biederman, Petty, Clarke, Lomedico, & Faraone, 2011).

A decrease in ADHD symptoms in adolescence does not necessarily lead to a decrease of comorbid disorders (Gau et al., 2010). Moreover, recent findings further emphasize the role of comorbid disorders, suggesting a new dimension of ADHD subtype categorisation, one that takes into account the specific comorbid disorders in the diagnosis (Biederman et al., 2011).

Executive Function and ADHD

In addition to comorbid disorders, children with ADHD often exhibit deficits on neurocognitive tasks, particularly those related to Executive Function (EF). EF represents a set of cognitive processes that integrate information from working memory with information about context in order to select optimal action (Willcutt et al., 2005). EF has drawn considerable interest in developmental research over the past two decades. Models and theories that attempt to explain EF from a developmental perspective focus on the domains of working memory, set-shifting and inhibition (Garon et al., 2008).

EF deficits in children with ADHD have been reported in the domains of response inhibition and execution, vigilance, working memory, set and task-switching/cognitive flexibility and planning (Toplak et al., 2009; Willcutt et al., 2005). An earlier meta-analytical study of neuropsychological test performance in ADHD reported small to large effect sizes for tests commonly used to assess EF (Frazier et al., 2004). Lambek et al. (2011) reported that among 48 children with ADHD in the study, only half were classified as having EF dysfunction.

Boys and girls have been reported to perform differently on some EF tasks, such as working memory tasks (De Luca et al., 2003; Seidman et al., 2005), attention measures (Newcorn et al., 2001), and reaction time (Brocki & Bohlin, 2004). In general, girls have been found to be less impaired as compared to boys (Hasson & Fine, 2012).

The search for common deficits continues, as researchers attempt to address previous methodological shortcomings that may explain these inconsistencies in findings. Small sample sizes, the failure to account for comorbid disorders, and unclear treatment status are some of the weaknesses encountered in the literature.

Executive function and comorbid disorders

EF deficits are not specific to ADHD, but are also found in other psychiatric conditions. Several studies have reported an association between EF and symptoms of anxiety/depression (Chang et al., 2007; Emerson et al., 2005; Spitznagel & Suhr, 2002). Obsessive compulsive disorder (OCD) has been found to be associated with deficits in set-shifting/cognitive flexibility and impulsivity (Chamberlain et al., 2007; Shin et al., 2008).

Studies examining EF and ADHD with comorbid disorders are limited in number and reported inconsistent findings (Doyle, 2006). Using a behavioural rating of EF (BRIEF), Sørensen et al. (2010) found that children with ADHD and comorbid anxieties (N = 11) obtained higher scores on the inhibit subscale of the BRIEF and children with anxiety disorders (N = 24) obtained higher scores on the shifting subscale when compared to children without anxiety disorders. Jonsdottir, Bouma, Sergeant and Scherder (2006) compared planning and verbal working memory in 43 clinic-referred and 115 control participants. Along with reporting poorer performance in the clinical group on working memory, planning tasks and visual attention tasks, the authors found a significant negative relationship between teacher rated atypical and depression symptoms and the planning task, and teacher rated anxiety symptoms and the visual attention test (Jonsdottir et al., 2006). In a study comparing performance on working memory tasks between children with anxiety, with ADHD, with ADHD and anxiety (N = 108) and a control group, children with the dual diagnosis were found to display a similar impairment to children with ADHD only, relative to both the control group and anxiety only group (Manassis et al., 2007). In this study the anxiety group consisted of children with any anxiety disorder except OCD and Post Traumatic Stress Disorder.

Using Tower of London, a planning task, Sarkis, Sarkis, Marshall and Archer (2005) compared children with ADHD and internalizing and externalizing comorbid disorders (N =

106). The authors reported that children with ADHD and comorbid mood disorders used more moves in the planning task as compared to the other groups. However, this difference did not reflect on overall task performance, suggesting that comorbid disorders do not have an effect on EF as measured by the Tower of London test.

Studies comparing children with CD with typically developing peers suggest that CD may have an effect on EF (Toupin et al., 2000). However, in the ADHD literature, the presence of comorbid ODD or CD does not seem to affect EF performance, as no differences were found between children with ADHD and comorbid ODD or CD and children with ODD or CD alone, nor was a difference found between children with ADHD and comorbid CD or ODD and those with ADHD alone (Kalff et al., 2002). Oosterlaan, Scheres and Sergeant (2005) found that EF deficits, as measured by working memory and planning tasks, were associated with ADHD, and not with ODD or CD, in a sample of ninety-nine 6-12 year old children. High parent ODD/CD ratings were associated with fewer errors on the planning task. The authors used parent and teacher questionnaires to identify ADHD, ODD and CD and did not report whether children had any other comorbid disorders.

Fischer et al. (2005) found that at follow-up, adults with both ADHD and CD made more perseverative errors on a set-shifting task than adults with ADHD only. Similarly, in a comparison of adolescent girls with CD to peers without CD on a number of EF tasks, such as working memory, interference control, and set-shifting, Pajer et al. (2008) found that the girls with CD performed worse on a set-shifting task. This finding supports the notion that EF deficits may be more pronounced in adolescence and adulthood, underlining the role of development and brain maturation in EF, particularly in the clinical population.

A recently published longitudinal study reported that EF performance, specifically planning and inhibition, as measured in preadolescent girls with ADHD, predicted the social functioning assessed at the five-year follow up (Rinsky & Hinshaw, 2011). Moreover, this study reported that childhood planning predicted presence of comorbidity in adolescence and that working memory marginally predicted internalizing disorders in adolescence.

Given frequently observed EF deficit and the high rate of comorbidities in this population, the main aim of the current study is to examine the role comorbid disorders play on EF task performance in a large sample of children diagnosed with ADHD. We hypothesise that the presence of comorbid disorders will have an additive negative effect on EF performance, resulting in poorer performance by children with ADHD as compared to those with ADHD but without comorbidity. Specifically, we hypothesise that children with anxiety disorders will show more impairments in working memory. We expect that the presence of CD and ODD will not affect EF performance.

This study will contribute to identifying the impact of comorbidities on EF will allow clinicians to refine individual intervention. In addition, this study addresses the limitations of previous studies, particularly with respect to sample size and by using a thorough diagnostic and standardised assessment procedure.

Methods

Participants

Children ages 6 to 12 diagnosed with ADHD and referred to the ADHD clinic were recruited sequentially for the study as part of an ongoing Clinical and Pharmaco-genetic Study of ADHD (Grizenko, Bhat, Schwartz, Ter-Stepanian, & Joober, 2006). Participants were referred to the research team by their primary treating psychiatrist, paediatrician or school psychologists. Children were excluded from the study if they met the DSM-IV criteria for psychosis, had a chronic medical condition, pervasive developmental disorder, Gilles de la Tourette's syndrome, or had an IQ less than 70 as measured by Wechsler Intelligence Scale for Children 3rd or 4th edition (WISC-III: Wechsler, 1991). Since the data collection for this study began prior to WISC-IV publication, WISC-III was also used. The Median for WISC-III Full Scale IQ was 97, for WISC-IV Full Scale IQ was 96. The final sample consisted of 355 children, 267 boys and 88 girls. The mean age for the group was 9.40 years (SD = 1.66), with no statistical difference in age between boys and girls.

Design and setting

The study was conducted at a university affiliated mental health institute located in Montreal, Canada. Internal Research Ethics Board approval was obtained for the study protocol.

Study procedure

All participating parents completed standardised interviews and questionnaires while their child was assessed using EF measures. Children who were taking methylphenidate (MPH) or other medication for treatment of the ADHD symptoms at the time of the study underwent five day medication washout period prior to completing the assessment. All EF measures were administered in the morning, to minimize the possible effects of fatigue on task performance.

Clinical Assessment

Intake interviews consisted of a clinical assessment by the team psychiatrists, and interviews with primary caregiver (herein referred to as parent) and the child. All children were assessed by a research team psychiatrist to confirm the ADHD diagnosis. If the child met the criteria for diagnosis of ADHD he or she was retained in the study.

A trained research assistant interviewed a parent, using *The National Institutes of Mental Health Diagnostic Interview Schedule for Children 4th edition* (Shaffer et al., 2000). The Diagnostic Interview Schedule for Children (DISC – IV) is a highly structured, DSM-IV diagnostic interview which assesses most common mental disorders in children and adolescents during the past year. The interview uses a decision tree approach, taking into account the frequency of the symptoms, the duration of the symptoms, if the symptoms interfere with the child's functioning and if symptoms occur in multiple settings (i.e., at school and at home). DISC-IV was used to determine the presence of comorbid disorders and ADHD symptoms. The following comorbid disorders were examined in the study: Oppositional Defiant Disorder (ODD), Conduct Disorder (CD), and Anxiety Disorders. The child was considered to have Anxiety disorder if he or she met the diagnostic criteria for one or more DSM-IV Anxiety disorders.

Child measures

Wechsler Intelligence Scale for Children – 3rd (WISC-III) or 4th (WISC-IV) editions was used to assess the children's general cognitive ability. The WISC was administered by an advanced doctoral level psychology student. The WISC was not re-administered if the child was assessed within one year of participating in the study. Thus, in some instances children were assessed while being treated for ADHD symptoms. Studies have found that psychostimulants may have up to seven point effect on IQ (Jepsen, Fagerlund, & Mortensen, 2008). Also, some of the EF areas assessed in this study are also part of the WISC-IV full scale IQ. Due to these constraints, and to avoid over-controlling, the full scale IQ (FSIQ) was used only as an exclusion criteria in the current analysis. Children with a FSIQ below 70 were excluded from the study.

The EF tasks were administered when participants were not taking any medication for ADHD symptoms or comorbid disorders. All assessments were conducted in the morning in English or French, depending on the language the child was schooled in or was most comfortable with. The following tests were used: Conners Continuous Performance Test (CPT), Wisconsin Card Sorting Test (WCST), Tower of London (ToL), Self Ordered Pointing Test (SOPT), and Finger Windows (FW).

CPT. The CPT is a widely used computerized test of attention, response inhibition and executive control (Conners et al., 2003; Homack & Riccio, 2006; Riccio et al., 2006). During the task a set of letters randomly appear on a black screen, one at a time. The participants are instructed to press the space bar as soon as they see a letter except the letter “X”. The letters are presented with a different speed through the test (six blocks of different times for a total of 14 minutes). The following CPT variables were used for the analysis: the number of omissions, number of commissions, hit reaction time (RT), RT standard error, hit RT block change and the hit RT inter-stimulus interval (RT-ISI).

WCST. The WCST is among the most widely used executive function tasks in both clinical and applied research. The task assesses set-shifting in children and adults. Participants complete the computerized version of the WCST where the child is first presented with four stimulus cards that differ in shape, colour and number, which remain on the screen throughout the test. The child is then presented with one card at a time and is asked to match this card with one of four stimulus cards. Children are not told according to what rule or category they should match but after each try a feedback is given whether the choice was correct or not. The rule for matching the cards changes after the child successfully matches 10 consecutive cards. The test is discontinued after the child successfully completes 2 sets matched by colour, 2 sets by shape and

2 sets by number or when all 128 cards are used. The variables used for analysis in this study are: perseverative responses, perseverative errors, non-perseverative errors, number of categories completed, failure to maintain set and number of trials to complete the first category variable. Although the last variable does not reflect the set-shifting ability of the participant, it gives information about the initial concept formation and problem solving ability (Barcelo, 2001).

ToL. The ToL is a planning task, based on Tower of Hanoi and consists of 3 different height polls (tall, medium and short) and 3 coloured balls (red, blue and green). The participant is presented with the polls where the three balls are arranges in a starting position and a picture of a target pattern. The participant is instructed to move the balls in order to match the pattern on a picture while following the rules. Each picture specifies how many moves should be done to complete the pattern. A total of 12 pictures were presented, starting from simple patterns requiring 2 moves to more difficult ones requiring 5 moves. There have been many different methods of administration and scoring the ToL. The ToL administration version and standard scores used in this study was adopted from Anderson, Anderson and Lajoie (1996). For the analysis, the ToL Standard Score was used.

SOPT. The SOPT, is a visual working memory task, primarily planning and monitoring aspects of working memory (Petrides & Milner, 1982). In this task, first the participant is presented with a set of six pages where each page has six randomly arranged pictures. The same six pictures are repeated on each one of the six pages but with a different arrangement on each page. The participants are asked to select a picture, then turn the page and select a different picture and continue until all six pictures are chosen (or all six pages completed). The same set is administered three times after which a new set with eight pictures and eight pages is presented. The same procedure is repeated with eight, 10 and 12 pictures. If the child pointed to the same picture more than once on one trial, then an error was recorded. Total number of errors across all trials and sets were calculated and used in the analysis.

Finger Windows. The FW is part of the Children's Memory Scale battery and is a measure of visiospatial working memory. In this task the participants are presented with a board that contains multiple holes. The administrator puts a pencil through a sequence of holes and asks the participant to repeat the same sequence. The test progressively becomes more difficult. FW scaled scores were used for the analysis.

Statistical Analysis

Statistical analyses were conducted using the SPSS software, Chicago, IL, USA. Continuous variables were expressed as means ± standard deviation (SD). Categorical variables were expressed as proportions (%). Chi Square tests were used to compare proportions between groups. SPSS General Linear Model procedure (GLM) multivariate analysis of variance (MANOVA) or univariate analysis of covariance (ANCOVA) were used to examine the effect of multiple fixed factors and control for confounding variables.

Results

Clinical Profile

The demographic information about the sample is presented in Table 1. The three most common comorbid disorders were used for this manuscript: Anxiety disorders, ODD and CD. Only 31% of children did not meet the criteria for any of the three examined comorbidities. According to the DISC-IV interview, almost half of the group (44.5%) met the criteria for one or more anxiety disorders, 42.8% for ODD and 12.7% for CD. As many as 110 children were diagnosed with more than one comorbid disorder.

No age (F(1,353) = .054, p = .816) or gender differences (χ^2 (1, N = 355) = .527, p = .468) were found between children with and without comorbidities. Significant association was found between presence of comorbid disorders and DSM-IV ADHD subtype (χ^2 (2, N = 355) = 20.23, p < .001, Cramer's V = .239). Specifically, an association was found between subtypes and ODD (χ^2 (2, N = 355) = 20.74, p < .001, Cramer's V = .242).

The significant association between ADHD subtypes and comorbid disorders was also reflected in the ADHD symptom presentation across the comorbid disorders (Table 1). Overall, the presence of comorbid disorders was associated with more ADHD symptoms, both inattentive (F(1,353)=11.11, p =.001, η_p^2 = .031, Power = .914) and hyperactive (F(1,353) = 34.36, p < .001, η_p^2 = .089, Power = 1.0). Children with Anxiety disorders presented with more inattentive symptoms (F(1,353) = 9.34, p = .002, η_p^2 = .026, Power = .862) and hyperactive symptoms (F(1,353) = 5.71, p = .017, η_p^2 = .016, Power = .664), children with CD more hyperactive symptoms (F(1.353) = 21.24, p < .001, η_p^2 = .057, Power = .996), and children with ODD with more inattentive (F(1,353) = 11.45, p = .001, η_p^2 = .031, Power = 921) and hyperactive symptoms(F(1,353) = 27.22, p < .001, η_p^2 = .072, Power = .999).

Cognitive profile

The Full Scale IQ for the group was within the average range (Table 1). No significant IQ differences were found between boys and girls (FSIQ: F(1,325) = .081, p = .776). No significant difference was found between full scale IQ and presence of comorbid disorders. When children in different comorbid groups were compared on four IQ indices (verbal, perceptual reasoning, working memory and processing speed) as shown in Table 1, children with ODD were found to have significantly higher scores on Full Scale IQ (F(1,325) = 4.77, p = .030, η_p^2 = .014, Power = .586), working memory (F(1,249) = 6.78, p = .010, η_p^2 = .027, Power =

.737), and processing speed ($F(1,249) = 7.37$, $p = .007$, $\eta_p^2 = .029$, Power = .772). However, once gender was controlled, significant differences were found between children with CD and without CD on verbal index ($F(3,326) = 4.014$, $p = .046$, $\eta_p^2 = .010$, Power = .445), children with CD having obtained lower scores compared to children without CD.

Executive Function

Most WCST and CPT variables were correlated with age. Significant difference was found between boys and girls on one of the EF measures which remained significant after controlling for age. Boys obtained higher score on ToL ($M_{boys} = 111.28$; $M_{girls} = 105.05$; $F(1,353) = 11.561$, $p = .001$, $\eta_p^2 = .034$, Power = .938).

Comorbid Disorders and Executive Function

The analyses were conducted in two steps: first, multivariate analysis were conducted for CPT, WCST, and working memory (SOPT and FW) variables, and a univariate analysis of variance was conducted using the ToL, without including any confounding variables in the model. Then, the analyses were repeated controlling for age and gender.

CPT. Table 2 presents the CPT and comorbid disorders data. Children with or without comorbid disorders differed significantly on the CPT ($F(6,340) = 2.260$, $p = .037$, $\eta_p^2 = .038$, Power = 789), which remained significant after controlling for age and gender ($F(6,340) = 2.200$, $p = .037$, $\eta_p^2 = .038$, Power =.776). A main effect of age was also observed ($F(6,337) = 19.614$, $p = .000$ $\eta_p^2 = .259$, Power = 1.0), while no main effect of sex was found ($F(6,337) = .625$, $p = .710$), a trend was observed for the interaction between sex and comorbidity ($F(6,337) = 2.105$, $p = .052$, $\eta_p^2 = .036$, Power = 754). Children with comorbidities were found to have poorer performance on CPT number of commission errors ($F(1,342) = 5.584$, $p = .019$, $\eta_p^2 = .016$, Power = 654) and RT standard error ($F(1,342) = 4.561$, $p = .033$, $\eta_p^2 = .013$, Power = .567).

When individual comorbid disorders were examined no significant effect of Anxiety disorders on CPT were observed (*F* (6,340) = 1.516, $p = .172$), however, when age and gender were added, significant main effect was observed for anxiety ($F(6,337) = 2.693$, $p = .014$, $\eta_p^2 = .046$, Power = .866) and age ($F(6,337) = 19.654$, $p < .001$, $\eta_p^2 = .259$, Power = 1.0). Children with anxiety disorders obtained higher T scores on commission errors, RT standard error, and RT inter-stimuli-interval change.

No significant multivariate effect of CD was found ($F(6,338) = 1.574$, $p = .154$), which remained not significant after age and gender were added to the analysis. Similarly, no significant effect of ODD was observed on CPT performance ($F(6,340) = .767$, $p = .596$), regardless of gender or age.

The interaction effects between different comorbid disorders were also examined and found to be not significant for both Anxiety and ODD ($F(6,338) = 1.377$, $p = .223$) or Anxiety and CD ($F(6,338) = 1.00$, $p = .425$).

WCST. The WCST results showed no multivariate comorbidity effect ($F(6, 348) = .776$, $p = .589$), including when age or sex were included in the model. A significant age effect was found ($F(6,348) = 10.261$, $p < .001$, $\eta_p^2 = .151$, Power = 1.0).

When each comorbid disorder was examined separately, no significant multivariate effect of Anxiety disorders ($F(6,348) = .645$, $p = .694$), CD (F(6, 348) = 1.429, $p = .203$), or ODD ($F(6, 348) = 1.023$, $p = .410$) was found, however, when age and sex were included in the analysis a significant effect of age continued to be present ($F(6, 345) = 10.087$, $p < .001$, $\eta_p^2 = .149$, Power = 1.0). In addition, after controlling for sex and age a significant multivariate CD effect was found ($F(6,345) = 2.55$, $p = .020$, $\eta_p^2 = .043$, Power = .844) and CD by sex interaction effect was found ($F(6, 345) = 2.173$, $p = .045$, $\eta_p^2 = .036$, Power = .770). Children without CD obtained lower scores on perseverative and non-perseverative errors, completed less categories and required more trials to complete the first category indicating poorer performance. Sex by CD interaction was found for non-perseverative errors and number of trails to complete the first category. Boys with and without CD obtained similar scores on the non-perseverative errors (*M* = 94.02, SD = 16.17; *M* = 94.71, SD = 14.69), while girls with CD obtained substantially lower scores (*M* = 84.55, SD = 10.85) compared with girls without CD (*M* = 96.86, SD = 14.35) or boys in either group.

The interaction effects between the comorbid disorders were examined by including Anxiety and CD and then Anxiety and ODD in the analysis. No significant CD by Anxiety ($F(6,346) = 1.320$, p = .247), or ODD by Anxiety ($F(6,346) = 1.137$, $p = .341$) interaction effects were observed, which remained not significant after the age and sex were controlled.

ToL. Univariate analysis of variance showed no significant group differences between children with and without comorbid disorders ($F(1,353) = .299$, $p = .585$). After controlling for age and gender a significant gender effect was observed ($F(1,350) = 11.127$, $p = .001$, $\eta_p^2 = .031$, Power = .914). Boys, obtained higher scores on this task (*M* = 111.28, SD = 13.57) then girls (*M* = 105.04, SD = 16.93).

When specific comorbidities were examined no significant effect of anxiety ($F(1, 353) = 1.856$, $p = .174$), CD ($F(1,353) = .026$, $p = .873$) or ODD ($F(1,353) = .080$, $p = .778$) on ToL was found. The results remained unchanged after the age and sex were included in the analysis. The main effect of age remained significant.

Working Memory. Multivariate analyses of variance were conducted using SOPT and FW. Since SOPT is not a standardized measure all analyses were completed controlling for age. Overall presence of comorbid disorders did not have significant effect on working memory

($F(2,351) = .397$, $p = .673$) while significant age effect was observed ($F(2,351) = 22.34$, $p < .001$, $\eta_p^2 = .113$, Power = 1). The results remained not significant after sex and ADHD symptoms were included in the analysis.

A significant multivariate effect of anxiety was observed ($F(2,351) = 3.387$, $p = .035$, $\eta_p^2 = .019$, Power = .636). Children with anxieties obtained significantly lower scores on FW compared with children without anxiety ($F(1,352) = 6.753$, p=.010, $\eta_p^2 = .019$, Power = .736). No other significant effects of comorbid disorders were observed (CD: $F(2,352)$=.497, p=.609; ODD: $F(2,352)$= .433, p= .649). However, when gender was included the effect of anxiety was no longer present ($F(2, 349) = 1.458$, p=.234).

Discussion

The current study examined attention, inhibition and EF in children with ADHD, both with and without comorbid disorders. Our findings suggest that the presence of comorbid disorders at least in part affects children's performance on the examined tasks. First, we found several differences in performance between children with and without anxiety disorders. Specifically, on the CPT, children with anxiety disorders had more difficulty refraining from responding to the non-target stimuli, resulting in higher commission errors. Children with comorbid anxiety disorders were also more inconsistent in response speed (i.e. had a more erratic response style throughout the test). Finally, as the speed between targets increased, their reaction time decreased. Contrary to other reports, we found no interaction between anxiety and gender with respect to performance on the CPT task. In an earlier study, Newcorn et al. (2001) found girls with ADHD and only comorbid anxiety disorders to be less impulsive on CPT than girls with ADHD only. On working memory tasks, children with comorbid anxieties had more difficulty with FW, a spatial working memory task. Comorbid anxiety disorders have been reported to play a significant role in working memory performance in children with ADHD, including diminishing the benefits of treatment with psychostimulants (Bedard & Tannock, 2008; Tannock, Ickowicz, & Schachar, 1995).

The second finding was related to children with comorbid CD, who were found to perform differently on the set-shifting task, but only after age and gender were controlled. Children with CD made more perseverative and non-perseverative errors and therefore completed fewer categories on the WCST. In addition, children with CD had difficulties with initial concept formation and problem solving, as they required more trials to complete the first category. Gender was also found to play a significant role in the performance of this task: girls with CD appeared to be the most disadvantaged as they made the most non-persevarative errors. In addition to differences on the set-shifting task, children with comorbid CD were found to have a lower verbal IQ as compared to children without CD. This finding supports the recent report by Murray and Farrington (2010), who found low IQ to be a predictor of CD. No other differences were found on other measures. Similar to our findings, Barnett, Maruff and Vance (2009) found no differences between children with ADHD and children with ADHD and comorbid CD or comorbid ODD on several working memory and planning tasks; however, their study did not include a set-shifting task.

Identifying the clinical profile of children with ADHD and CD is particularly important for clinical practice. It is well established that the presence of CD is associated with antisocial outcomes and substance use later in life (Brook, Brook, Zhang, & Koppel, 2010; Pardini & Fite, 2010). Further investigation is required in order to identify whether low verbal IQ, in combination with ADHD, and difficulties with cognitive flexibility are risk factors for developing CD in childhood. The current finding suggests that having more severe ADHD symptoms combined with difficulties in verbal communication may exacerbate behavioural problems, resulting in the kinds of disruptive behaviour reflected in a diagnosis of CD.

The third finding was related to gender differences, irrespective of comorbid disorders. We found that boys with ADHD performed better on the planning task than did girls with ADHD. Similarly O'Brien, Dowell, Mostofsky, Denckla and Mahone (2010) compared girls and boys with ADHD on various EF tasks and found that girls demonstrated poorer performance on a planning test. Gender differences in EF performance could be explained by the neuroanatomical brain differences seen between boys and girls. These gender differences may also play a role in the differences seen between boys and girls in the clinical presentation of ADHD.

The overall clinical profile of the sample was similar to those reported in the literature. As expected, many children presented with at least one comorbid disorder (Gau et al., 2010). Multiple comorbidities were also frequent, which is similar to reports in the literature (Larson, Russ, Kahn, & Halfon, 2011; Pliszka, 2000). In a recent publication that reports on data collected in the US from the National Survey of Children's Health, Larson, Russ, Kahn, and Halfon (2011) found that 33% of children with ADHD had at least one comorbid disorder and that 16% had two comorbid disorders. In our sample, the proportion of children with comorbid disorders was larger, and as many as 110 (31%) children had a double diagnosis of either CD and anxiety disorders or ODD and anxiety disorders, in addition to the diagnosis of ADHD. This was expected, since the sample was drawn from clinical population. Also as expected, children without comorbid disorders presented with less severe ADHD symptomatology. ADHD subtypes are not discussed here as the relationship between ADHD subtypes and EF warrants a more thorough examination, which is beyond the scope of this manuscript.

Strength and Limitations

This study has several strengths, the first of which lies in addressing some of the methodological limitations in current literature. The comparably large sample size allowed us to investigate subgroups of children with multiple comorbidities, as well as examine gender differences. All the children in this study underwent a thorough diagnostic process, including clinical diagnosis by a child psychiatrist and parent interviews using a structured DSM-IV interview, which included the level of impairment and interference with functioning in two settings as part of its diagnostic algorithm. The comorbid disorders were identified using the same DSM-IV structured diagnostic interview. The administration of the EF battery was standardised; all children were assessed in the morning to avoid fatigue, and children who were being treated for ADHD symptoms at the time of assessment discontinued their medication at least five days prior to the assessment to control for potential effects of medication on EF task performance.

Alongside these strengths, the study has limitations as well. As we did not include a control group, no comparisons can be made with typically developing children. While the assessments for the comorbid disorders were made using a thorough diagnostic tool used with parents, the study would have benefited from the inclusion of a child report measure of comorbid disorders. Finally, no teacher ratings of ADHD symptoms were included in this analysis.

Conclusion

Our findings demonstrate that the presence of comorbidities and gender differences may explain the heterogeneous nature of ADHD among elementary school-age children. These differences can also contribute to the inconclusive findings previously reported in the literature. Given the reported relationship between EF and social functioning (Miller & Hinshaw, 2010; Rinsky & Hinshaw, 2011) and EF and academic functioning (Miller & Hinshaw, 2010; Rogers, Hwang, Toplak, Weiss, & Tannock, 2011) in individuals with ADHD, identifying EF deficits should be an integral part of assessment, prior to intervention design, for this population.

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Table 1

Demographic and Clinical Characteristics of Children Grouped According to Comorbid Disorder status

	ANX		ODD		CD		No Com.	Total
	Yes n=158	No n=197	Yes n= 152	No n=203	Yes n=45	No n=310	n=110	n=355
Age Mean(SD)	9.43 (1.68)	9.37 (1.65)	9.40 (1.74)	9.39 (1.60)	9.08 (1.55)	9.44 (1.67)	9.37 (1.62)	9.40 (1.66)
VCI Mean(SD)	96.20 (12.86)	96.35 (14.59)	97.62 (14.27)	95.34 (13.50)	92.65 [b] (14.02)	96.83 [b] (13.76)	96.69 (14.30)	96.29 (13.84)
PRI Mean(SD)	101.86 (13.77)	103.32 (14.34)	104.04 (12.84)	101.73 (14.88)	102.77 (14.60)	102.68 (14.04)	102.08 (15.50)	102.69 (14.09)
WMI Mean(SD)	92.33 (12.53)	94.01 (12.26)	95.64* (11.05)	91.58* (13.05)	93.16 (10.92)	93.33 (12.55)	91.94 13.42	93.31 12.38
PSI Mean(SD)	96.88 (13.10)	96.99 (13.76)	99.59** (13.47)	94.98** (13.16)	94.48 (13.78)	97.22 (13.43)	94.71 13.40	96.94 13.46
FSIQ Mean (SD)	96.99 (12.32)	97.4 (13.49)	99.07* (12.18)	95.91* (13.39)	95.93 (13.35)	97.41 (12.93)	96.30 (14.21)	97.22 (12.98)
DISC-IV Inattentive symptoms Mean(SD)	7.29** (2.16)	6.56** (2.28)	7.35** (2.04)	6.54** (2.35)	7.07 (2.39)	6.86 (2.24)	6.30** (2.22)	6.89 (2.26)
DISC-IV Hyperactive symptoms Mean(SD)	5.47* (2.64)	4.79* (2.71)	5.93** (2.43)	4.47** (2.72)	6.78** (1.92)	4.85** (2.71)	3.90** (2.57)	5.10 (2.69)
DISC-IV Total ADHD symptoms Mean(SD)	12.77** (4.05)	11.37** (3.76)	13.28** (3.54)	11.03** (3.97)	13.91** (3.45)	11.71** (3.94)	10.20** (3.54)	11.99 (3.94)

Note: [a] mean; * p<.05; **p<.01; SD = Standard Deviation; VCI = Verbal Comprehension Index; PRI = Perceptual reasoning Index, WMI = Working Memory Index; FSIQ = Full Scale IQ; ANX = anxiety disorders; CD = Conduct Disorder; ODD = Oppositional Defiant Disorder; No Com = no comorbid disorders.

Table 2

CPT and Comorbid Disorders

	Comorbid Disorders							
	Anx		ODD		CD		No Com	Total
	Yes	No	Yes	No	Yes	No		
Omission errors T score Mean(SD)	56.63 (14.81)	56.74 (15.57)	55.61 (14.49)	57.49 (15.71)	59.82 (15.82)	56.28 (15.10)	57.67 (17.94)	56.69 (15.21)
Commission errors T scores Mean(SD)	54.74 (8.01)	53.40 (8.05)	54.55 (8.52)	53.59 (7.68)	53.86 (7.10)	54.02 (8.19)	52.77 (7.88)	54.00 (8.05)
RT T scores Mean(SD)	52.31 (10.38)	51.52 (11.48)	51.06 (11.20)	52.48 (10.83)	53.26 (10.53)	51.67 (11.06)	52.80 (11.52)	51.87 (10.99)
RT Standard Error T scores Mean(SD)	58.66 (10.70)	56.41 (10.30)	57.23 (10.66)	57.57 (10.45)	60.17 (9.52)	57.02 (10.62)	56.28 (10.74)	57.42 (10.53)
RT Block Change T scores Mean(SD)	52.65 (12.62)	51.82 (11.50)	51.52 (11.75)	52.69 (12.20)	55.92 (11.43)	51.65 (12.01)	51.86 (12.13)	52.19 (12.01)
RT Inter –Stimuli - Intervalle T scores Mean(SD)	56.44 (14.65)	54.05 (12.07)	55.29 (13.82)	55.01 (12.98)	55.77 (12.83)	55.03 (13.42)	54.26 (12.82)	55.13 (13.33)

Note: SD = Standard Deviation; RT = Reaction Time; ANX = anxiety disorders; CD = Conduct Disorder; ODD = Oppositional Defiant Disorder; No Com = no comorbid disorders.

Table 3

WCST and Comorbidities

	Comorbid Disorders							
	Anx		ODD		CD		No Com	Total
	Yes	No	Yes	No	Yes	No		
WCST Perseverative responses SS Mean(SD)	97.20 (13.54)	98.99 (13.70)	98.60 (15.26)	97.90 (12.32)	94.9 (13.08)	98.66 (13.67)	99.58 (11.41)	98.20 (13.64)
WCST Perseverative Errors SS Mean(SD)	96.92 (13.43)	99.18 (12.40)	99.18 (13.46)	97.43 (12.43)	94.51 (12.98)	98.71 (12.82)	99.09 (11.59)	98.18 (12.89)
WCST Non Perseverative Error SS Mean(SD)	94.13 (14.58)	95.45 (14.92)	95.41 (15.22)	94.45 (14.43)	92.13 (15.63)	95.26 (14.62)	95.81 (14.52)	94.86 (14.76)
WCST number of categories completed SS Mean(SD)	4.28 (1.82)	4.60 (1.66)	4.48 (1.83)	4.44 (1.67)	3.89 (1.97)	4.54 (1.69)	4.69 (1.55)	4.46 (1.74)
WCST Trials to complete first category SS Mean(SD)	24.73 (28.53)	21.32 (21.97)	22.68 (25.16)	22.96 (25.15)	32.13 (37.45)	21.49 (22.56)	20.33 (20.25)	22.84 (25.12)
SOPT Total Mistakes Mean(SD)	15.68 (7.58)	15.22 (7.58)	15.30 (7.71)	15.53 (6.99)	16.36 (6.35)	15.29 (7.43)	15.43 (7.51)	15.43 (7.302)
FW SS Mean(SD)	9.27 (2.75)	10.06 (2.96)	9.88 (2.95)	9.59 (2.85)	9.29 (2.68)	9.77 (2.92)	9.91 (2.99)	9.71 (2.89)
ToL SS	110.92 (14.32)	108.78 (14.98)	109.99 (15.18)	109.55 (14.38)	110 (13.42)	109.69 (14.91)	109.10 (15.18)	109.74 (14.71)

Note. ANX = anxiety disorders; CD = Conduct Disorder; ODD = Oppositional Defiant Disorder; No Com = no comorbid disorders; WCST = Wisconsin Card Sorting Test; SOPT = Self Ordered Pointing Test; ToL = Tower of London; SS = Standard Score; SD = Standard Deviation.

CHAPTER 4

DISCUSSION

As the most common and heterogeneous psychiatric disorders among school-age children, ADHD continues to attract the attention of researchers. To aid in the understanding of the pathogenesis of ADHD, a number of investigators have focused on finding a common endophenotype for ADHD. In addition to benefiting the genetic research, endophenotypes, heritable traits that indicate an individual's likelihood to develop the disorder (Castellanos & Tannock, 2002), may help identify the pathophysiology of ADHD (Doyle et al., 2005). EF has been identified as one such possible endophenotype, specifically due to observed EF delays in the ADHD population and their unaffected siblings. However, findings in this area have been inconclusive, either because EF deficits are not specific to ADHD, or because of the methodological shortcomings that are found in many studies. For example some studies have small sample sizes, or lack proper diagnoses, while others do not take into consideration confounding factors, such as comorbid disorders and gender. Driven by these observations, the overarching objective of this dissertation was to begin untangling the complex relationship between ADHD and EF, while examining a relatively large clinical population of elementary school-age children clinically diagnosed with ADHD. The aim was to understand the role of the diagnostic subtypes and comorbid disorders, while addressing some of the methodological limitations seen in the literature.

The first study closely examined all three conventional diagnostic categories (DSM-IV subtypes). We also examined the less studied, but newly popular, sub-category: the SCT subtype. The second manuscript focused entirely on an examination of the three most common comorbid disorders: anxiety disorders, ODD and CD. Having a well diagnosed and relatively large sample size (n=363 for manuscript 1, and n=355 for manuscript 2) that included both boys and girls allowed us to study the interaction between comorbid disorders or subtypes and gender in both manuscripts.

Manuscript 1

While the current categorical approach to the disorder has been criticized in recent literature (Brocki, Fan, & Fossella, 2008), many continue to find the categories clinically meaningful, as is reflected in the retention of the three ADHD subtypes in the newly published DSM-5 (Bell, 2011). In this experiment, we found that children with a predominantly inattentive subtype diagnosis performed better than children with a combined subtype diagnosis on some aspects of an attention task. Namely, they made less omission errors, displayed more consistent reaction times during the test, and consistent reaction times independent of the speed at which the stimuli was presented. Once the inattentive subtype was divided into two groups: children with SCT and children with inattentive subtype and sub-threshold hyperactive symptoms (I/subH) — the significant difference was now specific to the SCT subtype, and not to the I/subH subgroup.

An examination of scores revealed that children diagnosed with combined or hyperactive subtypes obtained omission error scores within the mildly atypical range, while children with the inattentive subtype performed within the average range (Conners, 2000). Once the SCT subtype was identified and the data were reanalyzed, the SCT group obtained better scores than I/subH group. A similar pattern between the two groups was seen in reaction time scores.

In this study age was found to be an important moderator; once it was controlled for, the significant findings were no longer present. Moreover, when the subtype profiles were examined, children in the SCT subgroup were found to be significantly older than those in the other groups. In a recent general population study, children in the SCT group were also found to be significantly older than children in the ADHD group (Barkley, 2013). In addition, in our study, most of the attention task variables were correlated with a number of hyperactive symptoms, and not with inattentive symptoms. Gender did not play a significant role on this measure, and there was no interaction between gender and subtypes. These results highlight the important effects of age and hyperactive symptoms on CPT, a widely used attention task.

Findings on most EF measures were not significant in this experiment. Significant differences were found on two measures: the number of mistakes on the working memory task, and the number of categories completed on the WCST. Neither of these variables are age normed however; thus, once age was included in the analysis they were no longer significant.

Given the significant relationship found between age and task performance, as well as age and subtype, we concluded that maturation may be associated with the reduction of hyperactive symptoms, which in turn affects the child's ability to remain on task, resulting in better performance. It has recently been hypothesized that SCT may in fact be a different disorder from ADHD (Lee et al., 2013). Our results suggest that SCT could be included as a separate diagnostic category of ADHD. Our findings also support adopting a developmental and dimensional approach to ADHD diagnosis (Barkley, 2003) as opposed to the current categorical approach.

Manuscript 2

The second experiment undertook to understand what role comorbid disorders play in attention and EF task performance. Comorbid disorders are often overlooked, even though a large proportion of children diagnosed with ADHD exhibit symptoms consistent with other psychiatric conditions. In this experiment, only the three most common disorders were examined: anxiety disorders, oppositional defiant disorder and conduct disorder. On an attention task, children with anxiety disorders were found to be more impulsive, and have more inconsistent reaction times as compared to children without anxiety disorders, independent of age or gender. The effect of age was considerable, while the effect of the anxiety disorders was moderate.

On EF measures, children with anxiety disorders obtained lower scores on a visual special memory task, although the effect was low. After controlling for gender, the results were not significant. Anderson et al. (2001) also reported a significant gender effect on working memory tasks in typically developing children. In the same study, the authors found no gender differences on a planning task (Anderson et al., 2001), our experiment however, reported a significant difference between boys and girls on the same planning task. Wodka et al. (2008) compared children with ADHD to typically developing children and found the planning task to be the best discriminant between girls with ADHD and typically developing girls. Since we found girls with ADHD to have overall poorer performance on the planning task as compared to boys with ADHD, this suggests that girls with ADHD may be particularly disadvantaged on this specific task.

Finally, WCST results indicate that children with CD had significantly more difficulty with this task. They made more perseverative and non-perseverative errors, completed less categories and had more difficulty with initial conceptualization, as reflected in the number of errors made before completing the first category. We then examined whether gender played a role in the performance of this test and found a small gender-by-CD interaction effect. That is, girls with CD obtained the lowest scores on a number of non-preservative errors and needed more trials to complete the first category. This finding suggests that CD in girls and boys may have different presentations. WCST assesses cognitive flexibility, the ability to adjust responses according to feedback from the environment. Impairments in this area can reflect difficulties in adjusting to change, which in turn can result in frustration, leading to the types of behaviour observed in children with conduct disorder. Further investigation is needed to understand these gender differences as it may have significant clinical impact.

In this study, ODD had no effect on any of the examined measures. However, we did find significant differences on several IQ indices between children with and without ODD. Since IQ was not our primary outcome measure, and was only included to describe the population, we did not explore these findings further. Additional investigation of IQ and comorbid disorders is necessary, albeit beyond the scope of these manuscripts.

Conclusion

Our findings support the body of research that views ADHD as a developmental disorder that evolves over time, manifesting differently at different developmental stages rather than presenting as a stable, categorical disorder. They also suggest that SCT may be a distinct subtype of ADHD, and that children with this subtype may be less impaired in some areas as compared to children with other subtype diagnosis. We identified two distinct profiles (a), (b) within the ADHD population and a potential third profile (c): a) inconsistent reaction time and difficulty suppressing response to a non-stimuli distinguished children with anxiety disorders from those without anxiety disorders, b) difficulties in set-shifting distinguished children with conduct disorder from those without conduct disorder, and potentially c) difficulty with concept formation distinguished girls with CD from the rest of the group.

Future Directions

While a great deal of research has been conducted in the area of ADHD and EF, many questions remain unanswered. The findings from our first manuscript call for more longitudinal studies to determine the stability of subtypes, and the role of SCT subtype. If SCT is found to be a disorder distinct from ADHD, then children with this diagnosis may have a different etiology, different risk factors, and require different types of intervention than those practiced with children with ADHD. Thus far, children with SCT have generally been grouped together with ADHD inattentive subtype, which could have contributed to inconsistencies in findings. We suggest that EF may still be a useful endophenotype for a subgroup of ADHD.

Gender differences in clinical presentations of ADHD have been documented. In addition, girls and boys have been shown to have different brain development and maturation patterns (Mahone & Wodka, 2008). Our findings also point to the need to further investigate the cognitive and clinical profile differences between boys and girls with ADHD, differences that may be partly explained by possible anatomical brain differences between the genders. How are these differences reflected in task performance, and everyday functioning? Neuroimaging studies are needed to identify possible correlates between EF and structural and functional brain differences between individuals with ADHD and individuals with ADHD paired with more complex psychopathology.

The subgroup of girls with ADHD and comorbid CD requires more thorough examination focusing on cognitive profile, genetic and environmental risk factors and response to treatment, as it is likely that this subgroup may be distinct from other ADHD groups. Given our results, we can hypothesize that EF (specifically set-shifting) may be a marker for this specific subgroup. Since the proportion of girls with ADHD is relatively small, and the proportion of girls with both ADHD and CD is smaller yet, an even a larger sample of the

ADHD population is required to thoroughly examine this particular subgroup. Understanding the aetiology of combined ADHD and CD diagnosis is particularly important, as CD has been established as an additional risk factor for poor outcomes in adulthood and is thus essential for prevention and intervention programs.

Implications for School Psychology

ADHD has been found to be a strong predictor of poor academic performance in school-age children (Sijtsema, Verboom, Penninx, Verhulst, & Ormel, 2013). Moreover, there is now evidence that EF is also associated with poor school functioning (Clark, Prior, & Kinsella, 2002; Tseng & Gau, 2013). Parents, educators and clinicians face an ongoing challenge: to develop effective tools that will help children adjust to the demands of the school environment, including academic, emotional and behavioural challenges. To embark on such a quest requires an understanding of the underlying deficits associated with ADHD and their interaction with the disorder's developmental course. Integrating specific EF deficits in interventions can bring promising outcomes. For example, Green (2008) describes children with behavioural challenges as children who are lagging in skills that are necessary for completing many day to day tasks, lack that contributes to the behavioural and emotional difficulties observed at schools and at home. Some of these skills are EF skills that Green targets in an intervention programme. More research studies are emerging that assess the effectiveness of interventions specifically designed to improve EF (van de Donk & Lokhorst, 2013).

Schools often put modifications in place for children with ADHD in order to facilitate their learning process. These modifications are most often targeted at behaviours such as fidgeting, distractibility, inattention and slow processing speed. Our study highlights set-shifting, concept formation and working memory, as additional areas that should be targeted to help children with ADHD, particularly children with comorbid CD.

Our study further emphasizes the need to focus special attention on commonly co-occurring disorders, such as anxieties, ODD and CD. The literature demonstrates that it is common to combine ODD and CD into one group, as both disorders are seen as similar in nature. However, our findings suggest that children with CD, in the ADHD population at least, have a distinct EF profile. CD and ADHD have been identified as risk factors for later poor outcomes (Harty, Thorn, Kalmar, Newcorn, & Halperin, 2004). Understanding the types of deficits associated with these two disorders is pivotal in determining what types of intervention may be effective for children with these diagnoses. Our findings suggest that further attention should be paid to additional comorbid disorders, as well as EF deficits associated with more complex presentations of ADHD. The impulsivity and inconsistency seen in anxious children with ADHD, or the difficulty in cognitive flexibility seen in children with CD, could be and should be addressed in school settings to help children master these skills and cope with difficulties. Being aware of differences in clinical presentation between these sub-groups will help teachers and educators better understand their students and the challenges they face daily. Conduct disorder, for example, may now be viewed not only as a behavioural disorder, but rather, as a manifestation of certain behaviours triggered by an underlying cognitive and executive function deficit. Although further research is needed, this knowledge may help psychologists design intervention programs specifically tailored to this population.

In conclusion, the results of our study suggest that children with ADHD and comorbid disorders should have a routine EF assessment to identify possible working memory, cognitive flexibility and other EF deficits. Once identified, the Individualized Educational Plan should include tailored interventions to address the specific deficits discovered.

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