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Attention Deficit Hyperactivity Disorder in adults: Neuropsychological deficits and functional impairments

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Attention Deficit Hyperactivity in Adults with ADHD: Neuropsychological Deficits and Functional impairment

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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To my family

ABSTRACT

The overall aim of the present thesis was to investigate the role of neuropsychological deficits in adult ADHD.

Study I examined the psychometric properties of a new rating instrument, the Adult Executive Functioning Inventory (ADEXI), which focuses on deficits in working memory and inhibition. The internal consistency was high; the test-retest reliability was adequate, whereas the inter-rater reliability was low. The ADEXI correlated significantly with another executive functioning (EF) rating instrument. Few significant relations were found between the ADEXI and neuropsychological test scores. Adults with ADHD reported significantly higher deficits with regard to inhibition and working memory compared to both a clinical and a non-clinical control group.

Study II investigated how well neuropsychological measures can discriminate between adults with ADHD and adults with other psychiatric disorders. Adults with ADHD performed more poorly compared to clinical controls with regard to verbal memory, inhibition, set shifting, fluency, and delay aversion. The results remained significant when controlling for IQ, but only the effects of delay-aversion, fluency, and inhibition remained significant when controlling for basic cognitive functions. Sensitivity and specificity were adequate.

Study III investigated executive deficits and functional impairments in adults with ADHD and adults with other psychiatric disorders. ADHD subgroups with or without executive deficits were compared. Adults with ADHD had greater problems with academic, social, and daily life functioning, as well as with criminality. Adults with ADHD were also more often on sickness benefit, but less often unemployed compared to the clinical control group. The ADHD subgroup with executive deficits had poorer academic functioning, a higher proportion of individuals not working or on sickness benefits, and a higher rate of criminality.

Study IV investigated neuropsychological deficits (working memory, inhibition, planning, switching, fluency, speed of processing, and delay-related behaviors) in older adults with ADHD in comparison with both younger adults with ADHD and healthy older controls. Both variable- and person-oriented analyses were included. Older adults with ADHD differed from healthy controls with regard to working memory, inhibition, speed of processing, and delay-related behaviors. Older adults performed at a similar level with regard to working memory and verbal fluency, but significantly better with regard to inhibition and switching compared to younger adults with ADHD. Twenty percent (20%) of older adults with ADHD did not show a clear deficit in any neuropsychological domain.

In summary, adults with ADHD perform more poorly on neuropsychological tests compared to adults with other psychiatric disorders. There is a link between executive deficits and functional impairments, especially academic/occupational and social functioning. In line with current models of heterogeneity in ADHD, the present thesis has been able to demonstrate that only a subgroup of younger and older adults with ADHD have executive deficits.

LIST OF SCIENTIFIC PAPERS

The present thesis is based on the following publications, which are referred to in the text by their roman numerals (**Study I-IV**):

- I. Holst, Y & Thorell, L. B. (in press). Adult Executive Functioning Disorder (ADEXI): Validity, Reliability and relations to ADHD. *International Journal of Methods in Psychiatric Research*. DOI: 10.1002/mpr.1567
- II. Holst, Y & Thorell, L. B. (2017). Neuropsychological functions in adults with ADHD and adults with other psychiatric disorders: The issue of specificity. *Journal of Attention Disorders*, 21, 137-148.
- III. Holst, Y & Thorell, L. B. (2017). *Functional impairments in adults with ADHD and adults with other psychiatric disorders and links to executive deficits*. Manuscript submitted for publication.
- IV. Thorell, L. B., Holst, Y., Christiansen, H., Kooij, J. J. S., Bijlenga, D & Sjöwall, D. (2017). Neuropsychological deficits in adults age 60 and above with attention deficit hyperactivity disorder. *European Psychiatry*, 45, 90-96.

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LIST OF ABBREVIATIONS

ADEXI	Adult Executive Inventory
ALS	Amyotrophic Lateral Sclerosis
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variances
APA	American Psychological Association
BD	Bipolar Disorder
BDEFS	Barkley's Deficits in Executive Function Scale
BFIS	Barkley's Functional Inventory Scale
BPD	Borderline Personality Disorder
BRIEF-A	Brief Rating Inventory of Executive Function –Adult Version
CD	Conduct Disorder
CANTAB	Cambridge Neuropsychological Test Automated Battery
CHEXI	Childhood Executive Functioning Inventory
D-KEFS	Delis Kaplan Executive System
DSM	Diagnostic and Statistical Manual of Mental Disorders
EF	Executive Functioning
GAI	General Ability Index
IQ	Intelligence Quotient
ODD	Oppositional Defiant Disorder
MMSE	Mini Mental State Examination
MS	Multiple Sclerosis
RT	Reaction Time
SD	Standard Deviation
WAIS	Wechsler Adult Intelligence Scale
WM	Working memory
WURS	Wender Utah Rating Scale

1 INTRODUCTION

Attention Deficit/Hyperactivity Disorder (ADHD) is a psychiatric disorder characterized by inattention, hyperactivity, and impulsivity. ADHD has earlier mainly been diagnosed in children. However, ADHD is no longer seen as primarily a childhood disorder, but a disorder that often remains into adulthood. Its worldwide prevalence has been estimated in a meta-analysis to be 3.4% in children (e.g., Polanczyk, Salum, Sugaya, Caye & Rohde, 2015) and to vary between 1-8% in adults, depending on the population investigated, diagnostic criteria, and data collection method (e.g., review by Ramos-Quiroga, Montoya, Kutzelnigg, Deberdt & Sobanski, 2013). In adulthood, the symptoms of ADHD can be modified, deteriorate or be improved. Both children and adults with ADHD often have deficits in neuropsychological functioning such as planning, working memory, fluency, inhibition, delay aversion, and reaction time variability (see reviews by Boonstra, Oosterlaan, Sergeant, & Buitelaar, 2005; Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005). With regard to functional impairments in major life activities, it was concluded in a European consensus statement on the diagnosis and treatment of adult ADHD that adults with ADHD often have problems in work performance, social relations, and that they are also at risk of criminality and substance abuse (Kooij et al., 2010b). The most problematic impairments seem to be in the domain of work. ADHD is not only associated with much higher levels of unemployment compared to controls – adults with ADHD who are employed experience workplace impairment and reduced productivity, as well as behavioral and emotional issues such as irritability and low frustration tolerance (for a review, see Küpper et al., 2012).

The previous research described above indicates that ADHD is associated with multiple neuropsychological deficits as well as functional impairments in many domains of daily life. However, few studies have compared adults with ADHD to adults with other disorders. In addition, the link between neuropsychological deficits and functional impairments has seldom been examined. Finally, we know very little about ADHD in adults above age 60. The overall aim of the present thesis was therefore to investigate neuropsychological functioning and functional impairments in adult ADHD, including both younger and older adults and comparisons with clinical controls.

1.1 ATTENTION DEFICIT HYPERACTIVITY DISORDER

1.1.1 Diagnostic criteria

In order to meet the criteria for a diagnosis according to the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association [APA], 2013), the individual has to have at least 6 symptoms of inattention and/or hyperactivity/impulsivity (see Table 1), although this has been lowered to 5 symptoms for adults. Symptoms of inattention include for example “failing to give close attention, often make mistakes in work or schoolwork,” “has trouble following instructions, organizing tasks and

activities,” and “avoiding tasks that require mental effort.” Hyperactivity includes symptoms such as “having a tendency to always be on the go,” “restlessness” and “being driven by a motor.” Finally, impulsivity includes symptoms such as “often blurts out an answer before a question has been completed,” “often has trouble waiting his/her turn,” and “often interrupt or intrudes on others” (e.g., butts into conversations or games). The following other criteria for ADHD are also presented in the DSM-5 (APA, 2013): 1) several inattentive or hyperactive/impulsivity symptoms should have been present before the age of 12 years, 2) symptoms should be present in two or more settings, (e.g., at school, at home, at work, with friends or relatives; in other activities), 3) there should be clear evidence that the symptoms interfere with, or reduce the quality of, social, school, or work functioning, 4) the symptoms should not occur only during the course of schizophrenia or another psychotic disorder, and 5) the symptoms are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder or a personality disorder).

Previous editions of the DSM did not provide appropriate guidance to clinicians in diagnosing adults with the condition. In the latest, 5th edition (APA, 2013), the symptom criteria for ADHD have therefore been updated to more accurately characterize symptoms common in adults. This revision is based on nearly two decades of research showing that ADHD, although a disorder that begins in childhood, can continue through adulthood for some people. By adapting criteria for adults, DSM-5 aims to ensure that children with ADHD can continue to get care throughout their lives if needed. More specifically, the symptom criteria have been updated to include examples of the ability to function at work (e.g., overlooks or misses details, work is inaccurate, fails to return calls, and finish reports), as well as an explanation of how hyperactivity during childhood can develop into feelings of inner anxiety and restlessness in the adult individual.

1.1.2 ADHD subtypes

According to DSM-5 (APA, 2013), ADHD is divided into three subtypes: predominantly inattentive, predominantly hyperactive/impulsive, and combined subtype. The predominantly hyperactive/impulsive type often develops during early childhood, whereas the inattentive symptoms often emerge during the first school years (Loeber, Green, Lahey, Christ, & Frick, 1992). It has been suggested that the hyperactive/impulsive type is a developmental forerunner to the combined type before inattentive symptoms become more apparent (Barkley & Murphy, 1998). Hyperactive/impulsive symptoms seem to decline during adolescence (Biederman, Mick & Faraone, 2000), whereas levels of inattentive symptoms continue into adulthood (Wilens et al., 2009). Concerning differences between ADHD subtypes, some studies have reported significant differences with regard to daily life functioning or comorbidity. For example, adults with the hyperactive/impulsive or inattentive subtype have been shown to have more problems with substance abuse compared to adults with the inattentive subtype (e.g., McGough et al., 2005; Sobanski et al., 2008).

Table 1. Abbreviated DSM-5 Symptom Criteria for ADHD (APA, 2013)

A persistent pattern of inattention and/or hyperactivity-impulsivity as characterized by (1) and/or (2). For each domain, six or more (five for age 17 or above) symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

1. Inattention

- Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).
- Often has difficulty sustaining attention in tasks and play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).
- Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).
- Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., start tasks but quickly loses focus and is easily sidetracked).
- Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).
- Often avoids, dislikes, or is reluctant to do tasks that require mental effort (e.g., schoolwork, or homework; for older adolescents and adults; preparing reports, completing forms, reviewing lengthy papers).
- Often loses things necessary for tasks and activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).
- Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).
- Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).

2. Hyperactivity and Impulsivity

- Often fidgets with or taps hands or feet, or squirms in seat.
- Often leaves seat in situations when remaining seated is expected (e.g., leaves his/her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).
- Often runs about or climbs in situations where it is not appropriate (Note: for adolescents or adults may be limited to feeling restless).
- Often unable to play or take part in leisure activities quietly.
- Is often "on the go" acting as if "driven by a motor" (e.g., is unable to be or uncomfortable being still for an extended period, such as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).
- Often talks excessively.
- Often blurts out an answer before a question has been completed (e.g., completes people's sentences; cannot wait for turn in conversation).
- Often has trouble waiting his/her turn (e.g., while waiting in line).
- Often interrupts or intrudes on others (e.g. butts into conversations, games, or activities; may start using other people's things without asking, for adolescents and adults may intrude upon or take over what others are doing).

1.1.3 Etiology of ADHD

The etiology of ADHD still remains relatively unclear. However, family studies in clinical samples suggest an increased familial liability for adult ADHD compared to ADHD in children. Both common and rare genetic variants exist (for a review, see Franke et al., 2012). Twin studies have shown a 76% heritability and a very large number of genes seem to be involved in the etiology of ADHD (e.g., Burt, 2009; Faraone et al., 2005). The genetic influence should be considered the most important factor in the etiology of ADHD. However, it has also been argued that different family-environmental factors (e.g., complications during pregnancy or delivery, and a dysfunctional home environment) can also play an important role (for a review, see Tarver, Daley & Sayad, 2014). More specifically, environmental factors are believed to influence the development of the disorder over time and what type of comorbid disorder an individual with ADHD might develop.

1.1.4 Sex differences

ADHD is diagnosed more often in boys than girls during childhood. According to a meta-analysis by Gaub and Carlson (1997), ADHD is estimated to occur two to nine times more frequently in boys. In addition to sex differences in frequency of the disorder, they also found that girls with ADHD had greater intellectual impairments, lower ratings on hyperactivity, and lower ratings on externalizing and internalizing problems compared to boys with ADHD. A few years later, Gershon (2002) more or less replicated the results from this meta-analysis. Other studies have also found that boys with ADHD exhibit more disruptive and behavioral disorders and more learning problems than girls with the same disorder and that boys are therefore more likely to be referred for clinical evaluation (Biederman et al., 2002).

In studies of adults, the male-female ratio is not as uneven as it is for children. For example, Corbisiero, Hartmann-Schorro, Riecher-Rössler and Stieglitz (2017) found a balanced sex ratio when screening for adult ADHD in an outpatient population. With regard to other gender differences in adult ADHD, one of the largest studies in this area investigated the effects of ADHD, gender, and rates of psychiatric comorbidity and cognitive functioning in 219 adults with ADHD and 215 normal control subjects (Biederman, Faraone, Manuteaux, Bober, & Cadogen, 2004). Both males and females displayed the same ADHD symptom clusters of inattention, impulsivity, and hyperactivity. However, there were some differences with regard to the distribution of ADHD subtypes, with the inattentive subtype being more common in females. Females with ADHD also had significantly lower rates of conduct disorder and antisocial personality disorder compared to males. Both genders were shown to be at higher risk of substance use disorder compared to normal controls, although substance use disorder was more prevalent in ADHD males than in ADHD females. Further, this study showed similar impairment for ADHD males and females concerning psychosocial, cognitive, and school functions. Depression and anxiety were the most common comorbid disorders in both genders.

1.1.5 Main comorbid disorders in ADHD

The majority of children with ADHD develop comorbid disorders including externalizing disorders such as oppositional defiant disorder (ODD) and conduct disorder (CD), as well as internalizing disorders such as depression and anxiety disorders (Hofvander, Ossowski, Lundström & Ankarsäter, 2009). In adult ADHD, the most common comorbid disorders are the following: mood disorders (e.g., depression, anxiety, and bipolar disorder), personality disorders, and substance use disorders (Murphy & Barkley, 1996; Spencer, Biederman & Mick, 2007). It has been suggested that 90% of adults with ADHD have one or more comorbid psychiatric disorders (Nutt et al., 2007). The high rate of comorbid disorders in adult ADHD adds to the complexity of the disorder and renders an ADHD diagnosis more difficult to make in adults (Kooij et al., 2012). Among individuals referred to a psychiatric assessment in adulthood and later diagnosed with ADHD, ADHD symptoms have often not been recognized initially and they have instead been treated for other psychiatric disorders during childhood (Torgersen, Gjervan & Rasmussen, 2006). One reason why ADHD symptoms go unrecognized is that disorders such as depression, posttraumatic stress disorder, learning deficits, intellectual disability, and autism all include symptoms that can resemble those found in ADHD. In the present thesis, the most frequent comorbid disorders in the clinical control group are mood disorders (depression, anxiety, and bipolar disorder) and personality disorders. Thus, I will describe the link between ADHD and these disorders in more detail and only mention other comorbid disorders briefly.

1.1.5.1 Depression and anxiety disorders

In adults with ADHD, a prevalence of 18.6%-53.3% has been estimated for depression and of 47%-50% for anxiety disorders, depending on the type of sample investigated (for a review, see Katzman, Bilkey, Chokka, Fallu & Klassen, 2017; Kessler et al., 2006). With regard to patients with depression or anxiety, one study showed that a total of 22 out of 114 patients (19.3%) received an ADHD diagnosis, and the subgroup of patients with comorbid ADHD scored significantly higher on depression than did non-ADHD patients (Pehlivanidis, Papanikolaou, Spyropoulou & Papadimitriou, 2014). In another study of depressed patients, the occurrence of ADHD was found to be 7.5% compared to 3.3% in a normal control group (Di Nicola et al., 2014). A study from the Oregon Adolescent Depression Project (Meinzer et al., 2013) examined predictors of first-onset of depression in a young adult sample. People with childhood onset of ADHD had a significantly higher risk of developing depression through early adulthood (age 30) than did those without ADHD. ADHD remained a significant predictor of depression after controlling for gender, other psychiatric disorders, social and academic impairment, stress and coping in adolescence. Differences between studies regarding the percentage of ADHD patients with comorbid depression and anxiety are likely to be at least partly dependent on the characteristics of the sample, with higher prevalence of comorbid disorders being found in clinically-referred samples compared to population-based samples.

1.1.5.2 Bipolar disorder

Bipolar disorder (BD) and ADHD share some clinical characteristics such as hyperactivity, impulsivity, distractibility, high energy level, talkativeness, and shortened sleep duration. However, BD can be differentiated by episodic mood symptoms, which are not as prominent in ADHD. In a review conducted by Kent and Craddock (2003), support was found for a relation between some ADHD and manic-like symptoms in children. There are only a few available studies on BD and ADHD in adults. The presence of ADHD in bipolar disorder has been estimated at between 9.5% and 21.2%, and rates of bipolar disorder in ADHD at between 5.1% and 47.1% (e.g., Wingo & Ghaemi, 2007). In addition, Wilens, Biederman, Wozniak, Gunawardene, Wong and Monuteaux (2003) showed that a majority (88%) of adults with comorbid ADHD and BD had Bipolar type II (i.e., primarily depressive periods and only mild periods of hypomanic symptoms) and only a minority had Bipolar type I (i.e., regular periods of depressive symptoms followed by periods of manic symptoms). In addition, compared to the ADHD group without BD, the group with comorbid ADHD+BD had more symptoms of inattention, a larger number of other comorbid psychiatric disorders, and poorer overall functioning, compared to adults with ADHD without BD.

1.1.5.3 Personality disorders

ADHD has also been shown to be associated with personality disorders (Kooij et al., 2012). The prevalence of comorbid personality disorders in adults with ADHD has been estimated to be more than 50% (Katzman et al., 2017). Especially Borderline Personality Disorder (BPD) shares some core clinical features with ADHD, such as impulsivity and easily aroused aggression. In a study investigating differences between patients with ADHD, BPD, comorbid BPD+ADHD, and healthy controls, results showed that ADHD and BPD+ADHD patients displayed a higher level of impulsivity than both BPD only and controls without any psychiatric disorders. BPD+ADHD patients also had a higher level of substance abuse and displayed more aggression compared to the healthy control group and the pure ADHD group (Prada et al., 2014). Davids and Gastpar (2005) conducted a systematic review of observational and experimental studies demonstrating the differences and similarities between BPD and ADHD. A significant association between ADHD and BPD was found in relation to deficits in affect, regulation and impulse control, substance abuse, and disturbed relationships.

Previous research has also shown that ADHD symptoms in childhood are considered important risk factors for the development of antisocial personality disorder in adulthood (Babinski, Hartsough & Lambert, 1999; Holmes, Slaughter & Kashani, 2001; Lundström et al., 2014; Mordre, Groholt, Kjelsberg, Sandstad & Myrhe, 2011). It has been suggested that high levels of comorbid conduct problems in children with ADHD might explain this link. However, a recent review by Storebö and Simonsen (2016) concluded that there is an increased risk for later onset of antisocial personality disorder in children with ADHD, both with and without comorbid conduct disorder.

1.2 THEORIES OF NEUROPSYCHOLOGICAL FUNCTIONING IN ADHD

1.2.1 Barkley's hybrid model of executive functioning

Executive functioning (EF) can be described as an umbrella term for various complex cognitive processes and sub-processes that are necessary to maintain goal-directed behavior and, in turn, to achieve future goals (e.g., Welsh & Pennington, 1988). EF involves processes such as planning, working memory, set shifting, and inhibition. Successful performance on EF tasks is dependent on normal prefrontal cortex functioning. However, recent theories have suggested that subcortical regions may also play a key role (e.g., Elliott, 2003). In Barkley's hybrid model, response inhibition is seen as a central deficit in ADHD (Barkley, 1997).

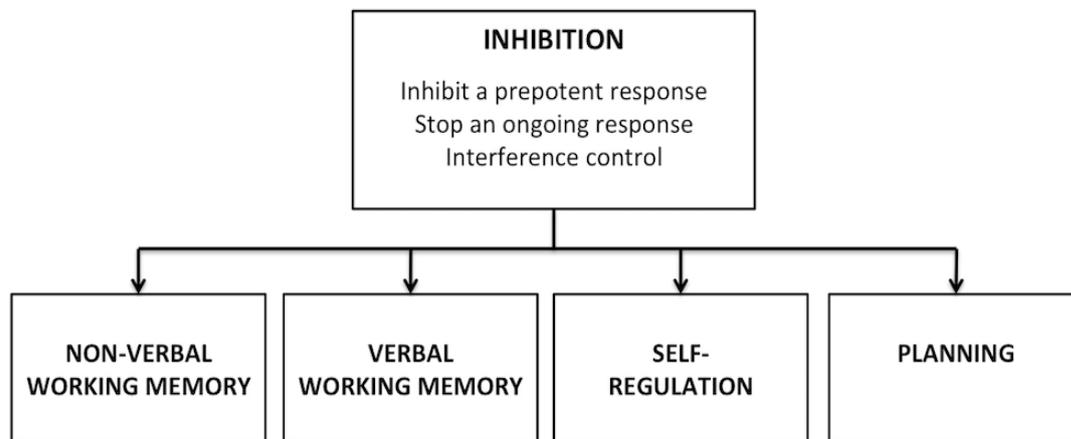


Figure 1. Simplified version of Barkley's Hybrid Model (Barkley, 1997)

Inhibition is the ability to resist impulses and stop a behavior at the appropriate time in order to choose another, more accurate response. In his model, Barkley refers to three distinct inhibitory processes: 1) inhibiting the initial response to an event so as to create a delay in responding, 2) interrupting an ongoing ineffective response in order to reevaluate the response and, 3) protect the goal-directed behavior from distraction and interference (see Figure 1). Inhibition is then believed to lead to secondary deficits with regard to four other executive functions: 1) non-verbal working memory, 2) verbal working memory, 3) self-regulation, and 4) planning. Working Memory (WM) refers to the ability to hold information in mind in order to complete a task. WM is important for carrying out activities in multiple steps, completing mental manipulations and following complex instructions. With regard to self-regulation, Barkley involves the regulation of emotion, arousal and motivation. Planning refers to the ability to set goals, develop strategies, and outline tasks and schedules to accomplish the goals.

A considerable body of previous research in children has supported a link between ADHD and executive deficits (e.g., Nigg, 2005; Willcutt et al., 2005), although as described further below, there are also subgroups of children with ADHD without these deficits (Nigg et al.,

2005). There are by now also a number of reviews on adult ADHD showing general executive deficits (e.g., Boonstra, Oosterlaan, Sergeant, & Buitelaar, 2005; Seidman et al., 2004), as well as support for Barkley's claim of an especially strong link between ADHD and inhibitory deficits (Boonstra, Kooij, Oosterlaan, Sergeant & Buitelaar, 2010).

1.2.2 Sonuga-Barke's dual pathway model

The dual-pathway model includes two ways of describing ADHD symptoms. The first pathway is characterized by deficits in executive functioning in the same way described in Barkley's hybrid model above. The second pathway is characterized as being dependent on the individual's motivation, and it has most often been operationalized as delay aversion, e.g., the tendency to choose a small immediate reward instead of a larger reward presented later (Sonuga-Barke, 2002).

In support of this model, previous studies on children have found independent effects of inhibition and delay aversion in relation to ADHD (Sonuga-Barke, Dalen & Remington, 2003). Thus, delay aversion does not appear to be just a secondary consequence of poor inhibitory control, but a central aspect of ADHD. However, previous studies have also found that the link between ADHD and delay aversion appears to be greatest during preschool (see Pauli-Pott, Dalir, Mingebach, Roller & Becker, 2014), and studies of school-aged children have failed to find significant differences between children with ADHD and controls (e.g., Scheres et al., 2006). It is not clear whether this reflects true age differences in the strength of the relation between ADHD and delay aversion, or whether this is a measurement issue (i.e., delay aversion tasks might be more suitable for younger children).

With regard to the link between ADHD and delay aversion in adults, few studies have examined this issue. However, a few studies using computerized tasks have found that adults with ADHD are more delay averse than normal controls are (Marx et al., 2010; Zhijie, Harrow, Song, Rucklidge & Grace, 2013), and self-ratings of delay aversion and delay discounting have been shown to be significantly related to ratings of ADHD symptoms in normally developing adults (Clare, Helps, & Sonuga-Barke, 2010). Another study found that delay aversion was specifically associated with ADHD combined and hyperactive type, but not with the inattentive type (Scheres, Lee, & Sumiya, 2007).

1.2.3 Sergeant's Cognitive Energetic Model

According to Sergeant's (2005) Cognitive Energetic Model, another factor of importance for ADHD is reaction time (RT) variability. In Sergeant's model, RT variability is regarded as a measure of state regulation (i.e., a measure of whether the individual has the energy necessary to meet task demands). High RT variability has been consistently associated with ADHD among children (for a review, see, e.g., Castellanos, Sonuga-Barke, Milham & Tannock,

2006), but there are far fewer studies on adults. However, existing studies do indicate that high RT variability is a prominent feature of ADHD in adulthood as well (for a review, see Klein, Wendling, Huettner, Ruder, & Peper, 2006). One study even reported that measures of RT variability showed the largest group differences both when comparing adults with ADHD with normal controls and when comparing them with adults with anxiety disorders (Epstein, Johnson, Varia, & Conners, 2001).

1.3 FUNCTIONAL IMPAIRMENTS IN ADHD

Many adults with ADHD have problems with major life activities, such as poor academic achievement and work performance, poor social relations, criminality and substance use (Barkley, Fischer, Smallish & Fletcher, 2006; Biederman et al., 2006b; Kooij et al., 2010b). In addition, ADHD in childhood is a major predictor of an array of physical, mental, and financial problems in adulthood (Brook, Brook, Zhang, Zeltser & Finch, 2013). Academic outcomes over time were found to be adversely affected by ADHD, but could improve with pharmacological, non-pharmacological, and multimodal treatment (for a review, see Arnold, Hodgkins, Kahle, Madhoo & Kewley, in press). In the present thesis, we focus on the following domains: academic/occupational functioning, social functioning, and criminality. The link between these domains and ADHD are therefore described in more detail below.

The most problematic impairments in ADHD seem to be in the domain of work. For example, Gjervan, Torgersen, Nordahl, and Rasmussen (2012) investigated the prevalence of functional impairments and occupational status in a clinically referred sample of 149 adults with ADHD. Only 22.2% had ordinary work as their main source of income, compared with 72% in the general population. In addition to high rates of unemployment, adults with ADHD who are employed experience workplace impairment and reduced productivity, as well as behavioral and emotional issues such as irritability and low frustration tolerance (for a review, see Küpper et al., 2012). With regard to other functional impairments, Küpper and colleagues (2012) showed that adults with ADHD are at increased risk of experiencing accidents, trauma and workplace injuries. The review also emphasized that indirect effects of ADHD on occupational health include poor academic achievement and increased rates of both substance abuse and criminality. Overall, ADHD in adults has a substantial economic impact as a result of absenteeism and lost productivity.

Adults with ADHD often experience social and interpersonal difficulties (Biederman et al., 1993; Kooij et al., 2010b; Rapport, 2002; Wilens & Dodson, 2004). More specifically, they more often than controls have unstable relationships and marital difficulties, resulting in higher rates of separation and divorce (Barkley, 2002; Weiss & Murray, 2003). Able, Johnston, Adler and Swindle (2007) also found that undiagnosed adults with ADHD scored higher on a scale measuring social difficulties, and displayed higher likelihood of being separated, divorced, or remarried compared to adults without ADHD.

The co-existence of an antisocial personality disorder and ADHD can contribute to and constitute the foundation for later development of criminal behavior (Mannuzza, Klein & Moulton, 2008; Satterfield et al., 2007; Söderström, Sjödin, Carlstedt & Forsman, 2003). Previous studies have suggested that 40% of long-term adult inmates in prisons have ADHD (Ginsberg, Hirvikoski & Lindfors, 2010). Finally, adults with ADHD are also at risk for health-related impairments such as physical injuries, suicide, obesity, diabetes, sleep, and substance abuse (for a review, see Nigg, 2013).

1.4 THE LINK BETWEEN NEUROPSYCHOLOGICAL DEFICITS AND FUNCTIONAL IMPAIRMENTS

As described above, individuals with ADHD often have functional impairments, at least when comparing them with normal controls. However, there is great variation within the group of individuals with ADHD, with some functioning relatively well in daily life. It is thus important to further understand the reason for this variation in impairment among adults with ADHD. One possible reason for it is that ADHD is a heterogeneous disorder with regard to its underlying neuropsychological deficits, with only a subgroup having pronounced executive deficits (e.g., Nigg et al., 2005). It should therefore be considered important to investigate the link between neuropsychological deficits and the functional impairments associated with ADHD. If it can be shown that, for example, deficits in working memory can explain poor academic achievement among individuals with ADHD, this would allow us to identify a subgroup with especially high risk of poor academic performance. In addition, this would provide important information about what areas to target in interventions focused on improving daily functioning among individuals with ADHD.

Few previous studies have examined the link between neuropsychological deficits and functional impairments in individuals with ADHD. However, Barkley and colleagues conducted two studies in which they showed that poor executive functioning appears to be a good predictor of occupational status among adults with ADHD, with relations being stronger for rating instruments of executive functioning compared to laboratory tasks (Barkley & Murphy, 2010; Barkley & Fischer, 2011). In addition, Halleland, Sörensen, Posseryd, Haavik and Lundervold (in press) compared adults with ADHD with and without executive function deficits. The results showed that 100% of the ADHD patients without executive deficits were employed compared to only 6.7% of ADHD patients with such deficits. The ADHD group with executive function deficits also had a higher frequency of reading and writing problems. However, no group differences were found with regard to psychiatric comorbidity. Concerning the link between delay aversion and functional impairments, two recent studies have addressed this issue. The first showed that adults with ADHD were more likely to meet criteria for problem gambling than normal controls were, and that probability discounting, but not delay discounting, explained a significant amount of the variance in gambling-related measures after controlling for ADHD symptoms (Zhijie et al., 2013). In the second study,

ratings of delay-related behavior were significantly associated with substance abuse, criminality, and money management (Thorell, Sjöwall, Mies, & Scheres, 2017).

The findings presented above suggest that different neuropsychological functions might explain at least some of the variance in functional impairments among individuals with ADHD. However, only a few studies are available and we need further studies to gain more knowledge about the link between different types of neuropsychological functions and functional impairments in adult ADHD.

1.5 CRITICAL ISSUES IN RESEARCH ON ADULT ADHD

1.5.1 The importance of short screening instruments

Previous research has shown that neuropsychological tests are generally only weakly related to everyday abilities that are believed to be dependent on well-functioning executive skills such as academic achievement, social relations, work performance, criminality, and substance abuse (Barkley & Fischer, 2011; Barkley & Murphy, 2010; Barkley & Murphy, 2011; Szuromi, Bitter, & Czobor, 2013). On the other hand, EF deficits measured through self-ratings have been shown to be strongly linked to functional impairments, and EF tests and EF ratings have shown only weak correlations (Barkley & Fischer, 2011; Barkley & Murphy, 2010). It has therefore been argued that EF tests should not be relied on as the sole source when measuring EF deficits. However, existing EF rating instruments have some important limitations. First, most of them include items measuring ADHD symptoms. Second, the available rating instruments often capture general cognitive functioning (e.g., information processing) or emotion regulation. Third, the rating instruments are often long, making it difficult for a person with ADHD and executive function deficits to answer all the questions. This emphasizes the need for a short screening instrument capable of assessing EF deficits.

Thorell and Nyberg (2008) developed a questionnaire for measuring executive functions in children called the Childhood Executive Functioning Inventory (CHEXI). To allow measurement of EF in adults as well, an adult version of the CHEXI – the Adult Executive Functioning Inventory (ADEXI) – will be introduced as part of the present thesis.

1.5.2 The importance of including a clinical control group

It is well known that symptoms of ADHD, especially inattention, are unspecific and can be found in many other psychiatric disorders (e.g., Tamm et al., 2012). With regard to neuropsychological functioning, deficits in executive functioning have been reported in patients with depression (e.g., Godard, Grondin, Baruch, & Lafleur, 2011; Gohier et al., 2009; Hammar, Strand, Årdal, Schmid, Lund & Elliot, 2011; Rose & Ebmeier, 2006), bipolar

disorder (e.g., Godard et al., 2011; Robinson et al., 2006), general anxiety disorder (Gualtieri & Dexter, 2008), and obsessive compulsive disorder (Vandborg, Hartmann, Egedal Bennedsen, Pedersen, & Thomsen, 2014; Bannon, Gonsalvez, Croft, & Boyce, 2006). These studies have made comparisons with normal controls. Thus, a serious limitation of previous research is that few studies have made a direct comparison between adults diagnosed with ADHD and adults with other psychiatric disorders. To what extent neuropsychological deficits are specifically linked to ADHD will therefore be addressed here.

1.5.3 The issue of sensitivity and specificity

One important limitation of previous research is that most studies have only investigated group differences, even though it has been argued that group differences alone are insufficient indices of the discriminant ability of neuropsychological measures (Doyle, Biederman, Seidman, Weber, & Faraone, 2000). Discriminant ability should preferably be examined using measures of sensitivity and specificity. Specificity is the probability of a normal test score given that a person does not have the diagnosis. Sensitivity is the probability of an abnormal test score given that the person has the diagnosis. Studies of children have found that neuropsychological tasks are better at excluding normal children from the ADHD category than at confirming ADHD in children diagnosed with the disorder (e.g., Barkley & Grodzinsky, 1994; Doyle et al., 2000). Thus, neuropsychological tests generally have high specificity, but lower sensitivity. Similar conclusions have been drawn in samples of ADHD adults (e.g., Lovejoy et al., 1999), but very few studies have examined this issue. Not only is it important to examine sensitivity and specificity when comparing patients with ADHD and healthy controls. If a neuropsychological test is considered to have good discriminatory ability for ADHD, it should also be able to discriminate between ADHD and other psychiatric disorders. The present thesis will therefore include direct comparisons of individuals with ADHD and clinical controls, and group differences as well as measures of sensitivity and specificity will be presented.

1.5.4 Control for basic cognitive functioning

In order to conclude that deficits in executive functioning are of central importance in ADHD, it is necessary to use adequate control variables (Boonstra et al., 2010). Previous studies are limited in that they have not controlled for basic cognitive processes such as speed, perception and memory. However, it has been argued that performance on EF tasks is dependent on these basic processes, and when using such measures as control variables, significant group differences between adults with ADHD and normal controls were only found for inhibition and set shifting (Boonstra et al., 2010). Thus, there appears to be an important overlap between deficits in executive functioning and more general intellectual functioning in adults with ADHD. In the present thesis, we aim to explore this issue further

by comparing adults with ADHD and a clinical control group as well as by controlling for basic cognitive functions.

1.5.5 Studying ADHD in older adults

It is currently well known that ADHD often persists into adulthood. However, very few studies have included patients 60 years of age and above. This is an important limitation, as making the transition into old age poses specific challenges that might be especially problematic for individuals with ADHD. These challenges can include, for example, increasing somatic problems and loss/illness of one's partner. It is therefore of great importance that more studies be carried out to increase our knowledge about ADHD in this age group, thereby allowing psychiatric clinics and care centers to provide the help that is needed. In the present thesis, we aim to explore this issue by comparing older adults with ADHD not only with healthy controls, but also with younger adults with ADHD. Such a comparison could identify important age-specific obstacles in this disorder.

1.6 AIMS OF THE PRESENT THESIS

The overall aim of the thesis is to investigate the role of neuropsychological deficits in adult ADHD. More specifically, the four studies included in the thesis addressed the following research questions:

- 1) What are the psychometric properties of the ADEXI, a brief screening instrument for assessing inhibition and working memory? (**Study I**)
- 2) Do adults with ADHD have more severe neuropsychological deficits compared to adults with other psychiatric disorders? (**Study II**)
- 3) Do possible group differences in neuropsychological functioning between adults with ADHD and adults with other psychiatric disorders remain significant when controlling for basic cognitive functioning? (**Study II**)
- 4) Do adults with ADHD have more severe functional impairments compared to adults with other psychiatric disorders (**Study III**)
- 5) Do ADHD subgroups with and without executive deficits differ with regard to functional impairments? (**Study III**)
- 6) Are older (age 60-75 years) adults with ADHD deficient with regard to executive functioning when compared to either younger adults (age 18-45) with ADHD or older healthy controls? (**Study IV**)
- 7) What is the link between neuropsychological deficits and daily life functioning in older adults with ADHD? (**Study IV**)

2 SUMMARY OF EMPIRICAL STUDIES

2.1 STUDY I

Adult Executive Functioning Inventory (ADEXI): Validity, reliability, and relations to ADHD.

2.1.1 Aims and background

As described in the introduction above, adult patients with ADHD often have deficits in executive functioning, and as a consequence of this they have difficulties completing long rating instruments. Thus, there is a need for short and comprehensive screening instruments that can assess different aspects of EF deficits such as working memory and inhibition in a valid and reliable way. It is important that a new rating instrument capture executive deficits specifically, as one limitation of available instruments is that they often include items measuring cognitive functioning more generally or ADHD symptom levels.

To address the limitations of available EF rating instruments, the overall aim of Study I was to examine the psychometric properties of the ADEXI, a newly developed rating instrument. The ADEXI is an adult version of the CHEXI (Thorell & Nyberg, 2008). The child version is used for ratings made by either parents or teachers. The ADEXI will be developed as a self-rating instrument and an instrument used by a relative or close friend. More specifically, the present study aimed to address the following aspects:

- 1) Use factor analysis to investigate whether the two major factors found for the childhood version of the questionnaire (i.e., inhibition and working memory) can be replicated using the ADEXI.
- 2) Study the reliability of ADEXI scores.
- 3) Study the convergent validity of the ADEXI by investigating the association between ADEXI scores and scores from both another EF rating instrument and laboratory measures of executive functioning.
- 4) Examine to what extent ADEXI scores can be used to discriminate between adults with ADHD and adults either with or without another psychiatric disorder.

2.1.2 Method

2.1.2.1 *Participants and procedure*

Study I included 202 participants from three groups: a clinical group of adults with ADHD (n = 51, 39% men); a clinical group of adults diagnosed with other psychiatric disorders (n = 46, 28% men); and a non-clinical sample consisting of individuals from a random sample and a

sample of university students ($n = 105$, 42% men). The groups did not differ significantly from one another with regard to age, $F = 1.23$, *ns* (ADHD group: $M = 27.43$, $SD = 6.31$; Clinical controls: $M = 25.65$, $SD = 4.76$; Non-clinical controls: $M = 26.50$, $SD = 5.57$) or gender ($\chi^2 = 2.56$, *ns*). However, there was a significant difference with regard to educational level. The two clinical groups had a similar educational level, but they both had a lower educational level compared to the non-clinical controls.

The participants in the two clinical samples were recruited through advertisements at three outpatient psychiatric clinics, and they visited the clinic on two occasions to perform the neuropsychological testing. Questionnaire data were also collected from a close relative or friend of each participant. The participants in the ADHD group underwent a neuropsychiatric assessment conducted by a licensed psychologist. The assessment included a clinical judgment using the second version of the Diagnostic Interview for ADHD in Adults (DIVA 2.0; Kooij & Francken, 2010a). This semi-structured interview consists of two parts: one for assessing the presence of all 18 criteria in the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; APA, 1994) during childhood and in the present; the other for assessing impairment in five areas of functioning (i.e., education, work, family, social/relationships, and self-confidence) in childhood and in the present. In addition, current levels of ADHD symptoms were assessed using self-report on the Adult ADHD Self-Report Scale (ASRS-v1.1; Kessler et al., 2005). The psychologist also interviewed a close relative of the participant, in most cases his/her mother, to obtain a detailed anamnesis. All participants in the ADHD group met the full diagnostic criteria according to the DSM-5 (APA, 2013). Finally, all participants underwent testing of global intellectual ability using the fourth edition of the Wechsler Adult Intelligence Scale (WAIS-IV; Wechsler, 2008). Exclusion criteria were an IQ score of < 80 on WAIS-IV and the presence of substance-related disorders. In addition to a primary ADHD diagnosis, participants in the ADHD group also met the criteria for the following comorbid diagnoses: mood disorders including “major depression” (15.8%), bipolar disorder (5.3%), unspecified anxiety disorder (UNS) (5.3%), panic disorder (3.5%), obsessive compulsive disorder (1.7%), social phobia (1.7%), and personality disorders (5.3%). Five of the participants had more than one comorbid diagnosis.

The diagnoses in the clinical control group were the following: mood disorders including “major depression” (43.4%), bipolar disorder (11.3%), anxiety disorder UNS (15.1%), social phobia (9.4%), panic disorder (1.8%), obsessive compulsive disorder (5.7%), general anxiety disorder (5.7%), posttraumatic stress disorder (5.7%), eating disorders (1.8%), and personality disorders (11.3%).

The study also included two non-clinical groups – a random sample and a sample of university students – which were combined in all analyses included in the present study. The random non-clinical sample of adults was recruited from a larger random sample recruited from a national population-based register. From this sample, a subsample of 44 adults (41% men) matched to the clinical ADHD sample with regard to age and gender were included in the present study. In addition, a convenience sample of university students ($n = 61$, 43% men)

was recruited through advertisements on the university campus. The exclusion criterion in the two non-clinical control groups was the presence of any psychiatric disorder.

2.1.2.2 Measures

ADEXI. The ADEXI is a 14-item questionnaire measuring working memory and inhibition. Several of the items from the CHEXI are also included in the ADEXI. However, a few items that were considered irrelevant to adults (e.g., “Has difficulty following through on less appealing tasks unless he/she is promised some type of reward for doing so”) were deleted. We also tried to minimize item overlap so the ADEXI could be completed as quickly as possible (14 items in the ADEXI versus 24 in the CHEXI), while still including enough items to capture the most central aspects of working memory and inhibition.

BDEFS. In addition to the ADEXI, the non-clinical sample also completed Barkley’s Executive Functioning Scale (BDEFS; Barkley, 2011a). The BDEFS includes the following six subscales: Self-organization/Problem Solving (24 items), Self-management of Time (21 items), Self-restraint/Inhibition (19 items), Self-regulation of Emotion (13 items), and Self-motivation (12 items). There is also a short version of the BDEFS, which includes 20 items.

Working memory was measured by two subtests from the WAIS-IV (Wechsler, 2008): Letter-Number Sequencing and Digit Span. In Letter-Number Sequencing, participants have to repeat a series of randomly mixed letters and numbers starting with the numbers in ascending order followed by the letters in alphabetical order. For Digit Span, the mean raw score (i.e., number of correct trials) for Digit Span Backwards and sequencing was included. In the backwards condition, participants have to repeat the series in a backwards order, and in Digit Span Sequencing, the numbers are randomly presented and must be repeated in the correct number order.

Inhibition was measured using the Color Word Test from the D-KEFS (D-KEFS; Delis, Kaplan & Kramer, 2001). Only the third trial (i.e., interference trial) was used. In this trial, participants are presented rows of words printed in dissonant colors and are instructed to inhibit reading the words and instead name the dissonant colors in which the words are printed. The number of seconds (i.e., raw score) needed to complete the trial was used as a measure of inhibition.

2.1.3 Results

2.1.3.1 Factorial validity of ADEXI scores

First, we did a factorial analysis of the ADEXI scores. Both a two- and three-factor solution were examined. The two-factor solution showed two clear factors. An oblique rotation method was chosen, as the two factors were shown to be highly correlated, $r = .69$. The two-factor solution explained 50.02% of the variance. The first factor included items from the a priori subscale tapping working memory and the second factor included items from the a

priori subscale tapping inhibition. Item 10 (“I sometimes have difficulty stopping an activity that I like”) had a similar factor loading on both factors. Based on the a priori subscales, this item was selected to be part of the inhibition subscale.

Table 2. Reliability and convergent validity for the ADEXI

	Adult Executive Functioning Inventory (ADEXI)		
	Full scale	Inhibition	Working Memory
Internal consistency			
Total sample (n = 461)	.91	.77	.90
Non-clinical sample (n = 364)	.89	.72	.88
Clinical sample (n = 97)	.90	.73	.89
Test-retest reliability			
Bivariate correlations (n = 105)	.71	.72	.68
Intra-class correlations (n = 105)	.67	.72	.62
Inter-rater reliability			
Bivariate correlations (n = 88)	.53	.38	.56
Intra-class correlations (n = 88)	.49	.34	.54
BDEFS subscales (n = 127)			
Self-organization/Problem solving	.71***	.51***	.72***
Self-management of Time	.66***	.51***	.65***
Self-restraint/Inhibition	.64***	.62***	.57***
Self-regulation of Emotion	.58***	.48***	.55***
Self-motivation	.64***	.57***	.59***
BDEFS short version	.70***	.58***	.66***

*** p < .001

2.1.3.2 Reliability of ADEXI scores

Results showed high internal consistency for scores on the ADEXI full scale as well as for scores on the inhibition and working memory subscales. As seen in Table 2, the test-retest reliability was found to be adequate. However, the inter-rater reliability for the full scale between self-ratings and other-rating was low. The concordance between self- and other-ratings was especially low with regard to inhibition, but also relatively low for working memory. The mean scores for both the full scale and the two subscales were all significantly higher (i.e., indicating more problems) for self-ratings compared to other-ratings.

2.1.3.3 Convergent validity of ADEXI scores

Regarding convergent validity, the results showed relatively strong relations (r s between .48 and .72) between all three ADEXI scores and scores on the BDEFS subscales. As expected, scores on the working memory subscale of the ADEXI were most strongly related to scores on the BDEFS subscale “Self-organization/Problem solving,” whereas scores on the ADEXI Inhibition subscale were most strongly related to scores on the BDEFS subscale referred to as “Self-restraint/Inhibition.” With regard to self-ratings, scores on the ADEXI full scale and ADEXI working memory subscale were significantly correlated with scores on the Color-Word Task measuring inhibition in both samples (i.e., clinical and non-clinical), all r s $>$.19, p s $<$.05. Scores on the ADEXI working memory subscale were related to the two working memory measures, although only in the non-clinical sample. With regard to ratings on the ADEXI made by a close relative/friend, no significant relations were found between the three ADEXI measures and scores on the digit span task.

2.1.3.4 Discriminant validity of the ADEXI

When studying group differences, the ADHD group reported higher scores than both the clinical and the non-clinical control group for all three measures. In the logistic regression analyses (see Table 3), we first compared the ADHD group with non-clinical controls. The results showed that the ADEXI scores classified 85% of the participants in the correct category with a sensitivity of 86% and a specificity of 84% (Model 1). Second, we compared the ADHD group with the clinical control group. The results showed that this model was also significant and the ADEXI scores classified 76% of the sample correctly with a sensitivity of 80% and a specificity of 72% (Model 2).

Table 3. Results of the logistic regression analyses

	Sensitivity	Specificity	Total correctly classified
Model 1: ADHD vs. non-clinical controls			
Step 1. Only ADEXI	86.3%	84.1%	85.3%
Model 2: ADHD vs. clinical controls			
Step 1. Only ADEXI	80.4%	71.7%	76.3%
Model 3: ADHD vs. non-clinical controls			
Step 1. Only executive function tasks	64.4%	77.3%	70.8%
Step 2. Executive function tasks + ADEXI	86.7%	84.1%	85.4%
Model 4: ADHD vs. clinical controls			
Step 1. Only executive function tasks	64.4%	70.5%	67.4%
Step 2. Executive function tasks + ADEXI	84.4%	77.3%	80.9%

We also wanted to examine to what extent ADEXI scores could increase the proportion of correctly classified individuals, when entering ADEXI in a second step, after taking the effects of EF tests into account. When comparing the ADHD group with non-clinical controls

(Model 3), the results showed that scores from the executive function tasks classified 71% of the participants correctly. When adding ADEXI scores in the second step, this step was significant ($\chi^2 = 42.76$, $n = 95$, $p < .001$) and classified 85% of the participants in the correct category. The sensitivity was improved from 64 to almost 87%, the specificity from 77 to 84%. When comparing the ADHD group with the clinical control group (Model 4), the results showed that scores on the executive function tasks classified 67% of the participants correctly. When adding ADEXI scores in the second step, this step was significant ($\chi^2 = 24.00$, $n = 97$, $p < .001$) and could classify 81% of the participants in the correct category. In this model, the sensitivity was improved from 64 to 84% and the specificity from 70 to 77%.

2.1.4 Conclusions

Study I shows that ADEXI scores have adequate psychometric properties and that this instrument serves a partly different purpose compared to other available EF rating instruments for adults. Compared to the BRIEF-A, the ADEXI has a clear advantage of not including items that are more or less identical to the diagnostic criteria for ADHD, but instead focuses more specifically on EF deficits. In comparison with BDEFS, the ADEXI does not include at all as many different types of neuropsychological deficits, which could be seen as a disadvantage. However, individuals with EF deficits often have difficulties completing long rating instruments, and it might therefore be an advantage to have a quick and easily administered screening instrument focusing specifically on two central EF aspects (i.e., inhibition and working memory), and an instrument that is also freely available (www.chexi.se).

2.2 STUDY II

Neuropsychological functioning in adults with ADHD and adults with other psychiatric disorders: The issue of specificity.

2.2.1 Aims and background

The aim of Study II was to investigate how well measures of neuropsychological functioning discriminate between adults with ADHD and adults with other psychiatric disorders.

ADHD is believed to be a heterogeneous disorder that is related to multiple neuropsychological deficits, including executive function (EF) deficits, delay aversion, and high reaction time (RT) variability (e.g., Castellanos et al., 2006; Nigg et al., 2005). However, the theoretical propositions within the ADHD research area are primarily based on studies of children. There have been an increasing number of studies of ADHD in adulthood, but comparisons have most often been made to a normal control group. Thus, we still know very little about which neuropsychological deficits are truly specific to ADHD. The overall aim of the present study was therefore to compare adults diagnosed with ADHD to adults with other psychiatric disorders. In line with the view that ADHD is a heterogeneous disorder, we included a broad range of neuropsychological functions than have been used in most previous studies. In addition, we addressed important limitations of previous studies by including control tasks measuring basic cognitive functions (e.g., speed) and by complementing our group differences with measures of sensitivity and specificity.

2.2.2 Method

2.2.2.1 Participants and procedure

Study II included 57 participants (24 men/33 women) diagnosed with ADHD and 53 participants (16 men/37 women) in a clinical control group. The age of the participants ranged between 18-44 years ($M = 26.8$, $SD = 5.9$ in the ADHD group, $M = 25.5$, $SD = 5$ in the clinical control group, $t = 1.184$, ns). The participants in both groups were the same as the ADHD sample and clinical controls included in Study I, except that a few more participants were included in Study II because some participants did not complete the ADEXI and therefore could not be included in Study I. The procedure for recruitment and the diagnostic procedure are only described in Study I.

2.2.2.2 Measures

The neuropsychological tests used in Study II were selected from either Delis Kaplan Executive System (D-KEFS; Delis, Kaplan & Kramer, 2001) or WAIS-IV (Wechsler, 2008). In addition, a few computerized EF tests used in previous studies on ADHD were used. Below follows a detailed description of all included measures.

Verbal working memory was measured using the Letter-Number Sequencing and the Digit Span Task from WAIS-IV, which are the same tasks as used in Study I and therefore not further described here.

Spatial working memory was measured using the Find-the-phone Task (Delosis, London). This task is similar in design to the spatial working memory task included in the Cambridge Neuropsychological Test Automated Battery (CANTAB; Owens, Downes, Sahakian, Polkey, & Robbins, 1990). In the version used in the present study (Sjöwall, Roth, Lindqvist & Thorell, 2013), a number of telephones are shown on the computer screen. Participants are instructed to find the telephone that is ringing by clicking on the phones using the computer mouse. If they find the correct telephone, the signal stops and a new telephone starts ringing until all telephones on the screen have rung once. Participants are told that each phone will only ring once and that the goal of the task is to find all the ringing phones without selecting the same phone twice. The adult version used in Study II included six sessions: two with six telephones, two with eight telephones, and two with ten telephones. The number of incorrect answers was used as a measure of spatial working memory.

Inhibition was measured using the Color Word subtest from D-KEFS and a Navon-like task. The Color Word Test has already been described in Study I and will therefore not be described further here. The Navon paradigm has been used previously (e.g., Miyake, Friedman, Emerson, Witzki and Howerter, 2000). In the present version (Delosis, London; Sjöwall et al., 2013), a circle consisting of small squares, or the opposite, a square consisting of small circles, is displayed on the computer screen. In one session, the participants are asked to respond to the local stimuli (i.e., the small squares making up the circle) and in the other session they are asked to respond to the global stimuli (i.e., the circle made up by the squares). In total, 20 objects (10 squares and 10 circles) were shown. The score used was mean reaction time.

Set shifting was measured using the shifting trials from both the Color Word Task and the Verbal Fluency Task from D-KEFS, and a third trial of the Navon task. During the shifting condition of the Color Word Task, the participants are asked to switch back and forth between naming the dissonant ink colors and reading the words. Completion time was used as a measure of set shifting. In the shifting condition of the Verbal Fluency Task, participants are instructed to alternate between saying words from two different semantic categories as quickly as possible for 60 seconds. Number of correct shifts was used as a second measure of set shifting. Finally, set shifting was measured using the Navon task (see description above under the heading “inhibition”). A third trial was performed in which participants had to shift between responding to the local or the global stimuli. Mean reaction time for the third trial was used as a measure of shifting.

Verbal fluency was measured using the Fluency Task from D-KEFS. During 60 sec/trial, the participants are requested to say as many words as possible that begin with a specified letter (F, A or S) or a designated semantic category (animals or boys’ names). The mean standard

score on the two conditions (i.e., letter fluency and category fluency) was used as a measure of verbal fluency.

Planning was measured by the Sorting test and the Tower test from D-KEFS. Sorting test (i.e., free sorting), the participants are instructed to sort cards into two groups according to as many different categorization rules as possible and to describe the concepts or the rule of categorization. In condition two (i.e., sort recognition), the examiner sorts the cards into two groups and the participant is asked to identify the correct categorization rule. The mean number of correct sorts was used as a measure of planning. For the Tower Test, the participants are instructed to build towers with disks (varying in size) in the fewest number of moves possible using pre-specified rules. The Total Achievement Score, which is the mean of three measures (i.e., number of moves to completion, the item-completion time, and correct number of towers), was used as a measure of planning.

Delay Aversion was measured using the “Quick Delay Questionnaire” (QDQ) developed by Clare et al. (2010). The QDQ is a 10-item self-rating instrument for adults that measures delay aversion and delay discounting. Ratings are made on a scale from 1 (do not agree at all) to 5 (agree fully), and high values indicate high levels of delay-related behaviors.

Reaction Time Variability was measured by the standard deviation of the participants’ reaction time for correct responses on the two non-set-shifting trials of the Navon-like task (see task description under the heading “inhibition” above).

Basic cognitive functioning, such as speed, verbal abilities and memory, was controlled for using the following three subtests from the WAIS-IV (Wechsler, 2008): Block Design, Vocabulary, and Digit Span Forward. In addition, measures of response speed (mean RTs) were collected from D-KEFS (i.e., Color-Word and Fluency Subtests) and the Navon Task. Finally, and in line with the D-KEFS manual (Delis et al., 2001), two of the measures of inhibition and the category fluency measure (see description above) were used as control variables when studying the effects of set shifting.

Intelligence was estimated using the General Ability Index (GAI) from the WAIS-IV (Wechsler, 2008). GAI is composed of the following subtest: Similarities, Vocabulary, Information, Matrix Reasoning, Block Design, and Visual Puzzles. Previous studies of the WAIS-III have found a very high correlation ($r = .96 - .97$) between GAI and Full-Scale IQ in clinical samples (Iverson, Lange, Viljoen & Brink, 2006; Tulsky, Saklofske, Wilkins & Weiss, 2001), indicating that GAI is a good measure of general intellectual ability.

Table 4. Means and standard deviations for all major variables included in the study and results of ANCOVAs

	ADHD		Control group		ANCOVA	ANCOVA	ANCOVA
	M	(SD)	M	(SD)	Sex	Sex + IQ	Sex + Control tests
					F	F	F
Verbal Working Memory							
Letter-Number Sequencing (Standard score)	8.5	(1.9)	9.8	(2.8)	6.18 (.06)*	6.92 (.07)*	1.05 (.01)
Digit Span Backwards (Standard score)	9.2	(2.6)	9.7	(2.9)	0.71 (.01)	0.56 (.01)	0.37 (.01)
Digit Span Sequencing (Standard score)	7.7	(2.3)	8.4	(2.2)	2.43 (.02)	1.75 (.02)	0.24 (.01)
Spatial Working Memory							
Find the Phone Task (Errors)	29.3	(20.1)	21.2	(18.2)	4.56 (.04)*	3.85 (.04) ⁺	1.99 (.02)
Inhibition							
Color-Word, Inhibition trial (Errors)	7.1	(3.8)	9.6	(3.3)	11.87 (.10)***	12.25 (.11)*	9.22 (.08)*
Navon, inhibition trials (Reaction times)	809.4	(321.8)	718.2	(223.1)	2.96 (.03)	1.93 (.02)	.81 (.01)
Set shifting							
Color Word, Shifting trial (Standard score)	7.1	(3.5)	9.5	(2.9)	13.78 (.12)***	12.65 (.11)*	3.27 (.03) ⁺
Category Fluency, Shifting (Standard score)	10.4	(3.2)	12.1	(3.5)	3.96 (.04)*	4.09 (.04)*	1.65 (.02)
Navon Task, Shifting trial (Reaction times)	1347.1	(479.4)	1151.7	(358.3)	6.54 (.06)*	5.49 (.05)*	0.39 (.01)
Fluency							
Letter fluency (Standard score)	10.79	(3.9)	12.4	(3.7)	4.10 (.04)*	4.32 (.04)*	5.76 (.06)*
Category fluency (Standard score)	11.2	(3.9)	12.6	(4.3)	2.20 (.02)	2.02 (.02)	3.18 (.03) ⁺
Planning							
Tower Test (Standard score)	10.2	(2.6)	11.2	(2.6)	3.99 (.04)*	3.70 (.03) ⁺	3.69 (.04) ⁺
Reaction Time Variability							
Navon Task (SD in reaction time)	1848.8	(574.5)	1630.4	(547.1)	4.15 (.04)*	2.79 (.03) ⁺	0.53 (.01)
Delay aversion							
Delay aversion questionnaire	3.3	(0.66)	2.8	(0.70)	10.8 (.10)***	9.99 (.10)*	7.06 (.071)**

+ p < .10 * p < .05, ** p < .01, *** p < .001

2.2.3 Results

2.2.3.1 Neuropsychological assessment of executive functioning

The results showed that for working memory, adults with ADHD performed more poorly compared to the clinical controls on the Letter-Number Sequencing Task and Find-the-phone Task. No significant group differences were found for the two Digit Span subtests. For inhibition, a significant group difference was found for the Color Word task, but not for the Navon task. For Set shifting, the results showed that the adults with ADHD performed more poorly than the clinical controls on Color Word, Category Switching, and the Navon task. For Fluency, the results showed that the ADHD group performed more poorly than the controls on letter fluency but not category fluency. Finally, the ADHD group was shown to perform more poorly compared to the clinical controls with regard to planning, reaction time variability and ratings of delay aversion.

When controlling for intelligence, all of the significant group differences reported above remained significant or marginally significant. However, when controlling for basic cognitive processing, only the following group difference remained significant or marginally significant: Color-word Task (both inhibition and shifting trials), fluency (both letter and category fluency), planning, and delay aversion.

2.2.3.2 Logistic regression analyses

To determine how well the neuropsychological variables could classify the participants into the correct group, three different logistic regression analyses were performed. First, we tested a full model with all of the ten variables for which significant group differences had been found in the ANCOVAs (Model 1). This model was shown to be statistically significant, $\chi^2 = 28, 37, p < .001$. Model 1 correctly classified 66% of the participants, with a sensitivity of 64% and a specificity of 67%. Only the effect of delay aversion significantly predicted group membership, with a marginally significant effect for Letter-Number Sequencing. A model with only these two variables was also significant, $\chi^2 = 22, 15, p < .001$. This model (Model 2) classified 71% of the participants correctly, with a sensitivity of 75% and a specificity of 66%. Finally, we examined a third model (Model 3), where we excluded delay aversion, as the importance of this variable may be inflated given that this function was measured using self-ratings rather than a laboratory task. Model 3 was significant, $\chi^2 = 17.99, p < .05$, and classified 64% of the participants correctly.

2.2.4 Conclusions

Study II aimed to investigate to what extent measures of neuropsychological functioning can discriminate between adults with ADHD and adults with other psychiatric disorders. Without controlling for IQ or control tests, we found significant group differences with regard to the following functions: verbal and spatial working memory, inhibition, set shifting, fluency,

planning, RT variability, and delay aversion. The effect sizes were small (below .06) to medium (between .06 - .14). After controlling for IQ, the significant effects remained for inhibition, set shifting, fluency, and delay aversion. When controlling for basic cognitive functions, significant group differences were only found for inhibition, fluency, and delay aversion. Effects of shifting and planning were marginally significant.

2.3 STUDY III

Functional impairments in adults with ADHD and adults with other psychiatric disorders and links to executive deficits

2.3.1 Aims and background

As described above in the general introduction, previous studies have concluded that adults with ADHD have impairments in major life activities such as academic achievement, occupational functioning, social and interpersonal difficulties, as well as antisocial behavior and criminality. A limitation of previous research is that few studies have compared daily functioning in adults with ADHD in relation to adults with other psychiatric disorders. However, there are a few studies available showing that adults with ADHD had poorer educational results, more impaired work performance, had more often been fired/dismissed from a job, as well as having higher levels of substance use, anti-social behavior, and criminal acts (Barkley, Murphy, & Fischer, 2008; Murphy & Barkley, 1996; Barkley & Murphy, 2010; Kooij et al., 2010b).

In addition to comparing adults with ADHD with adults with other psychiatric disorders, it should also be considered essential to study the importance of executive deficits in explaining why some individuals with ADHD function relatively well in daily life, whereas others have serious impairments. In the few previous studies examining the link between neuropsychological functioning and functional impairments in adult ADHD, it has been shown that, compared to the subgroup without EF deficits, the ADHD subgroup with EF deficits had significantly higher frequency of problems with regard to academic achievement and occupational functioning (Biederman et al., 2006a; Halletland, in press), as well as with criminality, traffic accidents, and social functioning in many areas of daily life.

The overall aim of Study III was to investigate functional impairments in adults with ADHD compared to adults with other psychiatric disorders. More specifically, we aimed to address the following research questions:

1. Do adults with ADHD differ from a clinical control-group regarding social relations, daily life functioning, criminality, as well as academic and occupational functioning?
2. Do ADHD subgroups with or without EF deficits differ from one another with regard to the functional impairments associated with the disorder?

2.3.2 Method

2.3.2.1 Participants and procedures

The present study included altogether 95 younger adults (age range 18-45 years) from two groups: a clinical group of adults with ADHD (n = 50, 40% men); and a clinical group of adults diagnosed with other psychiatric disorders (n = 45, 29% men). The participants are the

same samples as included in Study II and underwent the same neuropsychological assessment as described in Study II.

2.3.2.2 *Ratings of functional impairments*

Self-ratings assessing functional impairment were completed either at home or at the clinic. The following domains were included:

Academic functioning. For this domain of functioning, we used self-ratings of grade point average, grade retention, whether the participant had ever received special educational support in school, and highest obtained educational level.

Occupational functioning. For this domain of functioning, we used self-ratings of number of months in unemployment, number of months on sickness benefit (for sick leaves longer than one month), and current occupational status (i.e. working/studying, unemployed, or sickness benefit).

Social functioning. We assessed the participants' number of social relations using four questions ("How many close friends do you have?" "How many times/month do you have contact with your friends through e-mail, meetings, or phone calls?" "How many times/month do friends or family members visit you in your home?" and "How many times/month do you see your friends in your spare time?"). Ratings were made on a 4-point scale (less than one, 1-2, 3-4, 5 or more). We also assessed the quality of their relationships with friends and family. The question asked was the following: "During the past six months, how well have you gotten along with your brothers/sisters/father/mother/partner/children/friends?" Ratings were made on a scale from 0 (no contact at all) to 5 (very well); we combined some of the ratings to obtain measures for quality of relationships with family (i.e., mother, father, siblings, and children) and used two separate scores for the quality of relationships with partner and friends.

Daily Life Functioning. We used the ADHD Daily Problem Questionnaire (ADPQ; Thorell, Sjöwall, Mies, & Scheres, 2017) to assess daily life functioning in several areas. The ADPQ is similar in design to Barkley's Functional Impairment Scale (BFIS; Barkley, 2011b), in that it contains a list of daily activities, and participants (or a close relative/friend of the patient) are asked to rate their level of functioning on a scale from 0 ("no problem") to 9 ("very severe problem"). However, whereas the BFIS contains relatively broad items (e.g., problems "in your home life with your immediate family"), the ADPQ contains more specific items within four problem areas: (1) economic problems (2 items: e.g., "handling money in a responsible way"), (2) daily chores/responsibilities (4 items: e.g. "cleaning," "doing laundry,"), (3) time management (4 items: "keeping appointments"), and (4) social relations (2 items: e.g., "going to a party when I do not know the other guests well"). The reason for focusing on these four areas is that previous research has shown that the most serious impairments among individuals with ADHD are found in these areas (e.g., Barkley, Murphy, & Fischer, 2008).

Criminality. In order to measure criminal behavior, the patients were presented with a list of 15 criminal acts and asked to rate their own behavior on a 5-point scale (0 = never, 1 = 1 time, 2 = 2–3 times, 3 = 4–10 times, 5 = more than 10 times). This list included the following areas: (1) violent criminal behavior (e.g., physical abuse), (2) nonviolent criminal behavior (e.g., shoplifting, pickpocketing), and 3) driving-related problems (e.g., driving without a license, speeding). In the present study, the mean value for all fifteen items was used as a measure of criminality. In addition, we asked the participant whether he/she had ever been arrested by the police.

2.3.2.3 *Laboratory measures of executive functioning*

In Study III, we used the same laboratory measures of executive functioning as had been used in Study II and they will therefore not be described in detail here. However, as we wanted to classify patients into two subgroups (i.e., with or without executive deficits) based on tests for which normative data are available, only tests from either Delis Kaplan Executive System (D-KEFS; Delis, Kaplan & Kramer, 2001) or WAIS-IV (Wechsler, 2008) were included. In addition, we excluded measures that captured cognitive functioning more generally, such as measures of speed of processing, verbal fluency, or reaction time variability. Altogether, this meant that the following constructs were assessed: working memory (Digit Span Backward, Digit Span Sequencing, and Letter-Number Sequencing task), inhibition (interference trial from the Color Word Test) set-shifting (shifting trials from both the Color Word Task and the Verbal Fluency Task) and planning (Tower Test).

The classification of ADHD patients into those with and without executive deficits was conducted in the following way. First, and in accordance with the respective manuals for D-KEFS (Delis et al., 2001) and WAIS-IV (Wechsler, 2008), performance on each test was categorized as being average/above average (scaled score ≥ 8) or impaired (scaled score < 8 ; i.e., ≥ 1 SD below the mean) relative to available norms. Second, we followed recommendations from previous research (e.g., Biederman et al., 2006a) and defined individuals as having deficits in executive functioning if they had an impaired score on two or more of the neuropsychological tests.

2.3.2.4 *Ratings of neuropsychological deficits*

Executive functioning. The Adult Executive Functioning Inventory (ADEXI; Holst & Thorell, in press) was used to investigate executive functioning. Analyses similar to those conducted for the laboratory measures could not be made for the ADEXI self-ratings, as almost all ADHD participants (86%) were classified as having EF deficits when using the same cut-off as used for the tests (i.e., ≥ 1 SD below the mean). Instead, we used the median split to divide the ADHD group into those with low and high executive functioning.

2.3.3 Results

2.3.3.1 Group differences between the ADHD group and the clinical controls

With regard to academic functioning, adults with ADHD differed significantly compared to the clinical control group for all included measures. For occupational functioning, a significant difference was found between adults with ADHD and the clinical control group with regard to current occupational status (i.e., being employed, studying or being on sick leave), but not with regard to previous months of unemployment or previous months of sick leave. When studying the percentages for current occupational status in more detail, it was found that among adults with ADHD, the rate of unemployment was low, whereas the rate for sickness benefit was high, especially in the ADHD subgroup with EF deficits. The clinical control group, on the other hand, had a lower rate of individuals on sickness benefits, but a higher number of unemployed patients.

For the other domains of functioning, then results showed that compared to the clinical control group, adults with ADHD had a significantly lower number of social contacts, poorer quality of social contacts with family members, as well as more problems regarding time management, problems with money, social relations, and doing chores. Compared to the individuals in the clinical control group, adults with ADHD also reported a significantly larger number of criminal acts, and they had more often been arrested by the police.

2.3.3.2 Group differences between ADHD patients with and without executive deficits

In a next set of analyses, we compared ADHD subgroups with and without executive deficits with regard to functional impairments. The results showed that those with EF deficits based on EF tests reported significantly more often that they had repeated a grade or that they had received special educational support compared to those without EF deficits. The ADHD subgroup with EF deficits also reported a significantly lower educational level. Few significant differences were found between the two ADHD subgroups with regard to social functioning and daily life problems. However, the ADHD subgroup with EF deficits reported a significantly larger number of criminal acts, and had also more often been arrested by the police compared to the subgroup without EF deficits.

Finally, we compared subgroups with and without EF deficits based on self-ratings using the ADEXI. The results showed that very few significant group differences were found regarding educational, occupational, and social functioning, and criminality. However, patients with EF deficits were found to have significantly greater problems with time management, social relations, and completing daily chores compared to ADHD patients without EF deficits.

2.3.4 Conclusions

Study III demonstrates that daily life functioning is severely affected among adults diagnosed with ADHD, as they are significantly more impaired even compared to adults with

other psychiatric disorders. The study also shows that EF deficits appear to play a role in explaining these impairments, although primarily with regard to academic functioning, occupational status, and criminality.

2.4 STUDY IV

Neuropsychological deficits in adults age 60 and above with attention deficit hyperactivity disorder

2.4.1 Aims and background

Neuropsychological deficits have been shown to be of major importance in Attention Deficit Hyperactivity Disorder (ADHD) in both childhood (Castellanos et al., 2006) and adulthood (Boonstra et al., 2005). However, no previous studies have addressed this issue in a clinically referred sample of individuals with ADHD above 60 years of age. The overall aim of Study IV was therefore to investigate neuropsychological deficits among older adults with ADHD and compare them to both healthy controls in the same age range and younger adults with ADHD. More specifically, the study focused on deficits in executive functions (i.e., working memory, inhibition, switching, and planning), delay-related behaviors (i.e., the tendency to choose smaller immediate rewards over larger rewards that involve waiting), verbal fluency, and speed of processing. Studying neuropsychological deficits in older adults with ADHD should be considered an important topic, as we know from previous research that ADHD persists into older adulthood at prevalence rates between 2.8 and 3.3% (Michielsen et al., 2012; Guldberg-Kjär & Johansson, 2009). Older adults with ADHD have also been shown to have similar impairments as younger adults with ADHD, such as higher rates of comorbid depression, anxiety and poor perceived somatic health (Michielsen et al., 2013), as well as lower educational levels, higher rates of divorce, and more loneliness (Michielsen et al., 2015). Only one previous study (Semeijn et al., 2015) has investigated neuropsychological functioning in older adults with ADHD.

2.4.2 Method

2.4.2.1 Participants

The study included 158 participants in three groups: 1) older adults (60-75 years of age) diagnosed with ADHD (n=44), 2), healthy controls of the same age (n=58), and 3) younger adults (18-45 years of age) with ADHD (n=56).

Adults with ADHD were recruited from outpatient psychiatric units in Stockholm specialized in neuropsychiatric disorders; they all met the full diagnostic criteria according to DSM-5 (APA, 2013) as assessed by trained psychologists/psychiatrists. The diagnostic assessment was the same as the one in Study I-III and will therefore not be described further here.

Exclusion criteria for both clinical groups were: 1) an IQ score < .70 on the Wechsler Adult Intelligence Scale (WAIS-IV; Wechsler, 2008), 2) ongoing substance-related disorders, and 3) the presence of a serious neurological disorder such as Parkinson disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), or dementia. Among the older adults, we also

collected information on several factors that are relatively common among older adults because these factors could affect cognitive performance and therefore have to be taken into consideration in the analyses: 1) a score of < 24 on the Mini Mental State Examination (MMSE; Folstein, Folstein & McHugh, 1975), which is indicative of cognitive decline; 3) ongoing (i.e., during testing) migraine/severe headache, chronic or acute pain, severe physical disabilities, or seriously impaired vision after correction; 4) current use of neuroleptic, sedative, anxiolytic, or antiepileptic drugs. None of the participants (i.e., healthy controls or ADHD patients) who had agreed to participate in the study were found to have problems related to the factors mentioned above. Among older adults with ADHD, 22 were on stimulant medication, but withdrew the medication for at least 24 hours prior to testing. One participant was on non-stimulant medication (i.e., Atomoxetine). In the younger ADHD group, 38 participants were on stimulant medication, and 20 of them withdrew the medication for 24 hours. The remaining 18 participants were on medication during testing. However, results were very similar for both the variable- and person-oriented analyses when excluding these participants.

Healthy controls were recruited through local health care clinics and local organizations for senior citizens. Exclusion criteria were the same as those described above, with the addition of the presence of any psychiatric disorder. The controls did not differ significantly from the older ADHD group on the MMSE, $t = .88$, *ns*. Participants provided written informed consent after receiving a complete description of the study and the local ethics committee approved the study. All participants received approximately 70 Euros for taking part in the study.

The two groups including older adults did not differ with regard to age, and the three groups did not differ regarding male-female ratio, or general intellectual functioning (assessed using the Block Design Subtest from the WAIS-IV; Wechsler, 2008). However, significant group differences were found for educational level, with the healthy controls showing the highest educational level and the younger adults with ADHD the lowest.

2.4.2.2 Group differences in neuropsychological functioning

Older adults with ADHD performed at a significantly lower level compared to healthy controls regarding laboratory tests for all measures of working memory (i.e., Digit span backward and sequencing, and Letter-number sequencing). No group differences were found between younger and older adults with ADHD with regard to the laboratory measures of working memory. Regarding ratings on the ADEXI, older adults with ADHD rated themselves as having larger deficits in working memory compared to healthy controls, but less severe working memory deficits compared to younger adults with ADHD.

Older adults with ADHD performed worse compared to healthy controls, but better compared to younger ADHD patients with regard to all three measures of switching and inhibition. For both verbal fluency and speed in naming colors, older adults with ADHD did not differ significantly from healthy controls, but they performed better compared to younger ADHD

patients. Further, older adults with ADHD performed better compared to younger adults with ADHD on the task measuring speed of reading words.

In comparison with healthy controls, older adults with ADHD rated themselves as having higher problem levels with regard to both measures of delay-related behavior, but lower levels compared to younger ADHD patients for delay aversion. All significant group differences remained significant when controlling for ongoing comorbid depression or anxiety disorders, except for the Digit Span Task for which the main effect and the post hoc comparison between the older ADHD patients and controls were only marginally significant when controlling for depression.

2.4.2.3 Sensitivity and specificity

The number of correctly classified individuals in the ADHD group was 76.7 and the number of correctly classified individuals among the controls was 86.0. When entering the self-ratings in the second step, the sensitivity was increased to 88.4% and the specificity to 91.2%.

2.4.2.4 Person-oriented analyses

Person-oriented analyses showed that a majority of individuals in both the younger and older ADHD group performed within the average range for most of the tasks. In the chi-square analyses used to investigate group differences for the categorical variables, the results showed that the two ADHD groups showed similar levels of impairment in working memory, planning, and verbal fluency. However, older adults with ADHD were less impaired compared to younger adults with ADHD with regard to inhibition, switching and speed of processing. Thus, except for verbal fluency, these findings were the same as those found in the variable-oriented analyses. For the comparison between older ADHD patients and healthy controls, results were the same as the variable-oriented analyses with regard to working memory, verbal fluency, and speed of processing. However, unlike the variable-oriented analyses, the ADHD patients differed from controls also with regard to planning, whereas no significant differences were found for inhibition and switching.

A Venn diagram was used to illustrate the overlap between the following three domains: working memory, inhibition/switching, and speed of processing. As shown in Figure 1, 20% of older ADHD patients did not have a deficit within any domain, 43% had impaired performance within a single domain, and 36% showed impairment in multiple domains. The corresponding numbers for the younger adults with ADHD was 7% without deficits, 23% with single deficits, and 70% with multiple deficits. Working memory (64%) was the most common impairment among older adults with ADHD, whereas working memory and speed of processing were equally common (each one 68%) among younger adults with ADHD. Impairment in all three domains was more often found among younger adults (30%) compared to the older adults with ADHD (11%).

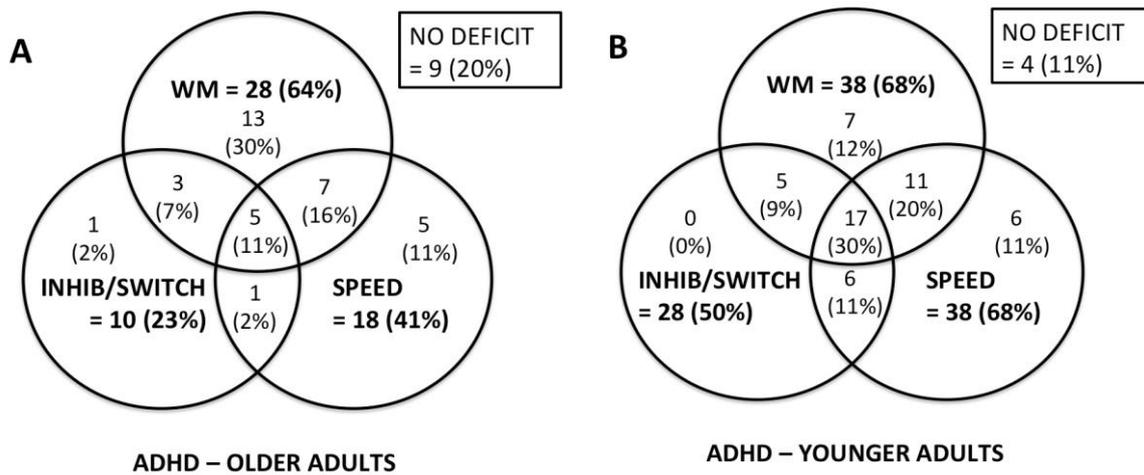


Figure 1. Venn diagram showing the number of older (A) and younger (B) adults with ADHD who had impaired performance with regard to the three domains: working memory (WM), inhibition/switching (INHIB/SWITCH), and speed of processing (SPEED).

2.4.3 Conclusions

The findings of Study IV support current models of heterogeneity in which ADHD is regarded as a disorder related to a range of neuropsychological deficits, but show that there is also a subgroup of ADHD patients without clear neuropsychological deficits (Castellanos et al., 2006; Nigg et al., 2005). Identifying neuropsychological subgroups within the ADHD population might therefore be of major importance, as this could help in detecting patients who are at particularly high risk of poor functioning in daily life.

3 GENERAL DISCUSSION

3.1 SUMMARY OF MAIN FINDINGS

In *Study I* we investigated the psychometric properties of the ADEXI, a short (14 items) questionnaire measuring two major executive functions: working memory and inhibition. Results showed that the internal consistency was high; the test-rest reliability was adequate, whereas the inter-rater reliability was low. Significant correlations were found between the ADEXI and another EF rating instrument. Discriminant validity analysis showed that individuals with ADHD reported significantly greater deficits with regard to inhibition and working memory compared to both a clinical and a non-clinical control group.

In *Study II* we investigated how well neuropsychological measures can discriminate between adults with ADHD and adults with other psychiatric disorders. Results showed that adults with ADHD performed more poorly compared to clinical controls with regard to verbal memory, inhibition, set shifting, fluency, and delay aversion. When controlling for IQ, the results remained significant. However, when controlling for basic cognitive functions (e.g., short-term memory, processing speed), only the effects of delay aversion, inhibition and fluency were significant. We also demonstrated that neuropsychological tests have a relatively poor ability to discriminate between adults with ADHD and clinical controls, with sensitivity ranging between 64% and 75% and specificity between 66% and 81%.

In *Study III* we investigated functional impairments in adults with ADHD and adults with other psychiatric disorders. The results showed that adults with ADHD had greater problems with academic functioning, daily life functioning, criminality, and some aspects of social functioning. With regard to occupational functioning, the groups did not differ with regard to previous number of months in unemployment or sickness benefits. Adults with ADHD were more often on sickness benefit and less often unemployed compared to adults with other psychiatric disorders. We also compared ADHD subgroups with or without executive deficits. Differences were only found in academic functioning, the proportion of individuals currently working or on sickness benefits, and criminality.

In *Study IV* we investigated neuropsychological deficits in older adults with ADHD in comparison with both younger adults with ADHD and healthy older controls. Older adults with ADHD differed from healthy controls with regard to working memory, inhibition, speed of processing, and delay-related behaviors. In comparison to younger adults with ADHD, they performed at a similar level with regard to working memory and verbal fluency, but significantly better with regard to inhibition and switching. Person-oriented analyses showed that a majority of older adults with ADHD performed within the average range on each test, and about 20% did not show a clear deficit in any neuropsychological domain.

3.2 ADHD AND NEUROPSYCHOLOGICAL FUNCTIONING

The studies included in the present thesis raise some critical issues that have not been fully addressed in previous studies. In summary, we have 1) introduced a new rating instrument, 2) compared adults with ADHD with a clinical control group of adults with other psychiatric disorders, 3) used a broader range of neuropsychological tests compared to many previous studies of adult ADHD, 4) studied sensitivity and specificity and not only group differences, 5) controlled for both IQ and basic cognitive functions (i.e., speed, verbal abilities and memory), and 6) investigated neuropsychological functioning in patients with ADHD above age 60. Below follows a more in-depth description of how the present results have generated new knowledge about the critical issues raised in the introduction.

3.2.1 Short screening instruments for adults with ADHD

In Study I, we emphasized the need for a short reliable rating scale focused on measuring EF deficits that do not include items measuring other related constructs or symptoms of ADHD. The ADEXI was created, as we did not feel any other instrument meeting these criteria was available. The present study showed that scores from the ADEXI generally have relatively good psychometric properties. However, due to the low correlations between ADEXI scores and those obtained from laboratory EF tests, the ADEXI should be used as a complement to rather than a replacement for neuropsychological tests. In addition, the low concordance between self- and other-ratings demonstrates the need to use ratings from multiple sources rather than relying solely on self-ratings.

The low correlation between EF ratings and EF tests found in Study I is in line with several previous findings (for a review, see Toplak, West & Stanovich, 2013). Because EF ratings have been shown to be more strongly related to daily life functioning, it has been argued that EF tests have poor ecological validity (Barkley & Fischer, 2011; Barkley & Murphy, 2010). However, the low correlations could also be taken as an indication that ratings and tests capture at least partially different constructs. Previous studies have argued that one important difference is that EF tests capture optimal performance, whereas EF ratings capture typical performance (Toplak et al., 2013). Furthermore, laboratory measures are usually assessed only once and could therefore be less sensitive for identifying deficits compared to ratings, which capture behavior over longer periods of time. Another way of describing the differences between EF tests and EF ratings has been formulated by Barkley and Murphy (2011). They argued that EF should best be viewed as a hierarchy, which involves several levels of increasingly complex behaviors. In their view, tests measure EF deficits at the lowest level, whereas ratings measure higher and more complex levels of EF deficits that cannot be measured with tests. Because daily life functioning largely involves complex EF demands, this may explain why EF ratings are more strongly related to daily life functioning.

When discussing the poor link between EF tests and daily life functioning, it is important to remember that EF ratings also have limitations. Two important limitations are that they are

affected by rater bias and that they usually capture more global levels of functioning rather than specific neuropsychological deficits (cf. Thorell & Nyberg, 2008). In sum, EF ratings and EF tests have different strengths and limitations, and one could therefore argue that these two sources of information should be used as a complement to rather than as a replacement for one another. In line with this thinking, the present study was able to show that sensitivity was greatly increased when the scores from both the laboratory test and the ADEXI were entered into the logistic regression model. By including several different sources of information, rater bias can also be minimized, and this could also be one way of controlling for non-credible EF performance/ratings (cf. Suhr, Cook, & Morgan, 2017).

3.2.2 Which neuropsychological deficits are specific to ADHD?

As described in the introduction of the present thesis, deficits in executive functioning have not only been reported in patients with ADHD, but also in patients with other psychiatric disorders such as depression (e.g., Godard et al., 2011; Gohier et al., 2009; Hammar et al., 2011; Rose & Ebmeier, 2006), bipolar disorder (e.g., Godard et al., 2011; Robinson et al., 2006), anxiety disorders (Gualtieri & Dexter, 2008), and obsessive-compulsive disorder (Vandborg et al., 2014; Bannon et al., 2006). One serious limitation of previous research is therefore that very few studies have made a direct comparison between individuals diagnosed with ADHD and individuals with other psychiatric disorders. Thus, we know very little regarding to what extent neuropsychological deficits are specifically linked to ADHD. By including a clinical control group and not only a normal control group, it is possible to determine whether neuropsychological differences are likely to be the result of specific ADHD-related deficits rather than of general psychopathology (Hervey et al., 2004).

The results of Study II showed that, when studying group differences, adults with ADHD performed more poorly compared to the clinical control group on neuropsychological tests measuring inhibition, working memory, set shifting, planning, and fluency. Adults with ADHD also showed more delay-averse behavior, and higher reaction time variability. These results could be said to be in line with all three theoretical models presented in the introduction, as they reveal the central importance of executive deficits (Barkley, 1997), delay aversion (Sonuga-Barke, 2002, 2003) and reaction time variability (Sergeant, 2005) for ADHD.

As argued in the introduction, it is important to not only study group differences, but also to report measures of sensitivity and specificity. In addition, it is important to be able to study whether neuropsychological tests can be used to discriminate not only between adults with ADHD and adults and healthy controls, but also between patients with ADHD and those with other psychiatric disorders. Few previous studies have conducted this type of analysis in adult ADHD, and the results of both Study I and II therefore contribute valuable new information by showing that, regarding the neuropsychological tests, the sensitivity ranged between 64% and 67% and the specificity between 70% and 81% when comparing adults with ADHD to

adults with other psychiatric disorders. The relatively low specificity of neuropsychological tests indicates that many of these deficits are present also among patients with other psychiatric disorders. The relatively low sensitivity is in line with current models of heterogeneity in ADHD (e.g., Nigg et al., 2005), in which only a subtype of patients with ADHD have clear neuropsychological deficits.

In sum, it can be argued that rather than describing ADHD as an executive disorder, which was often the case after Barkley's (1997) very influential theory was presented, there appears to be subgroups of patients with executive deficits included in many psychiatric disorders. This neuropsychological heterogeneity has been proposed to constitute a barrier to unraveling the mechanisms underlying the disorder and laying the foundation for effective treatments (Marquand, Wolfers, Mennes, Buitelaar, & Beckmann, 2016). In line with this, it has been stated in, for example, the Research Domain Criteria (RDoC), presented by the National Institute of Mental Health (NIMH; Insel et al., 2010), that psychiatric disorders should be characterized by underlying neurobiological deficits rather than behavioral symptoms. New disorders such as Working Memory Disorder, Inhibitory Control Disorder, or Emotion Regulation Disorder would then be introduced. In reality, making this transition to a more neuropsychologically based classification system has proven to be very difficult, at least partly owing to the relatively low ecological validity of many neuropsychological tests, as discussed above in relation to the ADEXI (see 3.2.1)

3.2.3 Control for basic cognitive functioning

Almost no previous studies have controlled for basic cognitive functions (i.e., speed, verbal abilities, and memory). However, conducting this control enabled us to examine whether adult ADHD is specifically linked to executive deficits or to cognitive deficits in general. In Study II, the effects of inhibition, verbal working memory, fluency, set shifting, and delay aversion remained significant when controlling for IQ. When controlling for basic cognitive functions, only the effect of inhibition, fluency and delay aversion remained significant. Boonstra and colleagues (2010), who did not include delay aversion, also found that the effect of inhibition remained significant when controlling for basic cognitive functions and IQ. This is also in line with Barkley's (1997) hybrid model of ADHD, where deficient inhibition is seen as the most central aspect of ADHD, which in turn leads to secondary deficits in other executive functions. The fact that delay aversion also remained significant in our study is in line with the dual pathway model proposed by Sonuga-Barke (2002), suggesting two separate pathways to ADHD: one motivational pathway, characterized by delay aversion, and one executive pathway, characterized by poor inhibitory control. The fact that so many executive constructs do not survive control for both IQ and basic cognitive processes could suggest that the sample of adults with ADHD also have deficits with regard to basic cognitive functions, and not only EF deficits.

3.2.4 Neuropsychological functions in older adults with ADHD

Study IV is one of the first studies ever to investigate neuropsychological deficits in adults above 60 years of age. Additional strengths of Study IV are also that we: 1) compared older adults with ADHD to both healthy older controls and to younger adults with ADHD, 2) included a broader range of neuropsychological functions (e.g., executive deficits, delay aversion, fluency and speed of processing) compared to previous studies, and 3) used a clinically-referred sample that was large compared with samples investigated in previous studies. Thus, the study contributes valuable new knowledge.

The results of Study IV showed that older adults with ADHD differed from controls with regard to working memory, inhibition and speed of processing. In comparison to younger adults with ADHD, they performed at a similar level for working memory and planning, but significantly better with regard to inhibition, switching, verbal fluency, and one measure of speed of processing. Overall, these results are in line with the view that ADHD is a heterogeneous disorder that is related to multiple neuropsychological deficits, including executive deficits and delay aversion, and that there is a subgroup of older adults showing no clear neuropsychological deficits (Castellanos et al., 2006; Nigg et al., 2005). With regard to more specific functions, we argue that the significant difference between the younger adults with ADHD and the older adults with ADHD with regard to delay aversion can possibly be due to a general age effect (i.e., that younger individuals are generally more delay averse than older individuals). Previous studies on age effects in normally developing samples have shown that younger adults have a tendency to choose more immediate rewards than older adults do (Green, Fry & Myerson, 1994; Li, Baldassi, Johnson & Weber, 2013). Li and colleagues (2013) found that older adults have more crystallized intelligence but lower levels of fluid intelligence and that delay-related behaviors are more dependent on crystallized intelligence. Crystallized intelligence involves knowledge that derives from prior learning and past experiences. Situations that require crystallized intelligence include reading comprehension and vocabulary exams. Fluid intelligence involves being able to think and reason abstractly and solve problems. It is considered to be independent of learning, experience, and education. Fluid intelligence tends to decline during late adulthood, and crystallized intelligence increases with age (Horn & Cattell, 1967).

In sum, the results of Study IV add some additional information regarding the role of neuropsychological deficits in older adulthood, but more studies are clearly needed as this age group has so seldom been the focus of ADHD research. As mentioned earlier in the summary, there are a few previous studies available showing that older adults with ADHD have impairments similar to those of younger adults with ADHD (Guldborg-Kjær & Johansson, 2009; Michielson et al., 2015). It is therefore of great importance that more studies be carried out to increase our knowledge about ADHD in this age group, thereby enabling psychiatric clinics and care centers to provide the help that is needed.

3.3 PRACTICAL IMPLICATIONS

When diagnosing ADHD in adults, it is important to collect a great deal of information about the patient's background and childhood symptoms of ADHD. The diagnostic process begins with the adult patient completing screening instruments – such as ASRS (Kessler et al., 2005) and Wender Utah Rating Scale (WURS; Ward, Wender & Reimherr, 1993) – aimed at measuring ADHD symptoms. If the screening results indicate that the patient has high levels of ADHD symptoms, a full investigation is initiated. This investigation involves interviewing the adult patient and a close relative, preferably a parent, in order to get a complete childhood anamnesis. The diagnostic process can be complemented by using a neuropsychological test battery, usually including WAIS-IV (Wechsler, 2008) for measuring IQ and tests measuring executive functions, such as the D-KEFS (Delis et al., 2001).

During the period in which the present research was conducted, administration of neuropsychological tests in the diagnostic process was reduced. The main reason for this change was that current models of heterogeneity (Castellanos et al., 2006; Nigg et al., 2005) have clearly shown that ADHD is comprised of several neuropsychological subgroups. ADHD is therefore no longer seen as an executive disorder, and the present results clearly support this claim. Neuropsychological tests should therefore not be used as a primary diagnostic tool for ADHD. In line with the diagnostic criteria presented in DSM-5 (APA, 2013), the most important components of the investigation should instead be the following: 1) anamnesis (i.e., being able to exclude that the symptoms are better accounted for by something else), 2) knowing whether there is a history of childhood symptoms of ADHD (i.e., symptoms need to have been present before age 12), and 3) whether the patient has significant impairments in daily life functioning.

The fact neuropsychological tests are more seldom used today raises the question: What role could neuropsychological tests play in assessments of ADHD? From a research-oriented perspective, it has been argued that it is important to investigate neuropsychological deficits in order to identify neuropsychological subgroups (Nigg et al., 2005). Perhaps these subgroups will be shown to differ with regard to important aspects, such as the biological underpinnings of the disorder, treatment response, impairments in daily life functioning, and symptom development over time. The aspect of biological underpinnings was not addressed in the present study. However, Sonuga-Barke (2002) argued that, for example, executive deficits and delay-related behavior are related to at least partially different brain regions, which is taken as support for the notion that these two neuropsychological deficits should be regarded as different pathways to ADHD.

With regard to treatment response, working memory training has been presented as one treatment option for ADHD. However, most studies have been conducted in childhood samples and there is a debate regarding the strengths of the treatment effects and to what extent possible effects can be generalized to daily life functioning (e.g., Titz & Karbach, 2014). One possible reason for these mixed findings is that most studies have only used an ADHD diagnosis as the inclusion criterion, without taking into consideration that only a

subgroup of these patients has clear deficits in working memory. If the intervention targets working memory deficits and these deficits are not present in a subsample of patients, it is not particularly surprising that the effects of treatment are limited. Thus, assessment of neuropsychological functioning as part of the assessment for ADHD could be important for identifying patients that might be helped by an intervention targeting working memory impairments. Another important link between neuropsychological assessment and treatment could be that some patients with ADHD may have such severe neuropsychological deficits in many domains that they have difficulty taking part in non-pharmacological treatment options such cognitive behavior therapy (CBT), which is seldom offered individually but rather in group settings (Hirvikoski, Lindström, Carlsson, Waaler, Jokinen & Bölte, 2017; for a review, see Mongia & Hechtman, 2012) or on the Internet (e.g., Pettersson, Söderström, Edlund-Söderström & Nilsson, 2017). Assessments of intellectual levels and socioeconomic status must be taken into consideration in future research, as suggested by, for example, Mongia and Hechtman (2012). In sum, neuropsychological assessment may be one way toward more individualized treatment options for patients with ADHD, although much more research is needed to determine how we can best identify neuropsychological subgroups.

Study III addressed the issue of the link between neuropsychological deficits and daily life functioning. A few previous studies have found that individuals in the ADHD subgroup with executive deficits are more impaired in daily life functioning compared to those in the subgroup without these deficits (e.g., Biederman et al., 2006a; Halleland et al., in press), but few studies have addressed this issue, at least in adult ADHD. The results of the present studies indicate that a number of issues need to be taken into consideration if neuropsychological assessment is to be an important source of information for better understanding the functional impairments associated with ADHD. First, the reason why the ADEXI was created (Study I) was that many of the available rating instruments do not only assess executive deficits, but also ADHD symptom levels. Thus, previous studies investigating the link between executive deficits and functional impairments using only ratings might have overestimated this link, both due to shared method variance and because their measures have included ADHD symptoms as well as executive deficits. The results of Study I also support previous research (Barkley & Fischer, 2011; Barkley & Murphy, 2010), by showing that the relation between ratings and tests of executive deficits is relatively weak. In Study III, the results showed that EF deficits appeared to play a role in academic functioning, current occupational status, and criminality. In comparison with previous research (e.g., Barkley & Fischer, 2011; Barkley & Murphy, 2010), the link between executive deficits and functional impairments was not as strong in our research when using EF ratings. This could be because we used measures that specifically targeted different EF constructs rather than more general cognitive functions and ADHD symptom levels. In sum, it is not clear how the information collected from ratings, preferably using multiple sources, and tests can be best combined to acquire the best information about the neuropsychological deficits that may be of importance to our understanding of the functional impairments associated with ADHD. Based on previous research on children, it appears clear that

executive deficits are of great importance to academic functioning, but perhaps less so to social functioning (e.g., Sjöwall & Thorell, 2014), and this was also supported by the results from Study III.

Finally, if neuropsychological subgroups of patients with ADHD can be identified, these subgroup may differ with regard to symptom stability over time. This issue was not addressed in the present studies, and it has seldom been addressed in studies on adults. However, a number of studies have shown that neuropsychological deficits in early childhood are related to a number of important outcomes later in life, including academic outcomes in late adolescence (e.g., Sjöwall, Bohlin, Rydell, & Thorell, 2017).

3.4 LIMITATIONS

In Study I, we compared the ADEXI, measuring deficits specifically in inhibition and working memory, with Barkley's Deficit Executive Function Scale (BDEFS), which includes subscales targeting: Self-organization/Problem Solving, Self-management of Time, Self-restraint/Inhibition, Self-regulation of Emotion, and Self-motivation. We argue that a short screening instrument for assessing executive deficits specifically (i.e., not including ADHD symptoms or cognitive deficits in general) is of great value and that the ADEXI can therefore serve an important purpose. However, it should be noted that owing to the small number of items included in the ADEXI, it is not possible to cover all neuropsychological deficits of importance to ADHD (e.g., delay aversion and emotion regulation), which could be seen as a limitation.

In Study II, there are some limitations that should be acknowledged. First, participants who were on medication with central stimulants were included together with medication-naïve participants. We conducted some complementary analyses that excluded participants with medication, and both group differences and the overall classification rates were relatively similar in these analyses. A second limitation is that not all of the included functions were studied using multiple measures. It would have been valuable to include more measures of inhibition and reaction time variability, and it would also have been valuable to include a laboratory test of delay aversion. However, in line with recent theories emphasizing the neuropsychological heterogeneity within ADHD (e.g., Castellanos et al., 2006; Nigg et al., 2005), we decided to prioritize studying a broad range of functions over studying fewer functions in more detail.

Study III is limited by the small sample size, especially concerning the comparison between the ADHD subgroups with and without EF deficits. However, because only a very limited number of previous studies on adult ADHD have compared these two ADHD subgroups with regard to functional impairment, the present study adds valuable new knowledge.

In Study IV, the sample size of older adults with ADHD was larger compared to previous studies. The number of participants with ADHD in this age group is still limited, although the

numbers are increasing as it is becoming more and more common to diagnose ADHD in adulthood. Older adults are more likely to suffer from different physical and mental disabilities, and are therefore less likely to participate in studies; thus, our sample might not include the most severely affected individuals. However, our sample is likely to be more severely affected compared to samples in previous studies of older adults with ADHD, because we used a clinically referred sample, whereas they used population-based samples. Another limitation worth mentioning is that we would have liked to include an even larger range of tasks. However, we could only include tasks for which standardized scores were available for older adults, given our interest in comparing to what extent older and younger adults with ADHD differed from one another relative to norms. It would have been valuable to include tasks assessing spatial working memory, reaction time variability, and reward processing, as well as additional tasks measuring inhibitory control. Ratings of emotional regulation would also have been valuable to include, as several studies of children have found strong links between ADHD and deficient emotion regulation (Shaw, Stringaris, Nigg & Leibenluft, 2014).

3.5 CONCLUSIONS AND FUTURE DIRECTIONS

In Study I, we showed that ADEXI scores have adequate psychometric properties and that this instrument serves a partly different purpose compared to other available EF rating instruments for adults. Compared to other rating instruments, such as the BRIEF-A or BDEFS, ADEXI has the clear advantage of being brief and less comprehensive, although this could also be seen as a disadvantage. However, individuals with ADHD and EF deficits usually have great difficulties completing long rating instruments, and it might therefore be an advantage to have a quick and easily administered screening instrument focusing specifically on two central EF aspects: inhibition and working memory. Future research should preferably collect normative data on the ADEXI using a large representative sample, because individual scores are of limited value from a clinical perspective without the availability of norms.

In Study II, we could conclude that adults with ADHD differ significantly from adults with other psychiatric disorders on a range of different neuropsychological functions. However, effect sizes were relatively small and only the effects of inhibition, fluency, and delay aversion remained significant after controlling for IQ or basic cognitive functions. In addition, the results demonstrate that, despite significant group differences, the ability of these tests to discriminate between groups was relatively poor, with about 25% to 30% being misclassified. It would be of great value if future studies were to compare adults with ADHD and clinical controls using a broader range of neuropsychological deficits. As mentioned above under limitations, one important domain that was not included in Study II, but which has been shown to be linked to ADHD, is emotion regulation (Shaw et al., 2014).

In Study III, we could demonstrate that daily life is severely affected among adults with ADHD. They are significantly more impaired even compared to adults with other psychiatric disorders. The study also showed that EF deficits seem to play a role in explaining these impairments, primarily with regard to academic functioning, occupational status, and criminality. Regarding future research, it would be of great value to investigate the specific effects of different neuropsychological deficits in relation to daily life functioning rather than just comparing ADHD subgroups with and without executive deficits. It would also be of great importance if future studies were to try to investigate whether executive functioning can be improved through cognitive training in adult ADHD, focusing especially on more long-term effects and whether effects can be generalized to daily functioning. It is also important to make appropriate adjustments in the work settings for adults with ADHD and executive deficits.

In Study IV, the results support current models of heterogeneity in which ADHD is regarded as a disorder related to a range of different neuropsychological deficits, but also show that there is a subgroup of older adults with ADHD without clear neuropsychological deficits. Future research should focus on identifying neuropsychological subgroups within the ADHD population, as this could help in detecting patients who are at particularly high risk of poor functioning in daily life. Longitudinal follow-ups of older adults with ADHD will be of major importance, as we do not know how specific neuropsychological deficits in older adults interact with either normal or abnormal cognitive decline. In addition, it would be of great value to further examine to what extent neuropsychological deficits among older adults with ADHD affect their daily life functioning and quality of life.

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