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A neuropsychological examination in a clinical referral context

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Chapter 1

General introduction

Goals of this thesis

This thesis aims to explore and further define the neuropsychological characteristics of attention-deficit/hyperactivity disorder (ADHD) in adulthood in order to improve the differential diagnosis of adult ADHD, optimize the neuropsychological evaluation, and develop more targeted and efficient treatment plans. More specifically, this thesis examines a broad range of neuropsychological functions of individuals in the clinical evaluation of adult ADHD and further defines the role of performance tests, self-reports, and informant reports in the clinical evaluation. Moreover, this thesis addresses the inter-relations of neuropsychological functions in adult ADHD and determines whether particular functions stand out and may play a more central role. Finally, this thesis examines whether core neuropsychological functions of adults with ADHD are stable or fluctuate over time in repeated clinical assessments.

Background

ADHD in adulthood

ADHD is a childhood-onset neurodevelopmental disorder and up to 65% of children with ADHD still experience ADHD symptoms in adulthood (American Psychiatric Association, 2013; Kooij et al., 2019; Owens, Cardoos, & Hinshaw, 2015). The global prevalence rate of adult ADHD was estimated to be 2.5 - 6.8% (Fayyad et al., 2017; Simon et al., 2009; Song et al., 2021). ADHD is characterized by symptoms of inattention and/or hyperactivity/impulsivity. Symptoms of inattention comprise, as defined by the current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013), distractibility, forgetfulness, losing things, daydreaming, carelessness, and having difficulty organizing tasks, while symptoms of hyperactivity/impulsivity include fidgeting, being unable to sit still and to concentrate on tasks, excessive talking and interrupting conversations. ADHD can be divided into three presentation types based on the main symptoms, including the predominantly inattentive symptom presentation, the predominantly hyperactive/impulsive symptom presentation, and the combined symptom presentation (American Psychiatric Association, 2013). Moreover, ADHD in adulthood usually co-occurs with other psychiatric disorders, of which depression, anxiety disorders, substance use disorders, and personality disorders are the most prevalent comorbidities (Barkley & Newcorn, 2009; Katzman et al., 2017; Sobanski, 2006). Adult ADHD is associated with more likely adverse outcomes compared to their typically developing peers, such as academic underachievement (Arnold et al., 2020;

Henning, Summerfeldt, & Parker, 2022), occupational issues (Fuermaier et al., 2021; Gjervan et al., 2012), sleep problems (Díaz-Román, Mitchell, & Cortese, 2018; Lugo et al., 2020), problems in social relationships (Michielsen et al., 2015; Wymbs et al., 2021), a poorer financial situation (Bangma et al., 2019; Beauchaine, Ben-David, & Bos, 2020), lower self-esteem (Harpin et al., 2016; Newark, Elsässer, & Stieglitz, 2016), and a lower quality of life (Agarwal et al., 2012; Thorell, Holst, & Sjöwall, 2019).

The clinical diagnostic evaluation of adult ADHD is commonly based on a structured diagnostic interview following ADHD diagnostic criteria as defined in the DSM-5 (American Psychiatric Association, 2013), and usually includes standardized inventories of self-report, reports of significant others, and objective information on symptoms and impairments, as it is outlined in current empirically-informed diagnostic guidelines (Sibley, 2021). The retrospective assessment of ADHD symptoms and impairments in childhood is a crucial but challenging aspect in the diagnostic process of first-time adult ADHD when no formal diagnosis has been established in childhood (Sibley, 2021). Moreover, a neuropsychological assessment using cognitive performance tests is also part of a routine clinical examination in many ADHD assessment settings, although performance tests are not mandatory to use and there is general agreement that performance tests are only of little help to establishing an ADHD diagnosis (Gallagher & Blader, 2001; Ramsay, 2015). So far, the role of a neuropsychological assessment in the clinical trajectory of adult ADHD is insufficiently defined, especially when differentiation to other clinical syndromes is required. Further, although a large body of evidence exists on neuropsychological deficits of adults with ADHD compared to typically developing individuals (Boonstra et al., 2005; Onandia-Hinchado, Pardo-Palenzuela, & Diaz-Orueta, 2021), less is known about the inter-relations between various neuropsychological functions, as well as about the stability or potential fluctuations in neuropsychological performance levels over time.

The assessment of neuropsychological functions using cognitive performance tests in adults with ADHD

Adults with ADHD are frequently reported to suffer from deficits in multiple neuropsychological functions when compared to healthy control groups, including processing speed, different aspects of attention, memory, and executive functions (Boonstra et al., 2005; Fuermaier et al., 2015; Hervey, Epstein, & Curry, 2004; Onandia-Hinchado et al., 2021; Pazvantoğlu et al., 2012; Schoechlin & Engel, 2005). However, the comparison of neuropsychological functions between individuals with ADHD and healthy control groups may not be representative for clinical practice, where individuals with ADHD are sought to be differentiated from individuals with subclinical levels of impairments or other psychiatric conditions (Barkley, 2010; Gentile, Atiq, & Gillig, 2006). The term ‘clinical controls’ refers to individuals who were referred for a diagnostic assessment of ADHD as they were suspected of having ADHD but who eventually did not reach the diagnostic criteria. Among those clinical controls, some of them may meet the diagnostic criteria of other psychiatric disorders, such as mood disorders, anxiety disorders, or addiction disorders, which are also known to be associated with deficits in various neuropsychological functions (Airaksinen, Larsson, & Forsell, 2005; Cotrena et al., 2016; Weiland-Fiedler et al., 2004). Comparisons of neuropsychological functions between individuals with ADHD and clinical controls are scarce, which makes firm conclusions about neuropsychological characteristics that are potentially specific for adult ADHD difficult to draw. For these reasons, the role of an objective neuropsychological assessment in the clinical evaluation of adult ADHD has not been agreed on, yet (Barkley, 2019; Mapou, 2019). The vast majority of researchers and clinicians agree that an objective neuropsychological assessment with cognitive performance tests is of little help in establishing the diagnosis of ADHD, as there is evidence showing that neuropsychological tests failed to discriminate well between adults with ADHD and adults with other psychiatric conditions, or even community samples without ADHD (Barkley, 2019; Marshall, Hoelzle, & Nikolas, 2021; Pettersson, Söderström, & Nilsson, 2018). However, others advocate the important role of an objective neuropsychological assessment and stress that performance tests could contribute to the comprehensive understanding of an individual’s functioning, as it helps clinicians to identify cognitive strengths and weaknesses, and could potentially guide treatment planning (Lange et al., 2014; Mapou, 2019). Thus, further neuropsychological research of adult ADHD and related disorders in the same referral context would benefit research and clinical practice by further defining the role of neuropsychological performance tests in assessment and treatment of adult ADHD.

The role of subjective reports on symptoms and impairments in adults with ADHD

Next to objective neuropsychological tests, a standardized assessment of symptoms and impairments with self and informant-report inventories is commonly applied in the clinical evaluation of adults with ADHD (Haavik et al., 2010; Marshall et al., 2021). A subjective assessment of neuropsychological functions can be understood as the individuals’ self-evaluation of their neuropsychological functioning in daily life activities (Fuermaier et al., 2015). Although both self-rated questionnaires (subjective assessment) and neuropsychological tests (objective assessment) have been shown to be sensitive measurements in revealing neuropsychological deficits in individuals with ADHD, research indicated that the objective neuropsychological test performances and subjective ratings of cognitive functioning were only marginally associated with each other (Fuermaier et al., 2015; Potvin et al., 2016). Conclusions about the relationships and distinct roles of subjective reports and objective measures in the neuropsychological evaluation of adult ADHD can, however, not be drawn because studies addressing this issue are scarce. Furthermore, the role of (symptom) self- and informant-reports in the diagnostic evaluation of adult ADHD is still a subject of research (Kooij et al., 2008; Magnússon et al., 2006). For example, a routine first-time diagnosis of ADHD in adults is recommended to include a subjective retrospective assessment of ADHD symptoms in childhood (e.g., as assessed with the Wender Utah Rating Scale, WURS; Ward, 1993) and an assessment of current ADHD symptoms (e.g., with the Conners' Adult ADHD Rating Scales, CAARS; Conners, Erhardt, & Sparrow, 1999) completed by patients themselves and their informants (see Sibley, 2021). However, although subjectively reported ADHD symptoms were shown to be substantially higher in individuals with ADHD compared to healthy controls, the comparisons of subjectively reported symptoms between individuals with ADHD and individuals with other psychiatric conditions are scarce and results are inconsistent. For example, the WURS was reported to successfully differentiate an ADHD group from clinical control groups suffering from other psychiatric conditions in some studies (Paucke et al., 2021; Suhr et al., 2008), which failed to be replicated by others (Suhr et al., 2009). Moreover, the comparison of subjectively reported symptoms between individuals with ADHD and clinical controls from the same referral context are presumably more challenging but also more relevant to the clinical practice of adult ADHD, as all individuals who are referred for a diagnostic evaluation of adult ADHD may show at least some ADHD-typical symptoms and/or impairments. Thus, more research is needed to define the role of subjective reports on symptoms and impairments in the clinical evaluation of adults with ADHD, especially in the differential diagnosis between individuals diagnosed with ADHD and clinical controls from the same referral context.

Inter-relations between neuropsychological functions of adults with ADHD

Although neuropsychological deficits have been frequently demonstrated in adults with ADHD in numerous research studies (Boonstra et al., 2005; Onandia-Hinchado et al., 2021), less is known about the inter-relations between different neuropsychological functions. In early reports on different pathway models of cognitive functions, it was suggested that individuals with ADHD may have impairments in one or more of several relatively independent neuropsychological functions, such as inhibition, working memory, timing, delay aversion, decision-making, and response variability (Coghill, Seth, & Matthews, 2014; Sonuga-Barke, Bitsakou, & Thompson, 2010; Sonuga-Barke, 2003, 2005). These conceptual studies support the argument that deficits in neuropsychological functions in adults with ADHD mainly occur relatively independently of each other. Yet, significant associations were reported between performance scores on relatively basic neuropsychological functions, such as processing speed and distractibility, and performance scores on more complex neuropsychological functions, such as inhibition and cognitive flexibility (Butzbach et al., 2019; Mohamed et al., 2021). In contrast to the view of largely independent neuropsychological deficits in adults with ADHD, these findings indicate that basic and complex neuropsychological functions are interrelated and deficits in basic functions may result in and lead to deficits in complex functions. Theoretically founded studies exploring the relationships between different neuropsychological functions of individuals with ADHD are, however, limited and no empirically founded conclusions can be drawn, yet. Moreover, clarifying the relationships between various neuropsychological functions is not only relevant for advancing our understanding of neuropsychological profiles of ADHD, but has also the potential to guide the clinical practice of adults with ADHD. For example, network analysis (Borsboom & Cramer, 2013; Fonseca-Pedrero, 2018; Hevey & Medicine, 2018) may be suited to indicate redundancy in extensive neuropsychological batteries, which could be a basis for adapting assessment batteries in order to save clinical resources in test administration, scoring, and interpretation. Further, network analysis may be suited to guide the development of more targeted treatment plans to improve neuropsychological performances, given specific functions can be identified that impact substantially on a range of other functions in the network.

Intra-individual variability of neuropsychological functions of adults with ADHD

Fluctuation in neuropsychological performance over short time intervals (e.g., in reaction time tasks over seconds or milliseconds), also known as intra-individual variability, has frequently been reported in adults with ADHD and is considered a central feature of the cognition (Klein et al., 2006; Kofler et al., 2013; Vaurio, Simmonds, & Mostofsky, 2009). Other than fluctuations in cognition, recent research also reported fluctuations in ADHD symptoms over days, weeks, or even months (Pedersen et al., 2020; Schmid et al., 2020). The observed fluctuations in ADHD symptoms may have implications for clinical practice, as, for example, it may indicate that one-time assessments may give a biased representation of an individual's functioning and that repeated assessments on different days may be helpful in getting a more accurate picture of the individual's symptomatology (Schmid et al., 2020). Similarly, the assessment of neuropsychological functions as it is commonly applied in clinical practice relies on the results of a one-time assessment, with the assumption that the performance scores represent stable characteristics of cognitive abilities. However, there is a lack of evidence on whether this assumption is correct or whether neuropsychological test performance also fluctuates from one assessment moment to the other as it is observed in symptom scores. Possible findings on intra-individual variabilities over time, if existent, may partly account for the inconsistent findings across studies of neuropsychological performance (Salomone et al., 2020; Tucha et al., 2008) or cognitive heterogeneity observed in individuals with ADHD (Luo et al., 2019; Mostert et al., 2015). Given the evidence of previous research suggesting a hierarchical relationship between basic and complex cognitive functions in adults with ADHD (Butzbach et al., 2019; Kooij et al., 2019; Mohamed et al., 2021), we suggest giving priority to the investigation of intra-individual variability in attention performance across different points in time.

Outline of the thesis

Chapter 2 *("Neuropsychological functioning of individuals at clinical evaluation of adult ADHD")* explores a wide range of neuropsychological functions of individuals at the clinical evaluation of adult ADHD by recruiting and assessing 199 individuals from an outpatient referral context. Participants were allocated into one of three groups, i.e., a group of participants who were diagnosed with ADHD (*n* = 78), a clinical comparison group including participants who did not meet the diagnostic criteria for ADHD but showed evidence for one or more other psychiatric disorders (*n* = 71), and a clinical comparison group of participants who did not meet diagnostic criteria for ADHD and who were also not diagnosed with any other psychiatric disorder (*n* = 50). All participants performed a comprehensive neuropsychological test battery that was developed to assess a wide range of neuropsychological functions that have been shown to be sensitive in this assessment context. This chapter aims, firstly, to describe the neuropsychological test performance of all individuals in the clinical evaluation of adult ADHD and, secondly, to examine whether significant and clinically meaningful differences exist in a wide range of neuropsychological functions between individuals who met the diagnostic criteria of ADHD and individuals who did not.

Chapter 3 *("The role of self- and informant-reports on symptoms and impairments in the clinical evaluation of adult ADHD")* examines the role of subjective reports on symptoms and impairments in the clinical evaluation of adult ADHD by recruiting and assessing 169 outpatients referred for a diagnostic evaluation of adult ADHD. Also, in this study we distinguished between a group of individuals with ADHD (*n* = 73) and two clinical comparison groups based on whether they show indications (*n* = 53) or no indications (*n* = 43) of psychiatric disorders other than ADHD. A set of clinically validated questionnaires was completed by participants themselves and their informants, tapping symptoms and impairments commonly seen in this assessment context. Neuropsychological test performance was also considered in this study. The main research questions of this chapter include whether significant and meaningful differences exist in subjectively reported symptoms and impairments between individuals who met the diagnostic criteria of ADHD and individuals who did not, whether subjective reports could predict an individual's diagnostic status, and whether subjective reports have predictive value for objective neuropsychological test performance.

Chapter 4 *("Networks of neuropsychological functions in the clinical evaluation of adult ADHD")* explores the relations between different neuropsychological functions of individuals in the clinical evaluation of adult ADHD using network analysis. A total of 319 participants from an outpatient referral context were recruited and divided into an ADHD group (diagnosis of ADHD was established, *n* = 173) or an n-ADHD group (participants did not meet the diagnostic criteria of ADHD, *n* = 146). All participants completed a comprehensive neuropsychological assessment that was designed to assess a range of neuropsychological functions of adults with ADHD. The aims of this study are, firstly, to explore whether the different neuropsychological functions are interrelated or isolated in the ADHD and n-ADHD groups, respectively, and, secondly, whether there is any significant difference between the neuropsychological function networks of the two groups. This study further aims to explore whether there are particular functions that stand out and may play a more central role in the networks of different neuropsychological functions.

Chapter 5 *("Neuropsychological attention performance of adults with ADHD is stable over time: Evidence from repeated assessments in one-month intervals")* examines whether attention performance on neuropsychological tests of adults with ADHD fluctuates or is stable over time in repeated assessments. A total of 21 adults diagnosed with ADHD took part in this study and completed tests for selective attention and vigilance three times in repeated assessments, each one month apart. In this study we present and depict the attention performance of all three assessments and then compare the attention performance between the three assessments in order to explore whether attention performance of adults with ADHD fluctuates or is stable over repeated assessments.

Chapter 6 *("General discussion")* elaborates on the main findings of the four empirical studies included in this thesis and critically discusses the implications of our findings for the understanding of the neuropsychological functioning of adults with ADHD and the clinical practice of individuals seeking a diagnostic evaluation of adult ADHD. Suggestions for future research will be discussed, as well as implications for the neuropsychological practice.

Chapter 2

Neuropsychological functioning of individuals at clinical evaluation of adult ADHD

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Abstract

Objectives: Numerous studies showed that adults with attention deficit hyperactivity disorder (ADHD) suffer from impairments in a range of cognitive functions when compared to healthy controls. However, only little is known about the neuropsychological functions when compared to various clinical control groups and whether a distinct neuropsychological profile can be identified for adult ADHD. **Method:** This retrospective study examined data of 199 outpatients referred for clinical evaluation of adult ADHD, allocated either to an ADHD group (n = 78) or to one of two clinical comparison groups, depending on whether they show indications (n = 71) or no indications (n = 50) for the presence of psychiatric disorders other than ADHD. All individuals performed a comprehensive neuropsychological test battery. **Results:** Data analysis revealed impairments in a range of cognitive functions in a substantial number of patients of all three groups. However, profiles of neuropsychological impairments were similar between groups. Furthermore, significant small to medium-sized correlations between basic and higher-order cognitive functions were revealed in the ADHD group and the clinical comparison group with indications for psychiatric disorders other than ADHD. **Conclusion:** Neuropsychological impairments are prominent in psychiatric outpatients seeking a clinical evaluation of adult ADHD but are not specific for ADHD. It is concluded that neuropsychological test performance may have limited incremental value to support the psychiatric differential diagnosis. Furthermore, a clinical trajectory may need to take into account that deficits in a range of higher-order cognitive functions can be substantially explained by deficits in basic cognitive functions.

Keywords: Adult ADHD, neuropsychology, cognition, assessment, diagnosis

Introduction

Attention deficit hyperactivity disorder (ADHD) is one of the most prevalent neurodevelopmental childhood disorders that persists into adulthood in a large proportion of cases (Biederman et al., 2011; Polanczyk et al., 2007; Stubbe, 2000; Weiss & Hechtman, 1993). ADHD is characterized by symptoms of inattention, hyperactivity, and impulsivity (American Psychiatric Association, 2013; Barkley & Murphy, 2006). A range of functional impairments are associated with ADHD in adulthood when compared to healthy controls, mainly including lower educational attainment and employment rate (Biederman, 2005; Faraone et al., 2000; Gjervan et al., 2012; Holst & Thorell, 2020; Sobanski et al., 2007), poorer financial situation (Bangma et al., 2019; Biederman et al., 1993), lower self-esteem (Canu & Carlson, 2007), more alcohol and drug abuse (Cumyn, French, & Hechtman, 2009; Torgersen, Gjervan, & Rasmussen, 2006), and a lower quality of life (Agarwal et al., 2012; Stern et al., 2017).

Because ADHD is by definition a disorder with predominant cognitive deficits that interfere with many tasks of daily living, a large body of neuropsychological research has been performed to elucidate the level of neuropsychological functioning of individuals with ADHD. Converging evidence from numerous studies revealed impairments of adults with ADHD in multiple domains of cognition, including different aspects of attention, processing speed, memory and executive functions (Barkley & Murphy, 2010; Boonstra et al., 2005; Brown, 2002; Fuermaier et al., 2015; Jacobson et al., 2011; Tucha et al., 2009). Research further revealed that neuropsychological functions appear to improve but do not normalize under pharmacological treatment with stimulants, as deficits are still present under stable medication especially in the domains of memory and attention (Fuermaier et al., 2017; Müller et al., 2007). Furthermore, studies showed that the impairments in the various domains of cognition may not be independent entities, but that impairments in basic cognition, such as processing speed and attention focus, may explain a considerable proportion of the impairments in the more complex cognitive functions, such as divided attention, memory, or executive functions (Boonstra et al., 2010; Holst & Thorell, 2017). Due to the cognitive impairments of adults with ADHD, the assessment of neuropsychological functions using cognitive performance tests has been suggested to be of added value to the clinical evaluation of adults with ADHD. In this respect, neuropsychological assessments are performed to characterize individual cognitive strengths and weaknesses, which may help to understand why an individual patient is experiencing problems in daily life (Barkley & Fischer, 2011; Mapou, 2019; Stern et al., 2017)

However, defining the role of a neuropsychological assessment in the clinical evaluation of adult ADHD is complicated because of the large heterogeneity of findings in previous research. For example, although adult ADHD was found in numerous studies to be associated with multiple cognitive impairments on a group level, not all adults with ADHD share the same type and degree of cognitive impairment, with some patients even showing not a single cognitive impairment in a cognitive test battery (Mostert et al., 2015; Nigg et al., 2005; Wåhlstedt, Thorell, & Bohlin, 2009). The heterogeneity of findings does not allow clear conclusions about what functions are more helpful in discriminating patients affected with ADHD from individuals not being affected with ADHD within a clinical evaluation (Dias et al., 2013). This heterogeneity is also reflected in a recent consensus report including international renowned experts in the field, which suggests as many as 16 cognitive functions to be relevant in a clinical neuropsychological assessment of adults with ADHD (Fuermaier et al., 2018).

Moreover, the majority of previous studies revealed cognitive differences between adults diagnosed with ADHD and healthy control group as recruited from the local community (Alderson et al., 2013; Boonstra et al., 2005). This comparison may not be representative for the use of neuropsychological assessment in the evaluation of ADHD in clinical practice, where individuals with ADHD are sought to be differentiated from clinical controls, which include individuals having other psychiatric conditions or individuals who do not reach diagnostic criteria for any psychiatric disorder but nevertheless had reasons for referral. In this respect, Holst and Thorell (2017), Pettersson, Soderstrom, and Nillson (2018) as well as Braek, Dijkstra, and Jolles (2011) found that patients with ADHD performed significantly poorer in a range of neuropsychological tasks compared to a clinical control group in an ADHD outpatient assessment, including measures of reaction time variability, attention, vigilance, inhibition, verbal (working) memory, verbal learning, set shifting, planning, fluency, and delay aversion (Holst et al., 2017; In de Braek, Dijkstra, & Jolles, 2011; Pettersson et al., 2018). However, effect sizes of group differences were mostly small to moderate, and neuropsychological tests were found to have a relatively poor ability to discriminate between adults with ADHD and clinical controls. In another study, Wiig and Nielsen (2012) revealed participants with ADHD to be significantly slower in a task for processing speed than both a healthy and a clinical control group, whereas no significant differences were observed between these two control groups (Wiig & Nielsen, 2012). In contrast to the findings differentiating adults with ADHD from clinical controls, Walker and colleagues (2000) could only demonstrate cognitive impairments of adults with ADHD when compared to a healthy control group, but not when compared to a clinical control group (Walker et al., 2000). Similarly, Marchetta, Hurks, Krabbendam, and Jolles (2008) reported a range of cognitive impairments of adults with ADHD when compared to a healthy control group, but significant difference to a clinical control group was found only in a task for mental flexibility (Marchetta, Hurks, Krabbendam, et al., 2008). Given these findings, it can be concluded that studies comparing cognitive functions between patients with ADHD and relevant clinical control groups in the same clinical setting are still scarce and that findings across studies remain inconsistent (Holst et al., 2017; In de Braek et al., 2011; Marchetta, Hurks, Krabbendam, et al., 2008; Pettersson et al., 2018; Walker et al., 2000; Wiig et al., 2012).

Due to the heterogeneity of the applied research (including differences in patient samples, control groups and cognitive measures applied), conclusions about what cognitive impairments are most characteristic for ADHD are difficult to draw. Thus, in order to further elucidate the role of a neuropsychological assessment in the clinical evaluation of adult ADHD, the present study employs a large sample of clinically referred individuals to an ADHD outpatient clinic (n = 248), who all performed a comprehensive test battery consisting of a broad range of measures, which was specifically composed for the neuropsychological assessment of adult ADHD. In this study, we aim to reveal differences in cognitive functions between individuals who receive a diagnosis of ADHD and individuals who have been referred for clinical assessment because of an assumed ADHD but who actually did not fulfill the diagnostic criteria of an ADHD. We expect that adults diagnosed with ADHD perform significantly poorer in several aspects of attention and executive function than individuals not reaching diagnostic criteria for ADHD. However, we expect that effect sizes of impairments between groups differ across functions and will not exceed small to medium size (Boonstra et al., 2005; Hervey et al., 2004; Marchetta, Hurks, Krabbendam, et al., 2008; Mostert et al., 2015; Pettersson et al., 2018). Moreover, as motivated by previous findings (Boonstra et al., 2010; Butzbach et al., 2019; Holst et al., 2017), we aim to quantify the effect of basic cognitive functions (i.e. processing speed and distractibility) on more complex cognitive functions (i.e. different aspects of complex attention and executive control) in adults with ADHD and seek to determine whether this hierarchical relationship is shaped differently in groups not having ADHD, such as being diagnosed with other psychiatric disorders or did not fulfill the diagnostic criteria of any psychiatric disorders.

Method

Participants

Two hundred and forty-eight participants were considered for inclusion in the present study. All participants were suspected to have ADHD (e.g. by general practitioners, neurologists, or psychiatrists) and were therefore referred for a diagnostic assessment to the ADHD outpatient clinic of the Department of Psychiatry and Psychotherapy, University of Duisburg-Essen, Germany. All individuals underwent a comprehensive diagnostic assessment by trained psychologists or psychiatrists. The diagnosis of ADHD was established based on the criteria as outlined in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM–5; American Psychiatric Association, 2013). The assessment procedure included a semi-structured interview to evaluate ADHD psychopathology (i.e., the Wender-Reimherr-Interview; Retz-Junginger et al., 2017) and the Essen Interview for school-days-related-biography (Grabemann et al., 2017). Furthermore, two self-report scales were completed by all participants to quantify the retrospective and current ADHD symptom severity (Rösler et al., 2008). The German version of the Wender Utah Rating Scale (WURS-K) was used to evaluate the retrospective symptoms in childhood (Retz-Junginger et al., 2003; Ward, 1993), while the German version of the ADHD Self-Report Scale (ADHS-SB) was administered to assess current ADHD symptoms (Adler et al., 2008; Adler et al., 2006; Kessler et al., 2005; Rösler et al., 2008). The diagnostic evaluation also included objective measures such as evidence derived from school reports and reports of failure in academic and/or occupational achievement, and comprised multiple informants for all individuals (e.g., employer evaluation, partner or parent-reports). The neuropsychological assessment using cognitive tests was part of the routine examination of all individuals in the ADHD outpatient clinic, however, cognitive test results were not part of the standard diagnostic decision process and decision making. All individuals agreed to their data being used for scientific purposes and gave written informed consent.

Forty-nine of the 248 participants were excluded from the present study, i.e. 47 participants were excluded because the diagnostic process was not completed or did not allow a formal diagnostic decision, and two participants were not considered because the neuropsychological assessment was not or only partly administered, leaving a sample of 199 participants for inclusion in the final data set that entered data analysis. All participants in this sample were allocated to one of three diagnostic groups, i.e. the ADHD group (diagnosis of ADHD was established, $n = 78$), the Clinical Comparison Group (CCG; participants did not meet diagnostic criteria for ADHD but showed evidence for one or more other psychiatric disorders; $n = 71$) and the Clinical Comparison Group-Not Diagnosed (CCG-ND; participants did not meet diagnostic criteria for ADHD and were also not diagnosed with any other psychiatric disorder; $n = 50$). Participants of the CCG showed evidence for one or more psychiatric disorders other than ADHD, including mood disorders ($n = 50$), addiction disorders ($n = 22$), anxiety disorders ($n = 5$), personality disorders ($n = 3$), eating disorders ($n = 3$), adjustment disorders ($n = 2$), schizoaffective disorders ($n = 2$), obsessive-compulsive disorders ($n = 1$), conduct disorders (n

= 1), and intellectual developmental disorders (*n* = 1). With regard to symptom presentations of ADHD, 66 patients with ADHD were diagnosed with the combined presentation and nine patients with the predominantly inattentive presentation, whereas the symptom presentation of three other patients with ADHD were not reported. Moreover, 31 of the 78 patients with ADHD showed evidence for one or more comorbid psychiatric disorders, including mood disorders (*n* = 19), addiction disorders (*n* = 5), adjustment disorders (*n* = 5), anxiety disorders (*n* = 3), obsessive-compulsive disorders (*n* = 2), personality disorders (*n* = 1), oppositional defiant disorders (*n* = 1), intellectual developmental disorders (*n* = 1), and autistic disorders (*n* = 1). Table 2.1 presents characteristics of the three groups (ADHD, CCG, CCG-ND) and revealed significant group differences in age, F (2) = 7.026, p = .001, sex, $\chi^2(2) = 6.553$, p = .038, education level, χ^2 (8) = 16.718, p = .033, childhood ADHD symptoms, F (2) = 24.486, $p < .001$, and current ADHD symptoms, F (2) = 12.060, $p < .001$. Compared to the CCG-ND, patients with ADHD had a significantly lower female-to-male ratio, and scored significantly higher on childhood and current ADHD symptoms. Compared to the CCG, patients with ADHD were on average significantly younger, more individuals attained a relatively low level of education, and obtained significantly higher scores in both scales for ADHD symptom severity. The CCG only differed significantly from the CCG-ND with regard to a higher score for childhood ADHD symptoms.

Table 2.1. Characteristics (M ± SD) of the ADHD group (ADHD), Clinical Comparison Group (CCG), and Clinical Comparison Group-Not Diagnosed (CCG-ND)

	ADHD (*n* = 78)	CCG (*n* = 71)	CCG-ND (*n* = 50)	F/χ^2	*p* value
Age (in years)	31.9 ± 10.3 [b]	38.8 ± 11.2	35.4 ± 12.1	7.026	0.001
Sex (female/male)	27/51 [a]	28/43	28/21 [6]	6.553	0.038
Education (1/2/3/4/5) [1]	4/23/15/22/13 [6 b]	0/11/29/18/12 [6]	0/14/12/16/8	16.718	0.033
Childhood ADHD symptoms [2]	44.6 ± 12.4 [a b]	34.5 ± 11.4 [a]	27.9 ± 12.5	26.486	< 0.001
Current ADHD symptoms [3]	35.5 ± 9.8 [a b]	29.6 ± 8.7	26.4 ± 11.7	12.060	< 0.001
Symptom presentation of ADHD [4]	66/9/0/3				
Psychiatric disorders other than ADHD [5]	19/5/3/1/0/5/0/2/1/1/1	50/22/5/3/3/2/2/1/1/1/0			

ADHD attention deficit Hyperactivity disorder; *CCG* clinical comparison group; *CCG-ND* clinical comparison group-not diagnosed

[1] Education (1/2/3/4/5) = no school-leaving qualification/compulsory schooling or intermediate secondary school/college or vocational training/Higher secondary school with university entrance qualification/university

[2] Childhood ADHD symptoms as measured with the German version of the Wender Utah rating scale-short version

[3] Current ADHD symptoms as measured with the German version of the ADHD self-report scale

[4] Symptom presentation of ADHD = combined/inattentive/hyperactive-impulsive/not reported

[5] Psychiatric disorders other than ADHD = mood disorders/addiction disorders/anxiety disorders/personality disorders/eating disorders/adjustment disorders/schizoaffective disorders/obsessive–compulsive disorders/conduct disorders/intellectual developmental disorders/autistic disorders
[6] Sex/education was not reported in one case
[a] $p < .05$ when compared with CCG-ND
[b] $p < .05$ when compared with CCG

Measures

Self-report scales for ADHD symptoms. The German version of the Wender Utah Rating Scale (WURS-K) was administered to assess childhood ADHD symptoms retrospectively (Retz-Junginger et al., 2003; Ward, 1993). The WURS-K includes 25 items, each answered on a 5-point Likert scale. The German version of the ADHD self-report scale (ADHS-SB, Adler et al., 2006; Kessler et al., 2005; Rösler et al., 2008) was used to quantify the severity of current ADHD symptoms. The ADHS-SB consists of 18 items, each answered on a 4-point Likert scale. A sum score was calculated for each scale.

Neuropsychological tests for cognitive functions. The test battery Cognitive Functions ADHD (CFADHD; Lara Tucha et al., 2013) of the Vienna Test System (VTS, Schuhfried, 2013) was administered to all participants. The CFADHD is a computerized test battery assessing cognitive functions in which adults with ADHD have been shown to commonly present difficulties.

Selective attention. The WAFS (Perceptual and Attention Functions-Selective Attention; Sturm, 2011) is administered to assess selective attention. In this test, a total of 144 stimuli (circle, triangle or square) were consecutively presented in the center of the computer screen, which will get lighter or darker or remain the same. The changes in circles and squares were defined as the target (30 targets). Participants were asked to press a response button as quickly as possible whenever a target (i.e., a circle gets lighter, a circle gets darker, a square gets lighter, or a square gets darker) was presented, and withhold a response if the target was not shown. The mean reaction time (RT in milliseconds) and dispersion of reaction time (SDRT) were registered. Moreover, the number of omission errors was recorded.

Vigilance. Vigilance is measured with the WAFV (Perceptual and Attention Functions-Vigilance; Sturm, 2012) of the VTS. In this test, a total of 900 squares were consecutively presented to the participants. A target is defined if the presented square becomes darker in shading (50 targets in total). Participants have to press a specific response button as quickly as possible when a target event occurs. The mean reaction time (RT in milliseconds) is registered. Moreover, the number of omission errors is recorded.

Working memory. A variant of the N-back task as originally introduced by Kirchner (Kirchner, 1958) was administered as a test for working memory, i.e. the 2-back version of the N-back verbal task (NBV; Schellig & Schuri, 2012). A total of 100 consonants are consecutively presented to participants. Participants are asked to respond to each consonant that is identical to the last-but-one (e.g., F – K – G – H – B – L – B – S). The number of correct responses is recorded.

Figural fluency. Figural fluency is measured with the 5-Point Test - Langensteinbach Version (Rodewald et al., 2014), which is based on the task paradigm of the Design Fluency Test (Jones-Gotman & Milner, 1977). An input field in the lower half of a divided screen is presented to participants, in which five symmetrically arranged dots are given. Participants are asked to create as many different patterns as possible in two minutes by connecting at least two dots. Dots can be connected by clicking on the space between two dots. All patterns that have been created are presented in the upper half of the divided screen. The total number of unique patterns created in two minutes is recorded.

Interference. Interference is assessed with the Stroop Interference Test (Schuhfried, 2016). This test is a variant of the color-word interference, which was introduced by Stroop (Stroop, 1935) as a measure of interference function. This test contains four conditions. The first condition is a color-word condition, in which color-words (BLUE, GREEN, YELLOW, RED) printed in grey are shown on the computer screen and participants are asked to press the button of the same color as the meaning of the color word. The second condition is a color-banner condition, in which colored banners (banners printed in blue, green, yellow and red) are presented. Participants are asked to press the button of the same color as the color of banners. The third condition is a reading-interference condition, in which color-words (BLUE, GREEN, YELLOW, RED) are printed in mismatching ink (e.g., BLUE printed in green ink). Participants are required to press the button of the same color as the meaning of the color word, ignoring the color the word was printed. The fourth condition is a naming-interference condition, which is analog to the reading-interference condition in which color-words are presented in mismatching ink (e.g., RED printed in blue ink). Participants are asked to press the button of the same color as the ink of the word. Participants are asked to respond as thoroughly as possible but at the same time as quickly as possible throughout the test. The main variables of interest are reading interference and naming interference. *Reading interference* is calculated by subtracting the time needed for completing the color-word condition from the time needed for the reading-interference condition. *Naming interference* is calculated by subtracting the time needed for completing the color-banner condition from the time needed for the naming-interference condition.

Processing speed and flexibility. The Trail Making Test - Langensteinbach Version (TMT-L; Rodewald et al., 2012) is administered as a test for processing speed and flexibility. The TMT-L is closely oriented on the Army Individual Test Battery (1944) and the original form of the Trail-Making Test by Reitan (Reitan, 1958). The TMT-L consists of two parts. In part A, the numbers 1 to 25 are simultaneously presented on the screen and participants are asked to join the numbers in ascending order as quickly as possible by clicking on them. In part B, the numbers of 1 to 13 and the letters of A to L are presented, and participants are requested to connect numbers and letters alternately in ascending order as quickly as possible (i.e., 1-A-2-B-3-C…). The times needed for part A and part B are registered. Part A is used as a measure of processing speed. Flexibility is assessed by the quotient of the times needed for part B by part A.

Planning ability. Planning ability is assessed with the Tower of London - Freiburg Version (TOL-F; Christoph et al., 2011) of the VTS. The TOL-F dates back to the design originally proposed by Shallice to measure planning ability (Shallice, 1982). The task requires participants to move balls of different colors (red, yellow, blue) that can be placed on three rods from given positions to certain target positions. Start state and goal state are presented on the lower and upper part of the computer screen, respectively. The left rod can hold three balls, the middle one can hold two, and the right one can hold only one. Participants are asked to convert a given start state into a goal state by using the minimum number of moves possible. The minimum number of moves to convert a given start state into a goal state is shown on the left of the screen. The item that is being worked on is automatically terminated after 60 seconds. If it has not been solved within this time, the next item will be presented. A total of 28 items are included in the test and presented in the order of an increasing minimum number of moves. The number of items solved in the minimum number of moves is registered.

Inhibition. Inhibition is assessed with a Go/No-Go test paradigm (Kaiser et al., 2016), as originally designed for the measurement of inhibitory control (Drewe, 1975). In this test, a series of triangles and circles are consecutively presented on the screen. Participants are asked to press a response button when a triangle is presented and to show no response to a circle stimulus. A total of 250 stimuli (202 triangles, 48 circles) is presented in the test, each for 200 milliseconds. The interstimulus interval is one second. The number of commission errors is recorded.

Task switching. Task switching is assessed with the SWITCH (Gmehlin et al., 2017) of the VTS. In this test, a series of visual stimuli with different forms (circle or triangle) and different brightness (light or dark) are consecutively presented. Participants are asked to respond to stimuli based on two rules that are applied alternately. One rule asks participants to react to form (circle or triangle) but ignore brightness. The other rule requires participants to react to brightness (light or dark) but ignore form. After every two stimuli, participants must change whichever rule is being applied and apply the other rule. The tasks requiring the same rules as used in the last are defined as repeated tasks and tasks requiring different rules as used in the last are defined as switch tasks. The main variable of interest is *task switch accuracy*. *Task switching accuracy* is calculated by subtracting the number of correct responses in switch tasks from the number of correct responses in repeated tasks.

Subjective experiences of cognitive functioning. The *Questionnaire on Mental Ability* (FLEI; Beblo et al., 2012) as part of the CFADHD on the VTS was administered to assess self-reported cognitive deficits. Items of this questionnaire ask participants to indicate to which extent everyday manifestations of problems in attention, executive functioning, and memory, apply to them. The FLEI includes 35 items scored on a 5-point Likert scale ranging from 0 (never) to 4 (very often). A sum score is computed to indicate the self-reported cognitive deficits.

Procedure

The diagnostic and neuropsychological assessment were both part of the standard clinical routine of all participants referred to the ADHD outpatient clinic of the University of Duisburg-Essen, Germany. All participants agreed and signed a written informed consent for their data being used for scientific purposes. Ethical approval for this procedure was provided by the local ethical review board (20-9380-BO). Participation was voluntary, unpaid, and it was stressed that the agreement to take part in research did not affect their clinical assessment or treatment. All participants were asked to complete a set of questionnaires at home prior to the diagnostic interview. The clinical evaluation started with the diagnostic interview, and continued with the neuropsychological assessment (cognitive testing) at the same or another day of convenience for the examinee. The neuropsychological assessment using cognitive tests took about two hours to administer, and was led by a trained psychologist or neuropsychological test assistant under close supervision. Participants were not informed about their diagnostic status at the time of the neuropsychological assessment.

Statistical analysis

Missing values occurred in 5.3% of the data due to administrative errors and were not replaced. Test data of all three groups are presented in descriptive statistics. Furthermore, neuropsychological test data are interpreted based on norm scores as provided by the test publisher, i.e. to derive the number of individuals having impairment in each of the functions assessed. An impairment is defined as an individual test performance that is equal or below the 16^{th} percentile (i.e. one SD below the mean) of the representative test norms as provided by the test publisher (Schuhfried, 2013).

Furthermore, neuropsychological functions are compared between groups using statistical significance tests and effect sizes. Because assumptions for parametric analyses (e.g. normality, homogeneity of variances) were not met in several variables, nonparametric statistical analyses were performed. Per test score, the ADHD group was compared with the CCG and CCG-ND, respectively, using Mann-Whitney U tests. The significance level was adjusted to $p < .01$ in order to control for alpha error growth in multiple testing. The effect size Cohen's r was calculated to indicate the magnitude of pairwise group differences. Cohen's r was chosen as it does not rely on the normality assumption. Based on Cohen's criteria for r, 0.1 indicates a small effect, 0.3 indicates a medium effect, and 0.5 indicates a large effect (Cohen, 1988).

In order to investigate the effect of basic on complex cognitive functions, functional domain scores were created representing different aspects of basic (i.e. processing speed and distractibility) and complex (i.e. different aspects of complex attention and executive control) cognitive functions (see Table 2.4). Basic cognitive functions were measured with the variables of the selective attention task (logarithmic mean of RT, logarithmic standard deviation of RT, omissions), vigilance task (logarithmic mean of RT and omissions) and TMT part A. With regard to complex cognitive functions, it is differentiated between working memory (NBV correct responses), inhibition/interference control (Go/No-Go omissions, Stroop Interference Test naming interference and reading interference), cognitive flexibility (TMT part B/TMT part A, SWITCH task switch accuracy), fluency (number of unique patterns created), and planning (TOL-F number of items solved). All test variables per defined functional domain are z-standardized based on scores of the CCG-ND and averaged in order to obtain one measure per functional domain. In addition, the association between basic cognitive functions and each aspect of complex cognitive functions is examined by Spearman rank correlation coefficients, separately for the ADHD group, CCG, and CCG-ND. The size of the association is interpreted as small (r = 0.1), medium (r = 0.3), and large (r = 0.5).

Results

Descriptive statistics of neuropsychological test performance as well as the percentage of impairment per test variable and neuropsychological function are presented in Table 2.2 and Figure 2.1. Decreased cognitive functions were found in all three groups compared to test norms, with a considerable proportion of individuals being impaired in aspects of attention, i.e. selective attention (52.0%, 54.9%, and 62.8% for the CCG-ND, CCG, and ADHD, respectively) and vigilance (49.0%, 51.4%, and 60.8%, respectively), inhibition (40.8%, 39.1%, and 49.3%, respectively), and interference control (30.6%, 40.6%, and 41.1%, respectively). Furthermore, the majority of individuals reported that they experience cognitive complaints in their daily lives (71.4%, 95.5%, and 89.2%, for the CCG-ND, CCG, and ADHD, respectively). The number of neuropsychological functions indicating impaired performance (Figure 2.2) differs largely across individuals, with the majority of individuals (98.0%, 98.6%, and 98.8%, for the CCG-ND, CCG, and ADHD, respectively) having either no impairment or impairments in up to six functions.

Table 2.2. Neuropsychological test performance and self-report of the groups ADHD, CCG, and CCG-ND

Neuropsychological variables	ADHD					CCG					CCG-ND				
	Range (min-max)	Mean	Median	SD	% percentile ≤16 [a]	Range (min-max)	Mean	Median	SD	%percentile ≤16 [a]	Range (min-max)	Mean	Median	SD	% percentile ≤16 [a]
Selective attention [b] - Logarithmic mean of RT	159 - 621	359	350	79	15.5	149 - 739	375	368	94	18.3	49 - 563	358	348	86	14
Selective attention [b] - Logarithmic SD of RT	0 - 5.43	1.43	1.28	0.80	54.5	1.09 – 9.08	1.41	1.25	0.97	36.6	1.11 - 9.82	1.43	1.25	1.21	40
Selective attention [b] - Omission errors	0 - 30	1.46	0	4.16	33.7	0 - 12	0.54	0	1.69	22.5	0 - 2	0.34	0	0.59	28
Vigilance [c] - Logarithmic mean of RT	253 - 688	458	458	76	16.4	307 - 706	462	447	82	19.7	341 - 726	457	459	71	8.2
Vigilance [c] - Omission errors	0 - 21	3.41	2	4.04	59.5	0 - 13	2.50	1	3.21	46.4	0 - 18	2.73	1	3.79	48.9
Speed of processing [d] - Time needed in seconds	2.2 - 37	21.11	20.30	5.73	22.1	13.5 – 43.1	23.47	23.1	5.99	32.3	11.1 - 34.7	20.43	19.9	4.71	10
Working memory [e] - Correct responses	0 - 15	10.91	12	3.49	22.1	0 - 23	11.23	12	4.01	16.9	0 - 15	11.02	12	3.73	24
Figural fluency [f] - Unique patterns created	11- 51	25.38	24	9.13	22.1	6 - 46	22.39	20	8.74	29.5	10 – 49,	25.56	23	9.56	18
Interference [g] - Reading interference	-0.03 - 1.1	0.22	0.18	0.17	38.3	-0.04 - 0.86	0.20	0.17	0.15	30.4	-0.04 - 0.49	0.17	0.14	0.13	24.5
Interference [g] - Naming interference	-0.01- 2.78	0.15	0.11	0.33	10.9	-0.07 - 0.46	0.14	0.11	0.10	17.1	0.02 - 0.46	0.14	0.13	0.08	12.2
Planning ability [h] - Number of items solved	7 - 22	13.49	14	3.04	17.2	7 - 22	14.45	15	3.44	14.9	8 - 21	15.02	15	3.64	14.3
Inhibition [i] - Commission errors	2 - 32	15.79	15	7.85	49.3	2 - 32	13.45	12	7.32	39.1	2 - 30	13.51	12	7.14	40.8
Flexibility [j] – Quotient score	0.76 - 3.85	1.58	1.50	0.47	10.5	0.95 – 4.67	1.61	1.52	0.54	18.3	0.62 - 2.62	1.48	1.41	0.35	8.3
Task switch accuracy [k] – Accuracy score	-8 - 20	2.80	2	5.84	25.3	-11 - 18	3.70	3	5.29	22.7	-10 - 32	3.90	3	6.50	22
Subjective experiences of cognitive functioning [l,1] – Impairment score	19 - 120	77.24	83	21.44	89.2	4 - 106	77.18	78	17.37	95.5	23 - 93	62.97	66.50	20.68	71.4

ADHD attention deficit Hyperactivity disorder; *CCG* clinical comparison group; *CCG-ND* clinical comparison group-not diagnosed

[a] Percentage of individuals with percentile rank ≤16 based on test norms. [b] Perceptual and Attention Functions-Selective Attention (WAFS). [c] Perceptual and Attention Functions - Vigilance (WAFV). [d] Trail-Making Test–A (TMT-A). [e] N-back verbal task (NBV). [f] 5-Point Test - Langensteinbach Version. [g] Stroop Interference Test. [h] Tower of London - Freiburg Version (TOL-F). [i] Go/No-Go test. [j] Time to complete TMT-B divided by time to complete TMT-A. [k] SWITCH task. [l] Questionnaire on Mental Ability (FLEI). [1] ADHD group reported significantly more problems of cognitive functioning than CCG-ND

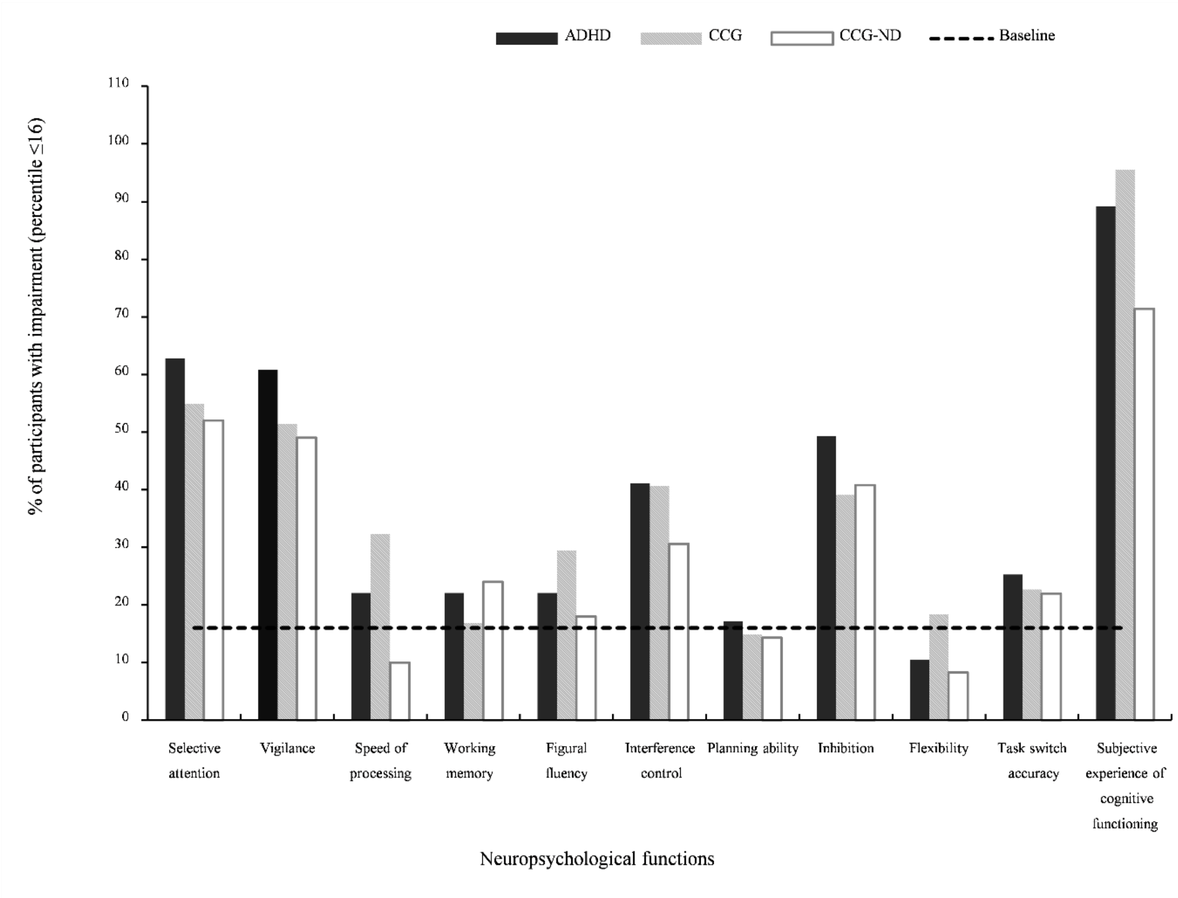

Fig.2.1. Percentage of individuals indicating impairment (percentile rank ≤ 16) in neuropsychological test performance and self-report.

Impairment per function is defined if test performance is impaired in at least one test variable of this function; Dotted line indicates 16% of participants having impairment (i.e. baseline if impairment is defined as percentile rank ≤ 16); *ADHD* Attention Deficit Hyperactivity Disorder; *CCG* Clinical Comparison Group; *CCG-ND* Clinical Comparison Group - Not Diagnosed.

Nonparametric group comparisons (Mann-Whitney U Tests) were computed to determine performance differences between the ADHD group and both the CCG and the CCG-ND. Test statistics of Table 2.3, as well as bar charts presenting the number of impairments in Figure 2.1 and 2.2, indicate no meaningful group differences. The only significant effect of medium size was observed in subjective experiences of cognitive functioning, i.e. the ADHD group reported significantly more problems of cognitive functioning in their daily lives than the CCG-ND. In addition, some effects did not reach significance but indicate a trend level effect of small size (Table 2.3). Specifically, when compared to the CCG, the ADHD group performed faster in the TMT-A and better in the figural fluency task (5-point test), but showed worse planning ability

(TOL-F). When compared to the CCG-ND, the ADHD group showed better naming interference ability in the Stroop task, but worse planning ability in the TOL-F. However, differences in processing speed between groups must be interpreted with caution,

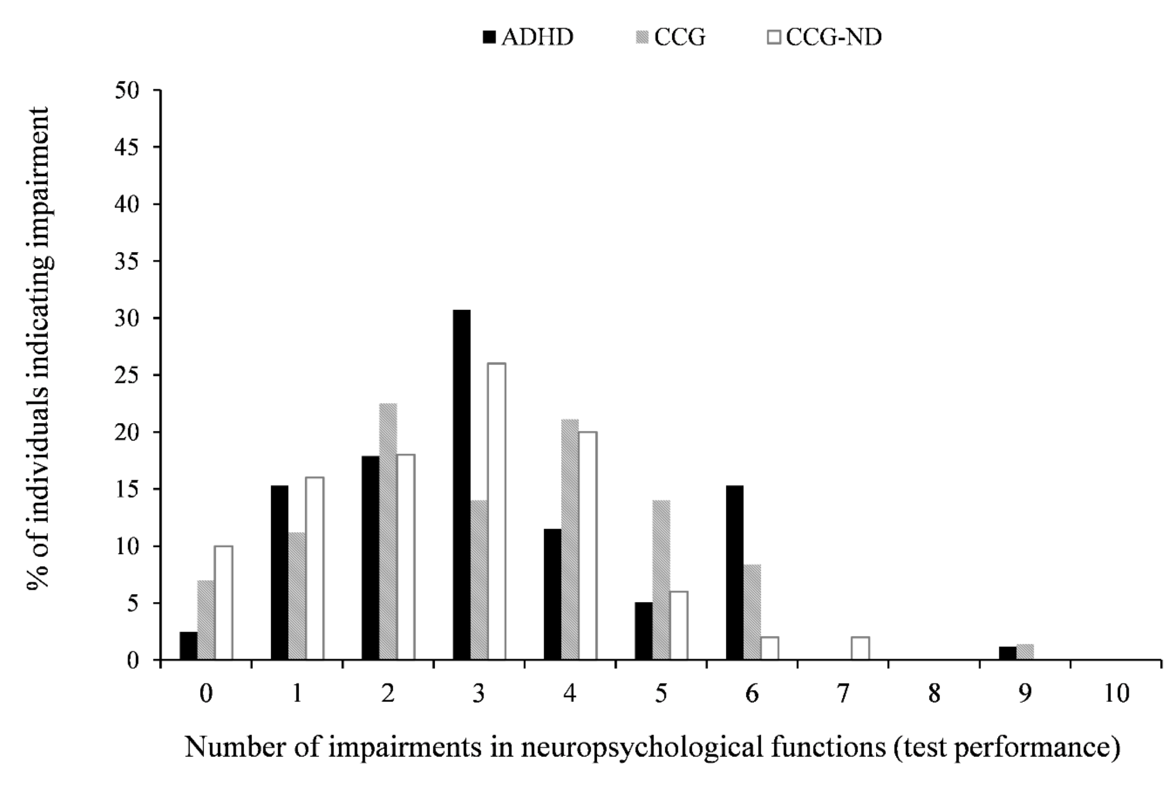

Fig.2.2. Percentage of individuals showing impairment in neuropsychological functions, ranging from 0 (no impairment) to 10 (impairment in 10 functions)
ADHD Attention Deficit Hyperactivity Disorder; *CCG* Clinical Comparison Group; *CCG-ND* Clinical Comparison Group - Not Diagnosed.

because groups differed substantially in age, and age was observed to be significantly associated to processing speed in medium to large-sized correlations, i.e. $r = 0.31$, $r = 0.34$, and $r = 0.26$, for CCG-ND, CCG, and ADHD, respectively.

Spearman's rank correlation coefficients between basic and complex aspects of cognitive functions in the three groups are presented in Table 2.4. For the ADHD group, a small-sized effect was found between basic cognitive functions and the total compound score of complex cognitive functions ($r = 0.28$). Differentiating between different aspects of complex cognitive functions, a significant association of medium size was obtained with inhibition/interference control ($r = 0.36$) and a significant association of small size with fluency ($r = 0.29$). For the

CCG, a significant and medium-sized effect was found for the total compound score of complex cognitive functions (*r* = 0.34), with a significant small-sized effect to inhibition/interference control (*r* = 0.26) and a significant medium-sized effect to fluency (*r* = 0.32). Finally, a small and nonsignificant association was found between basic cognitive functions and the compound score of complex cognitive functions of the CCG-ND (*r* = 0.15). Per domain of complex cognitive functions, a significant effect (medium size) was revealed only for the association with fluency (*r* = 0.45).

Table 2.3. Comparison of neuropsychological functions between ADHD, CCG, and CCG-ND

Neuropsychological variables	Group comparison [a]					
	ADHD vs. CCG			ADHD vs. CCG-ND		
	Z	*P*	*Cohen's r* [b]	*Z*	*P*	*Cohen's r* [b]
Selective attention [c] - Logarithmic mean of RT	- 0.87	0.38	- 0.07	- 1.38	0.89	+ 0.12
Selective attention [c] - Logarithmic SD of RT	- 1.67	0.09	+ 0.14	- 1.48	0.14	+ 0.13
Selective attention [c] - Omission errors	- 1.67	0.09	+ 0.14	- 1.05	0.29	+ 0.09
Vigilance [d] - Logarithmic mean of RT	- 0.21	0.83	+ 0.02	- 0.15	0.88	+ 0.01
Vigilance [d] - Omission errors	- 1.70	0.09	+ 0.14	- 1.39	0.16	+ 0.13
Speed of processing [e] - Time needed in seconds	- 2.45	0.014	- 0.20	- 0.71	0.48	+ 0.06
Working memory [f] - Correct responses	- 0.72	0.47	+ 0.06	- 0.41	0.68	- 0.04
Figural fluency [g] - Unique patterns created	- 1.92	0.05	- 0.16	- 0.11	0.91	+ 0.009
Interference [h] - Reading interference	- 0.30	0.77	+ 0.03	- 1.59	0.11	+ 0.15
Interference [h] - Naming interference	- 1.26	0.21	- 0.11	- 2.02	0.04	- 0.18
Planning ability [i] - Number of items solved	- 1.95	0.05	+ 0.17	- 2.32	0.02	+ 0.20
Inhibition [j] - Commission errors	- 1.77	0.07	+ 0.15	- 1.54	0.12	+ 0.14
Flexibility [k]- Quotient score	- 0.05	0.96	- 0.004	- 0.88	0.38	- 0.08
Task switch accuracy [l]- Accuracy score	- 1.12	0.26	- 0.09	- 0.98	0.33	+ 0.09
Subjective experiences of cognitive functioning [m] - Impairment score	- 0.31	0.76	- 0.03	- 3.44	0.001**	+ 0.33

ADHD attention deficit Hyperactivity disorder; *CCG* clinical comparison group; *CCG-ND* clinical comparison group-not diagnosed

**Statistically significant at $p < .01$.

[a] Mann-Whitney U Test. [b] Positive values indicate worse functioning in ADHD in the respective comparison, negative values indicate better functioning in ADHD in the respective comparison. [c] Perceptual and Attention Functions-Selective Attention (WAFS). [d] Perceptual and Attention Functions- Vigilance (WAFV). [e] Trail-Making Test–A (TMT-A). [f] N-back verbal task (NBV). [g] 5-Point Test - Langensteinbach Version. [h] Stroop Interference Test. [i] Tower of London- Freiburg Version (TOL-F). [j] Go/No-Go test. [k] Time to complete Trail-Making Test–B (TMT-B) divided by time to complete Trail-Making Test–A (TMT-A). [l] SWITCH task. [m] Questionnaire on Mental Ability (FLEI)

2

Discussion

This study aimed to explore neuropsychological functioning of individuals at clinical evaluation of adult ADHD, and examine the associations between basic and higher-order cognitive functions in this population. An analysis of neuropsychological test performance revealed that individuals with ADHD exhibit impairments in several of the neuropsychological functions assessed in this study. Considerable rates of impairment, as determined by use of test norms, were shown in adults with ADHD in selective attention, vigilance, inhibition, and interference control (63%, 61%, 49%, and 41% of participants, respectively). This is in line with the results of numerous previous studies showing impairments in adults with ADHD in various cognitive functions (Bálint et al., 2008; Boonstra et al., 2005; Pritchard, Neumann, & Rucklidge, 2008).

Table 2.4. Correlation coefficients (Spearman rank correlation) between basic cognitive functions and different aspects of complex cognitive functions in ADHD, CCG, and CCG-ND.

Complex cognitive functions	Spearman's *r* (*p*)		
	ADHD	CCG	CCG-ND
Working memory	0.138 (*p*=0.232)	0.161 (*p*=0.180)	-0.041 (*p*=0.780)
Inhibition/Interference control	0.355** (*p*=0.002)	0.264* (*p*=0.027)	-0.020 (*p*=0.893)
Cognitive flexibility	0.018 (*p*=0.873)	0.005 (*p*=0.964)	-0.206 (*p*=0.152)
Fluency	0.292* (*p*=0.010)	0.322** (*p*=0.006)	0.449** (*p*=0.001)
Planning	0.156 (*p*=0.222)	0.209 (*p*=0.089)	0.143 (*p*=0.325)
Total compound	0.282* (*p*=0.012)	0.344** (*p*=0.003)	0.146 (*p*=0.311)

Basic cognitive functions: Compound Z-score of selective attention task (logarithmic mean of RT, logarithmic standard deviation of RT, omissions), vigilance task (logarithmic mean of RT and omissions), and TMT part A; Working memory: Z-score of correct responses in NBV; Inhibition/Interference control: Compound Z-score of Go/No-Go omissions and Stroop Interference Test naming interference and reading interference; Cognitive flexibility: Compound Z-score of TMT part B/TMT part A and SWITCH task switch accuracy; Fluency: Z-score of number of unique patterns created in 5-Point Test; Planning: Z-score of number of items solved in TOL-F; Total compound: Compound Z-score of working memory, inhibition/interference control, cognitive flexibility, fluency, and planning

ADHD attention deficit hyperactivity Disorder; CCG clinical comparison group; CCG-ND clinical comparison group-not diagnosed

*Significant at the 0.05 level. **Significant at the 0.01 level

The present results conform to previous findings, demonstrating that slower responses, a greater reaction time variability, and more omission were commonly observed in adults with ADHD when compared to healthy control participants in tests of attention (Cross-Villasana et al., 2015;

Kofler et al., 2013; Mostert et al., 2015). The sensitivity of the vigilance task to reveal cognitive impairment underlines its central role in the neuropsychological assessment of adult ADHD, despite its long administration time may cost comparably many clinical resources. Furthermore, this study demonstrates marked cognitive complaints as reported by patients with ADHD. The pronounced experiences of cognitive impairments in daily life activities have been reported in earlier research on adults with ADHD (Fuermaier et al., 2014; In de Braek et al., 2011), and may also explain the referral reason of the present sample, as all individuals were seeking a clinical evaluation of adult ADHD as they thought to experience ADHD like problems in their daily lives. When comparing neuropsychological studies in ADHD across lifespan, it becomes apparent that ADHD is characterized by heterogeneous cognitive profiles with marked differences between individuals, but also across time (Luo et al., 2019; Seidman, 2006). For example, neuroimaging studies demonstrated morphological and physiological changes in ADHD over time to be associated with differences in neuropsychological functioning (Cortese, 2012; Hoogman et al., 2017; Krain & Castellanos, 2006). Furthermore, potential comorbid disorders that individuals with ADHD may grow into in adolescence and early adulthood, as well as drug abuse that often commences in this development phase, are likely to represent additional sources for marked inter-individual differences in neuropsychological profiles in young adults with ADHD (Marks, Newcorn, & Halperin, 2001; Rose et al., 2009).

Moreover, the present study demonstrates that individuals of the clinical comparison groups, i.e. the CCG and CCG-ND, showed a similar pattern of neuropsychological functioning and exhibited impairments in the same functions as observed in the group of patients diagnosed with ADHD, including selective attention, vigilance, inhibition, interference control, as well as in subjective ratings of cognitive functioning. This is also illustrated by an inspection of the number of impairments by group, which shows a similar distribution for the ADHD group, CCG, and CCG-ND. The vast majority of individuals have impairments in one to six functions (of ten functions assessed), with a peak at two to four impairments. The observation of similar patterns of neuropsychological functions between the three groups is consistent with the view of ADHD as dimensional construct, with ADHD-like symptoms and impairments occurring in large parts of the population, including the general psychiatric population (Sergeant, Geurts, & Oosterlaan, 2002). In this context, multifactorial models are discussed in the etiology of ADHD, with, for example, a large number of gene loci that may contribute to the clinical syndrome of ADHD (Bobb et al., 2005; Cortese, 2012; Demontis et al., 2019; Li et al., 2006). The notion of a similar pattern of neuropsychological functioning across the three groups is supported by group comparisons revealing mostly non-significant group differences, ranging from negligible to small size. A significant difference between groups was found in the subjective experience of cognitive functioning only. In this self-report, patients with ADHD indicate significantly more pronounced cognitive complaints compared to the CCG-ND. However, inspecting the magnitude of cognitive complaints of all three groups, it becomes apparent that the complaints may be no good indicator for differential diagnostic purpose, as pronounced and marked cognitive impairments are reported by all three groups at clinical assessment, which may explain their referral to an ADHD outpatient clinic. Taken together, data of this study, on the one hand, provide evidence for the notion that a neuropsychological assessment may have limited ability to discriminate between adult ADHD and other psychiatric disorders in a psychiatric assessment (Barkley, 2019; Holst et al., 2017; Pettersson et al., 2018; Solanto, Etefia, & Marks, 2004; Walker et al., 2000). On the other hand, marked cognitive impairments that are observed in the majority of individuals with ADHD in this study supports earlier seminal work which argued that a neuropsychological assessment using cognitive performance tests may contribute to the comprehensive understanding of an individual, including the characterization of individual cognitive strengths and weaknesses and potentially also guide treatment planning, such as the administration of cognitive remediation programs or acquiring compensation strategies to overcome consequences of cognitive deficits (Lange et al., 2014; Mapou, 2019; Pineda et al., 2007). Regarding cognitive remediation, there is yet an ongoing discussion on its usefulness in the treatment of adults with ADHD with nonconforming findings reported in different studies (Chevalier et al., 2017; Cortese et al., 2015; Rapport et al., 2013; Solanto et al., 2008). Further research is therefore needed on the extent to which neuropsychological tests can effectively be used to guide psychological interventions.

Finally, findings of earlier research (Butzbach et al., 2019; Holst et al., 2017) could be confirmed by demonstrating significant correlations between basic cognitive functions and higher-order cognitive functions in the ADHD group. The observed associations support the impairments in basic functions may lead to impairments in higher-order functions, such as aspects of complex attention and executive control. Noteworthy, the present study adds to previous research in demonstrating significant and medium-sized associations between basic and higher-order cognitive functions not only in the ADHD group but also in the CCG. This effect may indicate that the relationship between basic and higher-order cognitive functions may not be specific for adult ADHD, but may also hold true in individuals with other psychiatric disorders. In contrast, no such relationship was found in the clinical comparison group with no diagnostic status. The findings of a hierarchical relationship between basic and higher-order cognitive functions may not only be utilized to optimize neuropsychological assessment, but provides also implications for the treatment of cognitive deficits of patients with psychiatric conditions. Previous research already demonstrated that stimulant drug treatment improves basic cognitive functions, i.e. processing speed and reaction time variability, which in turn may indirectly improve higher-order cognitive functions (Bron et al., 2014; Butzbach et al., 2019; Kofler et al., 2013; Wong & Stevens, 2012). Similarly, cognitive remediation programs aiming to improve processing speed and other aspects of basic attention may have a broader area of effect than initially assumed, and may also impact on higher-order functions (Sonuga-Barke et al., 2014).

Limitations

This study needs to be seen in the context of several limitations. First, the group of patients with ADHD is a selected sample, with the majority being diagnosed with the combined symptom presentation and various comorbid psychiatric disorders. It is, therefore, difficult to evaluate how representative the present data are for the population of adults with ADHD when compared to clinical control groups, and whether the observed effects would hold in clinical samples with different characteristics.

Second, because the clinical assessment was designed mainly to determine the presence of adult ADHD, only clinical indications, but no verified diagnoses, could be given for the differentiation between other clinical conditions. Thus, the differentiation between individuals presumably having or not having psychiatric conditions, and subsequent group comparisons, must be interpreted with caution.

Third, the missing of more differences between groups may have been caused by similarities in group characteristics. For example, a similar range of psychiatric disorders are observed both in the ADHD group and the CCG. Further, given this context of an ADHD outpatient clinic, it must be considered that also individuals not being diagnosed with ADHD may suffer from a similar clinical pattern which may just not reach diagnostic threshold for ADHD.

Fourth, even though the neuropsychological assessment using cognitive tests was not part of the standard diagnostic routine of clinicians, results of the cognitive assessment were accessible to patients and clinicians, and may have guided clinical decision making. However, this may even support the notion that a neuropsychological assessment using cognitive tests may not contribute substantially to a differential diagnostic process of psychiatric disorders, if one takes into account that the neuropsychological assessment was not completely independent from the diagnostic assessment and still the ADHD group does not largely differ in neuropsychological functions from the two other clinical groups.

Conclusions

This study demonstrates that individuals seeking a clinical evaluation of adult ADHD show marked impairments in several aspects of cognitive functions, irrespectively from whether they fulfill diagnostic criteria for ADHD or not. This is underlined by group comparisons indicating no meaningful differences in cognitive functions between patients with ADHD, the clinical comparison group, and the clinical comparison group with no diagnostic status. We conclude that cognitive deficits are prominent in patients of this setting, but are not specific for ADHD. And a neuropsychological assessment using cognitive tests may not provide the clinician with incremental information for the differential diagnostic process of adult ADHD. Furthermore, we conclude and support earlier work that deficits in a range of cognitive domains can be substantially explained by deficits in lower-order cognitive functions, such as processing speed and basic aspects of attention and distractibility.

Chapter 3

The role of self- and informant-reports on symptoms and impairments in the clinical evaluation of adult ADHD

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Abstract: Little is known about which clinical features may aid the differentiation between attention deficit hyperactivity disorder (ADHD) and other clinical conditions. This study seeks to determine the role of self- and informant reports on symptoms and impairments in the clinical evaluation of adult ADHD and explore their association with objective neuropsychological test performance by examining data of 169 outpatients referred for a diagnostic evaluation of adult ADHD. Participants were assigned either to an ADHD group (ADHD, *n* = 73) or one of two clinical comparison groups, depending on whether they show indications (Clinical Comparison Group, CCG, *n* = 53) or no indications (Clinical Comparison Group—Not Diagnosed, CCG-ND, *n* = 43) of psychiatric disorders other than ADHD. All participants and their informants completed a set of questionnaires. Compared to the CCG-ND, the ADHD group obtained significantly higher scores on ADHD symptoms, impulsivity, cognitive deficits, and anxiety. Compared to the CCG, the ADHD group scored significantly higher on ADHD symptoms but lower on depression. Further regression analyses revealed that self- and informant reports failed to predict neuropsychological test performance. Self- and informant reported information may be distinct features and do not correspond to results of objective neuropsychological testing.

Keywords: adult ADHD; symptoms; impairments; clinical assessment; daily functioning

Introduction

Attention deficit hyperactivity disorder (ADHD) is a neuropsychiatric childhood disorder that persists into adulthood in a sizeable proportion of individuals and is characterized by symptoms of inattention, hyperactivity, and impulsivity (American Psychiatric Association, 2013; Asherson et al., 2016; Barkley et al., 2006; Biederman et al., 2011). ADHD in adulthood commonly occurs together with symptoms of other forms of psycho-pathology, which is underscored by research revealing a rate of up to 60–80% of patients with ADHD being diagnosed with one or more comorbid psychiatric disorders, with anxiety disorders (34%) and mood disorders (22%) being the most prevalent ones (Biederman, 2005; Cumyn et al., 2009; Kooij et al., 2019; Kooij et al., 2012). Additionally, ADHD symptoms can be observed in patients with anxiety (20%) and mood disorders (17%) (Bowen et al., 2008; McIntyre et al., 2010; Tannock, 2000). It has been demonstrated that symptoms of ADHD and comorbid conditions contribute to functional impairments that are commonly observed in this population, such as lower academic achievement (Advokat, Lane, & Luo, 2011; Arnold et al., 2020; Holst et al., 2020), lower employment rate (Faraone & Biederman, 2005; Gjervan et al., 2012), poorer financial situation (Bangma et al., 2019; Barkley, 2015), substance abuse (Kalbag, Levin, & misuse, 2005; Torgersen et al., 2006), and more frequent divorces and relationship breakups (Bruner, Kuryluk, & Whitton, 2015; Klein et al., 2012; Michielsen et al., 2015).

Symptoms and impairments of adults with ADHD are assessed by employing various types of instruments, usually distinguishing between subjective reports (self-report and informant-report) and objective neuropsychological tests. Neuropsychological research using cognitive tests demonstrated marked impairments in adults with ADHD in a range of cognitive functions when compared to healthy individuals, including aspects of attention, memory, and executive control (Alderson et al., 2013; Boonstra et al., 2005; Nigg et al., 2005; Quinlan & Brown, 2003; Salomone et al., 2020; Tucha et al., 2017). However, the differentiation between ADHD, other psychiatric disorders, and subclinical levels of impairment, as it is commonly seen in an outpatient referral context, appears to be more complex, as cognitive testing does not seem to provide incremental information for differential diagnostic purposes (Guo, Fuermaier, Koerts, Mueller, Diers, et al., 2021; Marchetta, Hurks, Krabbendam, et al., 2008; Walker et al., 2000). Patients' self-reports and, in many cases, also the ones of their informants are usually readily available and easily accessible and, thus, represent important sources of information in the clinical evaluation of adult ADHD (Kooij et al., 2008; Magnússon et al., 2006; Sibley et al., 2012). However, even though patients with ADHD differ in their experiences from healthy individuals in many aspects of functioning (Canu et al., 2020; Fuermaier et al., 2014; Gjervan et al., 2012), the diagnostic process in an outpatient referral context may be more puzzling, as adult ADHD is not only sought to be differentiated from healthy individuals but, also, from clinical conditions that may have overlapping clinical features and referral reasons. Thus, it remains a challenge for clinical research to identify characteristics, symptoms and impairments that are specific for adult ADHD and help the clinician to differentiate ADHD from subclinical levels of impairment and other clinical conditions.

Previous research in studying the role of self- and other reports for differential diagnostic purposes came to inclusive findings. Concerning ADHD symptoms, Suhr and colleagues demonstrated that the Conners' Adult ADHD Rating Scale (CAARS) failed to differentiate an ADHD group from a group being diagnosed with another psychiatric disorder; however, significant and large-sized differences were observed on the Wender Utah Rating Scale (WURS) in the way that the ADHD group endorsed more symptoms than the clinical control group. Yet, the WURS was found to be of only limited value to differentiate between ADHD and the other psychological disorders in a further study of the same group, which revealed a high rate of false positives (16%) in individuals who either were diagnosed with other psychological disorders or re-ported depressive symptoms (Suhr et al., 2008; Suhr et al., 2009). In contrast, in a more recent study, Paucke and colleagues highlighted the utility of both the WURS and some subscales of the CAARS in the differentiation of ADHD and major depressive disorder (Paucke et al., 2021). Further, McCann and Roy-Byrne examined the utility of a number of ADHD self-report scales for the diagnostic screening of adults referred for an ADHD evaluation. The authors found, on the one hand, that all scales were sensitive to the presence of ADHD (ranging from 78% to 92%); on the other hand, however, a high proportion of individuals with other diagnoses than ADHD were also screened positive for ADHD by these scales (ranging from 36% to 67%), especially individuals with a major depressive episode and dysthymia (McCann & Roy-Byrne, 2004; McCann et al., 2000). In another study, Young reported small to medium-sized group differences between patients with ADHD and clinically referred comparison individuals (primarily suffering from anxiety, depression, and personality disorders), as well as healthy comparisons in all four subscales of the Young ADHD Questionnaire, both in the self- and the informant report. Yet, further discriminant analyses showed that only the ADHD symptomatology subscale had significant discriminant value. Of note, the ADHD symptom severity of adults with ADHD was only weakly associated between the self- and informant report in this and some further studies (Kooij et al., 2008; Young, 2004). Nevertheless, moderate to large associations were reported in the German version of the CAARS (Christiansen et al., 2012).

The majority of the studies using self-reports to differentiate ADHD from clinical comparison groups were based on core symptoms of ADHD, including attention and concentration deficits, impulsivity, and hyperactivity, which are partly shared by other psychiatric conditions, such as mood disorders, anxiety disorders, impulsive-control disorders, and substance use disorders (Kooij et al., 2012; Moss et al., 2007). Given this well-documented overlap, it can be assumed that scales focusing on ADHD symptoms are not adequate instruments to serve the purpose of differential diagnosis but that measures for other clinical conditions with which ADHD is commonly confused may be more promising. In this context, Paucke and colleagues reported a large-sized difference between adults with ADHD and adults with major depressive disorder in self-reported symptoms of de-pression, as assessed with the Beck Depression Inventory-Ⅱ (BDI-Ⅱ; Paucke et al., 2021). However, this effect was not found in an earlier study comparing patients with ADHD and bi-polar disorder (Torralva et al., 2011). Similarly, Nelson and Gregg showed that college students with ADHD and dyslexia could not be differentiated from each other and, also, not from college students not having any diagnosis based on self-reported symptoms of depression and anxiety (Nelson & Gregg, 2012).

Considering no firm conclusions can be drawn so far about the role of self- and informant reports on symptoms and impairments in the differential diagnosis of adult ADHD, more research is needed, especially comparing clinical samples from the same referral context. Thus, this study aims to advance our understanding of the role of subjective reports in the clinical evaluation of adult ADHD and for differential diagnostic purposes specifically and to provide clinicians recommendations on how to use and interpret the standardized self- and informant reports. This study employs a large sample of 169 individuals clinically referred to an ADHD outpatient assessment. All individuals completed a comprehensive battery of self- and informant report rating scales for symptoms and impairments, including ADHD symptom domains in child-hood and adulthood, cognitive functioning, depression, anxiety, and impulsivity. By using a large clinical sample of individuals who all completed a comprehensive battery of self- and informant reports, this study aims to determine whether individuals meeting the diagnostic criteria of ADHD can be differentiated from relevant clinical controls in the same referral context by reported levels of symptoms and impairments. We expect (1) individuals diagnosed with ADHD to show more pronounced ADHD symptoms and impairments but less pronounced symptoms of depression and anxiety when compared to individuals not reaching diagnostic criteria of ADHD but showing evidence for other psychiatric disorders. However, when compared to individuals who did not show evidence for any psychiatric disorders, we expected (2) individuals diagnosed with ADHD to endorse higher symptom levels and more impairments on all scales applied. Furthermore, because of reliable findings showing symptom un-der-reported (Du Rietz et al., 2016; Manor et al., 2012; Sibley et al., 2012) or over-reported (Cook et al., 2018; Fuermaier et al., 2014; Suhr et al., 2008) in the self-report of individuals with ADHD, we expected (3) individuals diagnosed with ADHD to show a more pronounced discrepancy to informant reports compared to clinically referred individuals not reaching diagnostic criteria of ADHD. Finally, (4) on the basis of previous research questioning the relationship between subjective reports and an objective neuropsychological test performance (Barkley et al., 2010; Fuermaier et al., 2015; Hoelzle et al., 2019; Jarrett et al., 2017), this study seeks to further define the role of subjectively reported complaints by relating symptoms and impairments to test the scores of cognitive functions.

Materials and Methods

Participants

A total of 248 participants were considered for inclusion in this study. All participants were recruited from the ADHD outpatient clinic of the Department of Psychiatry and Psychotherapy, LVR-Hospital Essen, University of Duisburg-Essen, Germany. Individuals were referred for a diagnostic assessment, because they were suspected of having ADHD by GPs, neurologists, psychiatrists, or by themselves. Qualified psychologists or psychiatrists performed a comprehensive assessment for all participants based on the criteria as outlined in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (American Psychiatric Association, 2013). A semi-structured interview was conducted to evaluate ADHD psychopathology (i.e., the Wender-Reimherr-Interview and the Essen Inter-view-for-school-days-related-biography) (Grabemann et al., 2017; Retz-Junginger et al., 2017). Furthermore, all participants and their informants completed a battery of self- and informant report rating scales for symptoms and impairments commonly seen in ADHD, including ADHD symptoms in childhood, current ADHD symptoms, impulsiveness, anxiety, depression, and cognitive disturbances. Further, all individuals underwent cognitive testing using a battery of neuropsychological tests (see the Methods section for a detailed description of the applied measures). The diagnostic assessment also included objective measures of impairment (e.g. failure in academic and/or occupational achievement) and multiple in-formants (e.g. school reports, employer evaluation, partner or parent-reports) for all individuals.

Seventy-nine participants were excluded from data analysis for one of the following reasons, i.e., participants did not complete the diagnostic process, a formal diagnostic decision could not be established, or self- and informant report information was not assessed, resulting in a sample of 169 participants who were included in the final data analysis. All of those participants who were retained were assigned to one of three groups, i.e., the ADHD group (participants diagnosed with ADHD, n = 73), the Clinical Comparison Group (CCG; participants who did not fulfill diagnostic criteria for ADHD but showed evidence of one or more other psychiatric disorders; n = 53), and the Clinical Comparison Group-Not Diagnosed (CCG-ND; participants who did not fulfill diagnostic criteria for ADHD and were not diagnosed with any other psychiatric disorder; n = 43). Of those patients diagnosed with ADHD, 62 were diagnosed with the combined symptom presentation, and nine were diagnosed with the pre-dominantly inattentive symptom presentation, while the symptom presentation of an-other two participants was not reported. Moreover, 27 patients diagnosed with ADHD showed evidence for one or more comorbid disorders, including mood disorders (n = 16), anxiety disorders (n = 3), addiction disorders (n = 6), personality disorders (n = 2), adjustment disorders (n = 3), obsessive-compulsive disorders (n = 2), intellectual development disorder (n = 1), mixed receptive expressive language disorder (n = 1), and autistic disorders (n = 1). Individuals in the CCG showed evidence for one or more psychiatric disorders other than ADHD, including mood disorders (n = 37), anxiety disorders (n = 4), addiction disorders (n = 15), personality disorders (n = 1), adjustment disorders (n = 1), obsessive-compulsive disorders (n = 1), eating disorders (n = 3), and schizoaffective disorders (n = 1). The characteristics of all the participants are presented in Table 3.1. A strict significance level of $p < 0.01$ was applied to control for alpha error inflation. Significant difference was observed between the groups in age, $F(2) = 6.453$, $p = 0.002$, but not in sex, $\chi^2(2) = 4.500$, $p = 0.105$, and not in educational level, $\chi^2(8) = 17.268$, $p = 0.027$. Compared to the CCG, patients with ADHD were on average significantly younger but did not differ significantly in sex and education level. The ADHD group did not differ significantly from the CCG-ND in either age, sex, or educational level.

Table 3.1. Characteristics (M ± SD) of the ADHD group (ADHD), Clinical Comparison Group (CCG), and Clinical Comparison Group-Not Diagnosed (CCG-ND).

	ADHD	**CCG**	**CCG-ND**	**ANOVA/Chi-Square**		**Pairwise Comparisons**			
						ADHD vs. CCG		**ADHD vs. CCG-ND**	
	(*n* = 73)	**(*n* = 53)**	**(*n* = 43)**	F/χ^2	***p***	***p***	***Cohen's d***	***p***	***Cohen's d***
Age (in years)	32.4 ± 10.4	39.3 ± 11.0	33.7 ± 11.3	6.453	0.002*	0.001*	0.648	0.543	0.121
Sex (female/male)	26/47	23/30	24/19	4.500	0.105				
Education (% in 1/2/3/4/5) [1]	6/28.5/20/28.5/17	0/17/44/23/16	0/30/19/37/14	17.268	0.027				
Symptom presentation of ADHD [2]	62/9/0/2								
Psychiatric disorders other than ADHD [3]	16/3/6/2/3/2/1/1/1/0/0	37/4/15/1/1/1/0/0/0/1/1							

Note: ADHD = Attention Deficit Hyperactivity Disorder; CCG = Clinical Comparison Group; CCG-ND = Clinical Comparison Group—Not Diagnosed. [1] Percentage of individuals with different education levels per group (%). Education (1/2/3/4/5) = No school-leaving qualification/Compulsory schooling or intermediate secondary school/College or vocational training/Higher secondary school with university entrance qualification/University. [2] Symptom presentation of ADHD = combined/inattentive/hyperactive-impulsive/not reported. [3] Individuals were suffering from one or more psychiatric disorders other than ADHD: Mood disorders/anxiety disorders/addiction disorders/personality disorders/adjustment disorders/obsessive-compulsive disorders/intellectual development disorder/mixed receptive expressive language disorder/autistic disorders/eating disorders/schizoaffective disorders. * Statistically significant at $p < 0.01$.

Measures

The current study is part of a larger project on clinical and neuropsychological functioning of adults with ADHD in an outpatient referral context. Since the present study focuses on self- and informant-reported symptoms and impairments, it describes these instruments in detail. The role of objective neuropsychological test performance has been addressed in a previous study of our group on an overlapping sample (Guo, Fuermaier, Koerts, Mueller, Diers, et al., 2021). The current manuscript is therefore restricted to a brief description of neuro-psychological tests.

WURS-K. The German version of the Wender Utah Rating Scale (WURS-K) was administered to all participants to quantify self-reported retrospective ADHD symptoms (Retz-Junginger et al., 2003; Retz-Junginger et al., 2002; Ward, 1993). The scale includes 25 items on a 5-point Likert scale ranging from 0 (not at all or very slightly) to 4 (very much). Participants were asked to rate each item based on their recall of experiences in childhood. Internal consistency (Cronbach's alpha) of this scale was excellent and reported to be 0.91. A sum score was calculated for the se-verity of ADHD symptoms in childhood.

ADHD-SR. The German version of the ADHD Self-Report Scale (ADHD-SR) is a self-report scale used to assess the severity of current ADHD symptoms (Adler et al., 2006; Kessler et al., 2005; Rösler et al., 2004). The ADHD-SR comprises 18 items corresponding to the diagnostic criteria of DSM-IV. Participants are asked to rate each item based on how often an ADHD symptom occurred over the past six months on a scale ranging from 0 (never) to 3 (very often). The internal consistency (Cronbach's alpha) of this scale was high and reported to be 0.90. A sum score was calculated for the severity of current ADHD symptoms.

CAARS. The Conners' Adult ADHD Rating Scales (CAARS) is a self- and in-formant report instrument that was developed to assist in the assessment of ADHD in adulthood (Conners, Erhardt, & Sparrow, 1999). The present study includes both the self-report (CAARS-S:L) and observer report form (CAARS-O:L). Each scale includes 66 items, which are rated on a 4-point Likert scale ranging from 0 (not at all/never) to 3 (very much/very frequently). Item scores are summed up to derive eight subscale scores, including inattention (CAARS_SR_IA and CAARS_OR_IA for the self- and other report, respectively), hyperactivity (CAARS_SR_HA and CAARS_OR_HA), impulsivity (CAARS_SR_IM and CAARS_OR_IM), problems with self-concept (CAARS_SR_SC and CAARS_OR_SC), DSM-IV: inattentive symptoms (CAARS_SR_DSM and, CAARS_OR_DSMI), DSM-IV: hyperactive-impulsive (CAARS_SR_DSMH and CAARS_OR_DSMH), DSM-IV: total ADHD symptoms (CAARS_SR_DSMT and CAARS_OR_DSMT), and the ADHD index (CAARS_SR_Index and CAARS_OR_Index). Internal consistency (Cronbach's alpha) of the CAARS was excellent and ranged from 0.74 to 0.95 (Christiansen et al., 2012).

STAI. The State-Trait Anxiety Inventory (STAI) is a self-report scale designed to measure the presence and severity of anxiety symptoms in adults. The inventory consists of 40 items, each rated on a 4-point Likert scale. Twenty items assess the presence of anxiety as an emotional state (state anxiety, STAI-S), whereas other 20 items assess individual differences in anxiety proneness as a personality trait (trait anxiety, STAI-T) (Spielberger, 1983, 2010). Internal consistency (Cronbach's alpha) was reported to be 0.93 and 0.90 for state anxiety and trait anxiety, respectively (Barnes, Harp, & Jung, 2002). The sum scores were calculated for both state and trait anxiety, with higher sum scores indicating higher levels of anxiety.

BDI-Ⅱ. The Beck Depression Inventory-Ⅱ (BDI-Ⅱ) is a self-rated scale assessing the presence and severity of depressive symptoms in individuals aged 13 years and older. The BDI includes 21 items, each rated on a 4-point Likert scale (Beck, Steer, & Brown, 1996). To each item, participants are asked to select the statement that best characterizes their emotions and functioning in the past two weeks. The internal consistency (Cronbach's alpha) of the BDI-Ⅱ was reported to be high (alpha ≥ 0.84) (Kühner et al., 2007). Scoring of the BDI includes the calculation of a total score, with high scores indicating more severe depressive symptoms.

BIS-11. The Barratt Impulsiveness Scale (BIS-11) is a self-report questionnaire de-signed to measure impulsiveness (Patton, Stanford, & Barratt, 1995; Stanford et al., 2009). The scale consists of 30 items, each rated on a 4-point Likert scale ranging from 1 (rarely/never) to 4 (almost always/always). The internal consistency (Cronbach's alpha) of the BIS-11 was high (0.83) (Stanford et al., 2009). A total score was calculated for the BIS-11, with larger scores indicating higher levels of impulsiveness.

FLEI. The Questionnaire on Mental Ability (FLEI) was administered as a measure of subjectively experienced cognitive deficits (Beblo et al., 2012). In this scale, participants are asked to rate 35 statements regarding the presence of problems in attention, executive functioning, and memory in everyday life. The FLEI includes 35 items scored on a 5-point Likert scale ranging from 0 (never) to 4 (very often). The internal consistency (Cronbach's alpha) of the FLEI was high (0.94) (Beblo et al., 2012). A sum score is computed to indicate the severity of the cognitive deficits.

Neuropsychological test battery. A battery of neuropsychological tests was ad-ministered to all participants to assess several aspects of cognition, including selective function (Perceptual and Attention Functions-Selective Attention, WAFS), vigilance (Perceptual and Attention Functions-Vigilance, WAFV), working memory (N-back Task), interference (Stroop Interference Test), inhibition (Go/No-Go Test), figural fluency (5-Point Test—Langensteinbach Version), flexibility (Trail Making Test—Langensteinbach Version, TMT-L), planning ability (Tower of London—Freiburg Version, TOL-F), and task switching (SWITCH Task). All tests were retrieved from the test set Cognitive Functions ADHD (CFADHD), which is a computerized test battery assessing cognitive functions in which adults with ADHD commonly show difficulties (Lara Tucha et al., 2013; Schuhfried, 2013). The test variables recorded include the speed of responses (mean reaction time); variability of response times (SD of reaction time); and accuracy measures (i.e., number of omission errors, commission errors, correct responses, correctly produced patterns, or number of solved items). Based on the test variables, compound Z-scores per domain are computed, e.g., basic attention, working memory, inhibition/interference control, cognitive flexibility, and convergent/divergent thinking (for details, see Guo, Fuermaier, Koerts, Mueller, Diers, et al., 2021).

Procedure

The assessment of symptoms, impairments, and neuropsychological functions using the various approaches was part of the standard clinical procedure for all participants referred to the ADHD outpatient clinic of the department of psychiatry and psychotherapy, LVR-Hospital

Essen, University of Duisburg-Essen, Germany. All participants signed a written informed consent that declares their agreement for their data being used for scientific purposes. Furthermore, approval for this study was obtained from the ethical review board of the medical faculty of the University of Duis-burg-Essen, Germany (20-9380-BO). It was stressed to all individuals that agreeing to take part in this study was voluntary, unpaid, and would not affect their clinical assessment or treatment. All participants were asked to complete the battery of self- and informant report questionnaires and to perform the neuropsychological assessment around the date of their clinical interview. The clinical assessment, including all measures, took about four hours in total.

Statistical Analysis

Descriptive statistics of all measures of self- and other reports are presented per group. Furthermore, self- and other reports of the CAARS subscales for inattention, hyperactivity, impulsivity, self-concept, and total ADHD index were contrasted by calculating discrepancy scores per person (i.e., computing scores of self-reports minus other reports) and presenting the mean and standard deviation of the absolute discrepancy scores per group. After checking for assumptions of parametric testing, groups were compared on all measures employing ANCOVA and post-hoc pairwise comparisons between the ADHD group and the CCG and CCG-ND, respectively. As the assumption check for STAI variables indicated a violation of the normality assumption (presumably because of the small sample size resulting from missing values), results of ANCOVA were confirmed by nonparametric testing (Kruskal–Wallis Tests). Age was taken as a covariate to control for age differences between groups. A strict significance level of $p < 0.01$ was applied to control for alpha error inflation. Effect sizes (Cohen’s *d*) were calculated for significant pairwise group differences to indicate the magnitude of findings. Age-adjusted mean scores were used for the calculation of effect sizes to control for age differences. Based on the interpreting guidelines for Cohen’s *d*, $d < 0.2$ indicates a negligible effect, $0.2 \leq d < 0.5$ indicates a small effect, $0.5 \leq d < 0.8$ indicates a medium effect, and $d \geq 0.8$ indicates a large effect (Cohen, 1988).

Furthermore, to determine the validity of subjective reports in predicting an individual’s diagnostic status, two binary logistic regression models, using backward elimination of predictor variables, were calculated for distinguishing the ADHD group from both the CCG and CCG-ND, respectively. Only scales that showed significant effects on the group were included as predictors in the models. To reduce the influence of multicollinearity between STAI-T and

STAI-S, a new anxiety variable (STAI) was calculated by adding for each individual the scores of STAI-T and STAI-S and was included in a binary logistic regression analysis. Missing values (about 12% of the data) were replaced by group means for regression analyses to obtain a sufficiently large sample size.

Finally, the objective neuropsychological test performance per domain (i.e., basic attention, working memory, inhibition/interference control, cognitive flexibility, and convergent/divergent thinking) were presented per group and were compared using ANCOVA. In order to explore the predictive value of self- and other reports for objective neuropsychological test performance (following a clinically oriented order of pre-diction but not necessarily causal relationship), multiple linear regression models were computed for each group separately and the total group. To improve the power of regression models, binary correlation analyses were performed between all subjective reports and different aspects of objective neuropsychological test performance prior to the regression analyses. Only variables that were significantly correlated with the outcome in bivariate analyses were eventually included in multiple regression models. Additionally, backward elimination was used for potential predictor variables. All statistical analyses reported so far were performed using IBM SPSS 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Statistical power for the group comparisons was calculated with G-Power. These calculations indicate, based on a significance level of 0.05, large power to reveal medium (83.0%) and large effects (99.8%). However, in order to minimize the risk of running into a type-1 error, we decided to reduce the significance level to 0.01, which resulted in lower power for medium effects (63.0%) but retained high power for large effects (98.7%).

Results

Descriptive statistics and group comparisons (ANCOVA controlling for age, with post-hoc pairwise comparisons) of subjective reports of symptoms and impairments, as well as objective neuropsychological test performances, are presented in Table 3.2. Significant differences were found in symptom domains of ADHD, anxiety, depression, impulsiveness, and subjective experience of cognitive deficits, whereas no significant effects were observed in any of the discrepancy scores or in the neuropsychological test performance. Compared to the CCG, the ADHD group endorsed significantly higher symptom scores in the WURSK, ADHD-SR, and CAARS-SR-IM (medium to large effects) and significantly less symptoms of depression (medium effect). The ADHD group did not differ significantly from the CCG in any variables of the informant report, anxiety, impulsiveness, and subjective experiences of the cognitive deficits (effects up to medium size). Compared to the CCG-ND, the ADHD group (and their informants) indicated significantly more symptoms in the WURSK, ADHD-SR, CAARS-SR-HA, CAARS-SR-IM, CAARS-SR-Index, and CAARS-OR-HA (medium to large effects), significantly higher symptom scores in the STAI-T and STAI-S (large effects), BIS-11 (large effect), and FLEI (medium effect). Group differences between ADHD and CCG-ND on depression did not reach significance (negligible effect).

Table 3.2. Self- and other reports of symptoms and impairments in the various domains.

Variables	ADHD (*n* = 73)	CCG (*n* = 53)	CCG-ND (*n* = 43)	ANCOVA		Pairwise Comparisons: ADHD vs. CCG		Pairwise Comparisons: ADHD vs. CCG-ND	
	M ± SD	**M ± SD**	**M ± SD**	***F***	***p***	***p***	***Cohen's d***	***p***	***Cohen's d***
ADHD Symptoms									
WURS-K [a]	44.6 ± 12.5	34.1 ± 11.8	27.9 ± 12.5	25.771	<0.001*	<0.001*	0.86	<0.001*	1.34
ADHD-SR [b]	35.4 ± 9.8	30.1 ± 10.6	26.4 ± 11.8	11.012	<0.001*	0.002*	0.59	<0.001*	0.87
CAARS-SR-IA [c]	24.2 ± 8.0	22.6 ± 5.7	20.0 ± 8.4	3.776	0.025				
CAARS-SR-HA [c]	22.1 ± 7.1	18.2 ± 7.7	15.0 ± 8.6	10.275	<0.001*	0.015	0.53	<0.001*	0.92
CAARS-SR- IM [c]	22.2 ± 8.4	18.2 ± 6.8	17.6 ± 8.2	6.066	0.003*	0.005*	0.58	0.003*	0.58
CAARS-SR-SC [c]	11.4 ± 4.5	11.7 ± 4.1	10.6 ± 4.6	0.728	0.485				
CAARS-SR-Index [c]	23.3 ± 7.2	22.3 ± 5.3	19.1 ± 7.5	5.159	0.007*	0.295	0.23	0.002*	0.61
CAARS-OR-IA [c]	22.3 ± 9.4	21.6 ± 10.0	18.5 ± 9.2	1.958	0.145				
CAARS-OR-HA [c]	18.9 ± 9.8	15.8 ± 8.2	13.0 ± 6.7	5.706	0.004	0.057	0.38	0.001*	0.68
CAARS-OR- IM [c]	20.0 ± 9.5	17.9 ± 7.5	16.0 ± 7.5	2.948	0.056				
CAARS-OR-SC [c]	10.3 ± 5.1	10.2 ± 4.8	10.2 ± 4.7	0.029	0.971				
CAARS-OR-Index [c]	20.9 ± 8.4	19.1 ± 7.0	17.4 ± 6.5	2.571	0.080				
Symptom Discrepancy Between Self- and Other Reports									
Discrepancy-CAARS-IA [d]	7.2 ± 6.2	7.8 ± 6.0	8.4 ± 5.9	0.598	0.552				
Discrepancy-CAARS-HA [d]	6.5 ± 5.2	6.6 ± 5.8	5.9 ± 4.1	0.198	0.821				
Discrepancy-CAARS-IM [d]	6.9 ± 6.1	7.4 ± 5.5	6.0 ± 5.5	0.550	0.578				
Discrepancy-CAARS-SC [d]	4.0 ± 3.8	4.7 ± 3.7	3.7 ± 2.5	0.911	0.405				
Discrepancy-CAARS-Index [d]	7.3 ± 6.4	7.3 ± 6.3	6.3 ± 5.3	0.348	0.707				
Anxiety									
STAI-T [e]	43.6 ± 15.7	51.3 ± 12.2	31.4 ± 9.9	14.840	<0.001*	0.016	0.51	0.001*	0.87
STAI-S [e]	43.3 ± 17.8	48.6 ± 14.3	28.9 ± 11.2	10.975	<0.001*	0.213	0.26	<0.001*	0.92
Depression									
BDI-II [f]	17.6 ± 12.4	24.8 ± 9.3	15.7 ± 11.5	7.757	0.001*	0.002*	0.60	0.367	0.17
Impulsiveness									
BIS-11 [g]	80.9 ± 11.7	76.7 ± 10.4	70.6 ± 15.1	9.705	<0.001*	0.030	0.47	<0.001*	0.81
Subjective Experiences of Cognitive Deficits									
FLEI [h]	78.3 ± 21.9	78.5 ± 15.3	64.2 ± 20.6	7.774	0.001 *	0.743	0.07	<0.001*	0.68
Objective neuropsychological test performance									
Basic attention [i]	−0.19 ± 0.88	−0.08 ± 0.58	−0.0008 ± 0.54	1.569	0.212				
Working memory [j]	0.03 ± 0.86	0.04 ± 1.08	0.0009 ± 1.0	0.017	0.983				
Inhibition/interference control [k]	−0.12 ± 0.76	−0.06 ± 0.65	−0.02 ± 0.62	0.214	0.807				
Cognitive flexibility [l]	−0.02 ± 079	−0.04 ± 0.81	0.07 ± 0.74	0.327	0.720				
Convergent/divergent thinking [m]	−0.27 ± 0.65	−0.21 ± 0.69	0.002 ± 0.78	2.103	0.125				

Note: ADHD = Attention Deficit Hyperactivity Disorder; CCG = Clinical Comparison Group; CCG-ND = Clinical Comparison Group—Not Diagnosed. [a] Wender Utah Rating Scale for childhood ADHD symptoms. [b] ADHD Self-Report Scale for current ADHD symptoms. [c] Self-reports (SR) or other reports (OR) of Conners' Adult ADHD Rating Scales. IA, inattention, HA, hyperactivity, IM, impulsivity, SC, problems with self-concept. Index, ADHD index. [d] Absolute discrepancy between self- and other reports of ADHD symptoms. [e] Trait and State anxiety subscales of State-Trait Anxiety Inventory. [f] Beck Depression Inventory. [g] Barratt Impulsiveness Scale. [h] Questionnaire on Mental Ability. [i] Compound Z-score of measures of processing speed and distractibility in tasks of selective attention, vigilance, and processing speed. [j] Z-scores of the N-back task. [k] Compound Z-scores of the Go/No-Go and Stroop tasks. [l] Compound Z-scores of the TMT-B/A and SWITCH tasks. [m] Compound Z-scores of the Tower of London and 5-Point tasks. *Statistically significant at $p < 0.01$.

Furthermore, two significant binary logistic regression models were obtained for the differential diagnosis between the ADHD group and both the CCG and CCG-ND, respectively. Regarding the differentiation between the ADHD and CCG groups, subjective reports had a significant predictive value for an individual's diagnostic status, $\chi^2(4) = 47.54$, $p < 0.001$, with 31.4% explained variance (Cox and Snell). This model correctly classified 75.4% of the individuals. The contribution of each scale to the model is presented in Table 3.3. Significant effects are observed for WURS-K, CAARS_SR_IM, and BDI-II. Regarding the differentiation between the ADHD and CCG-ND group, subjective reports again had a significant predictive value for an individual's diagnostic status, $\chi^2(4) = 69.79$, $p < 0.001$, with 45.2% explained variance (Cox and Snell) and 84.5% of the individuals correctly classified. Table 3.3 shows that WURS-K, CAARS_SR_HA, BDI, and STAI had significant effects on predicting the group membership.

Table 3.3. Binary logistic regression models (backward elimination) based on the measures of self- and other reports to predict an individual's diagnostic status.

Predictors	**B**	***SE* B**	**Wald**	***p***	**Odds Ratio (95% CI [a])**
Prediction of the differential diagnosis of ADHD and CCG					
WURS-K [b]	0.075	0.021	12.825	<0.001*	1.078 (1.04~1.12)
CAARS-SR- IM [c]	0.092	0.036	6.733	0.009*	1.097 (1.02~1.18)
BDI-II [d]	−0.081	0.023	12.340	<0.001*	0.922 (0.88~0.96)
STAI [e]	−0.016	0.009	2.839	0.092	0.984 (0.97~1.10)
Total $R^2 = 0.314$ [f]					
Prediction of the differential diagnosis of ADHD and CCG-ND					
WURS-K [b]	0.095	0.025	14.290	<0.001*	1.099 (1.05~1.16)
CAARS-SR-HA [g]	0.093	0.040	5.440	0.020	1.098 (1.01~1.19)
BDI-II [d]	−0.064	0.028	5.201	0.023	0.938 (0.89~0.99)
STAI [e]	0.063	0.016	14.979	<0.001*	1.065 (1.03~1.10)
Total $R^2 = 0.452$ [f]					

Note: ADHD = Attention Deficit Hyperactivity Disorder; CCG = Clinical Comparison Group; CCG-ND = Clinical Comparison Group—Not Diagnosed. [a] Confidence interval. [b] Wender Utah Rating Scale for childhood ADHD symptoms. [c] Impulsivity subscale of self-report Conners' Adult ADHD Rating Scales. [d] Beck Depression Inventory. [e] State-Trait Anxiety Inventory. [f] Cox and Snell R^2. [g] Hyperactivity subscale of self-report Conners' Adult ADHD Rating Scales.
* Statistically significant at $p < 0.01$.

Finally, multiple linear regression models were computed to explore the predictive values of self- and other reports for objective neuropsychological test performances (Table 3.4). For the ADHD group, the CAARS-OR-IM (*Beta* = −0.261, *p* = 0.026) and discrepancy-CAARS-HA (*Beta* = −0.265, *p* = 0.022) have significant predictive values for convergent/divergent thinking (*F* = 6.356, *p* = 0.003). For the CCG group, two significant regression models were obtained, i.e., the CAARS-SR-IA (*Beta* = −0.392, *p* = 0.004) has a significant predictive value for basic function (*F* = 9.281, *p* = 0.004), and BDI-II (*Beta* = −0.391, *p* = 0.004) has a significant predictive value for inhibition and interference control (*F* = 9.186, *p* = 0.004). For the CCG-ND group, the BDI-II (*Beta* = −0.435, *p* = 0.004) has a significant predictive value for working memory (*F* = 9.585, *p* = 0.004). For the total group, two significant regression models were also obtained, i.e., the BIS-11 (*Beta* = −0.213, *p* = 0.005) and discrepancy-CAARS-SC (*Beta* = −0.167, *p* = 0.026) have significant predictive values for basic attention (*F* = 6.433, *p* = 0.002), whereas the CAARS_OR_HA (*Beta* = −0.238, *p* = 0.002) and FLEI (*Beta* = −0.141, *p* = 0.061) have significant predictive values for convergent/divergent thinking (*F* = 7.632, *p* = 0.001). However, adjusted R-square values remained below 17% for all models.

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Table 3.4. Multiple linear regression analyses of measures of self- and other reports (predictors) on objective neuropsychological test performances (criteria).

Criteria of Neuropsychological Test Performance	**Regression Models**				
	F		***R*-Square**	**Adjusted *R*-Square**	***p***
	***df* (Regression, Residual)**	***F*-value**			
ADHD (*n* = 73)					
Basic attention [a]	1, 71	5.182	0.068	0.055	0.026
Working memory [b]	-	-	-	-	-
Inhibition and interference control [c]	1, 71	6.450	0.083	0.070	0.013
Cognitive flexibility [d]	1, 71	5.400	0.071	0.058	0.023
Convergent/divergent thinking [e]	2, 70	6.356	0.154	0.130	0.003*
CCG (*n* = 53)					
Basic attention [f]	1, 51	9.281	0.154	0.137	0.004*
Working memory [g]	2, 50	3.962	0.137	0.102	0.025
Inhibition and interference control [h]	1, 51	9.186	0.153	0.136	0.004*
Cognitive flexibility [b]	-	-	-	-	-
Convergent/divergent thinking [b]	-	-	-	-	-
CCG-ND (*n* = 43)					
Basic attention [b]	-	-	-	-	-
Working memory [i]	1, 41	9.585	0.189	0.170	0.004*
Inhibition and interference control [b]	-	-	-	-	-
Cognitive flexibility [b]	-	-	-	-	-
Convergent/divergent thinking [j]	1, 41	5.460	0.118	0.096	0.024
Total (*n* = 169)					
Basic attention [k]	2, 166	6.433	0.072	0.061	0.002*
Working memory [b]	-	-	-	-	-
Inhibition and interference control [l]	1, 167	4.716	0.027	0.022	0.031
Cognitive flexibility [b]	-	-	-	-	-
Convergent/divergent thinking [m]	2, 166	7.632	0.084	0.073	0.001*

Note: ADHD = Attention Deficit Hyperactivity Disorder; CCG = Clinical Comparison Group; CCG-ND = Clinical Comparison Group—Not Diagnosed. Basic attention = Compound Z-score of measures of processing speed and distractibility in tasks of selective attention, vigilance, and processing speed. Working memory = Z-score of N-back task. Inhibition and interference control = Compound Z-score of Go/No-Go and Stroop tasks. Cognitive flexibility = Compound Z-score of TMT-B/A and SWITCH tasks. Convergent/divergent thinking = Compound Z-score of Tower of London and 5-Point tasks. [a] Model was estimated based on the candidate predictors CAARS-OR-HA and CAARS-OR-IM; CAARS-OR- IM was retained in the final model. [b] No regression estimated because no candidate predictor correlated significantly with the criteria. [c] Model was estimated based on the candidate predictors CAARS-OR-IA and CAARS-OR- HA; CAARS-OR- IA was retained in the final model. [d] The model was estimated based on the candidate predictors CAARS-SR- IM and CAARS-SR-SC; CAARS-SR-SC was retained in the final model. [e] The model was estimated based on the candidate predictors CAARS-OR-HA, CAARS-OR- IM, CAARS-OR-Index, discrepancy-CAARS-HA, and discrepancy-CAARS-IM; CAARS-OR-IM and discrepancy-CAARS-HA were retained in the final model. [f] The model was estimated based on the only candidate predictor CAARS-SR-IA. [g] The model was estimated based on the candidate predictors CAARS-SR-HA and discrepancy-CAARS-HA; both CAARS-SR-HA and discrepancy-CAARS-HA were retained in the final model. [h] The model was estimated based on the only candidate predictor BDI-II. [i] The model was estimated based on the candidate predictors BDI-II, CAARS-SR- IM, and discrepancy-CAARS-SC; BDI-II was retained in the final model. [j] The model was estimated based on the only candidate predictor BIS-11. [k] The model was estimated based on the candidate predictors WURS-K, ADHD-SR, BIS-11, CAARS-OR-IA, CAARS-OR-HA, CAARS-OR- IM, CAARS-OR-Index, and discrepancy-CAARS-SC; BIS-11 and discrepancy-CAARS-SC were retained in the final model.

[l] The model was estimated based on the candidate predictors CAARS-OR-IA, CAARS-OR-HA, and CAARS-OR-Index; CAARS-OR-HA was retained in the final model. [m] The model was estimated based on the candidate predictors WURS-K, ADHD-SR, BIS, CAARS-SR-HA, CAARS-OR-HA, CAARS-OR- IM, CAARS-OR-Index, and FLEI; CAARS-OR-HA and FLEI were retained in the final model. * Statistically significant at $p < 0.01$.

Discussion

This study aimed to explore the role of self- and informant reports on symptoms and impairments in the clinical evaluation of adult ADHD and examine the predictive value of self- and informant reports for objective neuropsychological test performance.

Group comparisons revealed various significant effects of medium to large sizes between the ADHD group and both the CCG-ND and CCG. Compared to the CCG-ND, the ADHD group reported, consistent to our expectations, significantly more pronounced symptoms and impairments in most of the self-report scales. In line with previous findings, both the scales for current (ADHD-SR; CAARS) and retrospective ADHD symptoms (WURS-K) unfold to have discriminative value to distinguish individuals with and without ADHD (Anbarasan, Kitchin, & Adler, 2020; Brevik et al., 2020; Christiansen et al., 2012; Murphy & Adler, 2004; Ustun et al., 2017). Further, in line with the core features of ADHD and commonly seen comorbidity, patients with ADHD indicated more pronounced symptoms of impulsivity (Winstanley, Eagle, & Robbins, 2006; Young & Gudjonsson, 2005), cognitive deficits (Alderson et al., 2013; Boonstra et al., 2005; Salomone et al., 2020), and higher levels of anxiety (Schatz & Rostain, 2006; Tannock, 2009). Against our expectations, however, depressive symptoms did not differ between the ADHD group and CCG-ND. This is surprising, considering the indications of a large number of comorbid mood disorders in the ADHD sample (16 of 73). The pattern of group differences between the ADHD group and the CCG-ND is also reflected in the logistic regression analysis, revealing that subjective reports significantly predicted an individual's diagnostic status with almost 45% explained variance. The strongest predictors were self-reported ADHD symptoms in childhood and current anxiety. The observed predictive value of anxiety is consistent with the widely recognized knowledge that anxiety is one of the major comorbidities of ADHD (Schatz et al., 2006; Tannock, 2009). Retrospective ADHD symptoms in childhood seem to stand out in the diagnostic process and appear to be most informative to identify ADHD in adulthood in a psychiatric outpatient referral context (Brevik et al., 2020). We conclude that the exploration of childhood onset and continuity of ADHD symptoms through adolescence and adulthood should be done with care and deserves sufficient time and resources in the assessment of first-time ADHD diagnosis in adulthood.

Comparing individuals with ADHD to the group of individuals showing indications of other psychiatric disorders (CCG), fewer differences were observed, i.e., the ADHD group reported higher scores on their current (ADHD-SR; CAARS) and retrospective (WURS-K) ADHD symptoms but lower scores on depression (BDI). Hence, also in differentiation to patients having other psychiatric disorders, ADHD symptomatology seems to have a key role and appears to have clinical value (McCann et al., 2000; Paucke et al., 2021; Suhr et al., 2008). Considering the fact that the majority of individuals in the CCG showed indications of mood disorders (37 of 53), higher depression scores appear logical and may serve as useful information to differentiate ADHD from depressive disorders. The discriminative value of self-reported ADHD symptoms in childhood and adulthood, as well as depressive symptoms, are underscored in the logistic regression analysis, with no other score adding significantly explained variance for group differentiation. Compared to other ADHD scales used in this study, the CAARS appeared to play a minor role in distinguishing the ADHD group from the CCG, which adds evidence to previous works stressing the limited value of the CAARS for a differential diagnostic purpose (Grogan et al., 2018; Harrison, Nay, & Armstrong, 2019; Solanto et al., 2004; Van Voorhees, Hardy, & Kollins, 2011). In contrast to differences in depression, no significant effects were found for the symptoms of anxiety, impulsivity, and subjective reports of cognitive deficits. As an explanation, one may consider that whether or not group differences in psychopathology can be observed may depend on the composition of samples (comorbid disorders to ADHD; diagnostic status of the clinical comparison group) and may be difficult to generalize. Additionally, nonsignificant differences on a variety of scale scores support the view that it is difficult to differentiate ADHD from other psychiatric disorders based on self-reported information only (Barkley & Brown, 2008; Faraone & Antshel, 2008; Montano & Weisler, 2011).

Furthermore, against our expectations, neither the informant report scores nor any of the discrepancy scores between the patients and their informants contributed to the differentiation between the ADHD group, CCG, or CCG-ND. Against previous evidence questioning, the reliability of patients' self-reports due to symptom under- or over-reporting of patients with ADHD (Cook et al., 2018; Du Rietz et al., 2016; Fuermaier et al., 2014; Jiang & Johnston, 2012; Manor et al., 2012; Nelson & Lovett, 2019; Sibley et al., 2012), the present study strengthens the role of patients' self-reports in the clinical evaluation of adult ADHD (Kooij et al., 2008; Magnússon et al., 2006; Young et al., 2005). This must not be confused with the conclusion that informant reports are of no added value to the clinical evaluation of adult ADHD, as it has been repeatedly demonstrated that ratings from multiple informants on symptoms and impairments increase the accuracy of clinical evaluations (Martel et al., 2015; Nelson et al., 2019). Besides, even though no significant effects of discrepancy were observed on group levels, disagreement between different sources of information (e.g., including self- and informant reports) is believed to provide unique and crucial information in clinical evaluations (De Los Reyes & Kazdin, 2005; Goodman, De Los Reyes, & Bradshaw, 2010). On an individual basis, this means that, independent from the diagnostic group, disagreements between self- and other reports may, for instance, give an indication for noncredible symptom reporting and may represent a risk factor for an adverse outcome (Ferdinand, van der Ende, & Verhulst, 2004; Guion, Mrug, & Windle, 2009; Sherman, Slick, & Iverson, 2020). Such a disagreement between self- and other reports, however, may also indicate that patients lack awareness of their symptoms or that they may apply efficient coping strategies so that their significant others do not experience the full degree of their difficulties.

Finally, a number of significant regression models of subjective reports on objective neuropsychological test performances have been obtained in this study. However, considering the negligible to small proportions of explained variance, and no reoccurring patterns of prediction across the models, it can be concluded that subjective reports of symptoms and impairments have no meaningful predictive value for objective neuropsychological test performances (Brooks, 2019; Draper & Smith, 1998). While both subjective reports and objective test performance have been advocated to provide the clinician with valuable information in a clinical evaluation and treatment planning, they seem to be distinct and nonredundant sources of information and should not be treated interchangeably (Barkley et al., 2011; Barkley et al., 2010; Biederman et al., 2008; Butzbach et al., 2019; Fuermaier et al., 2015; Kallweit et al., 2020; Nelson et al., 2019). It remains a challenge for future research to determine the value of any of the information derived in a clinical assessment to predict the sustainable change, long-term outcome, improvement in symptoms, impairments, and general well-being.

Limitations

Several limitations of this study must be considered. First, the representativeness of group differences in the various scales of psychopathology is difficult to determine, because this largely depends on the composition of groups regarding ADHD symptom presentation, comorbidity (ADHD group), and psychopathology (clinical control groups). Second, it must be stressed that the various comorbid disorders of patients with ADHD and psychiatric conditions of individuals in the CCG were suggested based on the clinical assessment for ADHD but were not confirmed by subsequent psychiatric evaluations per specific disorders. Third, this study is largely based on self-reports, which are known to be vulnerable to bias, including over-reporting, under-reporting, or careless responding (Cook et al., 2018; Nelson et al., 2019; Sibley et al., 2012). Fourth, because data were collected in a clinical setting and not under strict controlled experimental conditions, administrative challenges resulted in the occurrence of some missing values depending on the variable type, and individuals were not selected based on matching group criteria. Finally, the subjective reports and neuropsychological test results were accessible to clinicians establishing a diagnosis; thus, these data were not completely independent of diagnostic decision-making.

Conclusions

This study highlighted the role of self-reports of ADHD symptoms in the clinical evaluation of adult ADHD in an outpatient referral context, giving particular emphasis on the role of ADHD symptoms assessed retrospectively from childhood. Compared to self-reports, informant reports, and, also, the discrepancy between self- and informant-reported information unfolds to have limited values for the differential diagnosis of ADHD. While a comprehensive assessment of individual strengths and weaknesses, clinical diagnosis, treatment planning, and outcome assessments typically benefit from a comprehensive approach, including various types of information, self-reports still seem to be most informative for a differential diagnosis. This study also demonstrates that the present inventory of symptoms and impairments differentiated ADHD from a clinical comparison group without psychiatric disorders more successfully than from a clinical control group with indications of other psychiatric disorders. Comorbidities and shared features between ADHD and other psychiatric disorders may presumably be the main reasons for this effect. Finally, our data confirm previous evidence showing that subjective reports of symptoms and impairments on the one side and objective neuropsychological test performances on the other side are distinct and nonredundant information. The roles of various types of information for clinical evaluations, the prediction of outcomes, and sustainable improvement still need to be determined.

Chapter 4

Networks of neuropsychological functions in the clinical evaluation of adult ADHD

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Abstract: This study applied network analysis to explore the relations between neuropsychological functions of individuals in the clinical evaluation of attention-deficit/hyperactivity disorder (ADHD) in adulthood. A total of 319 participants from an outpatient referral context, i.e. 173 individuals with ADHD (ADHD group) and 146 individuals without ADHD (n-ADHD group), took part in this study and completed a comprehensive neuropsychological assessment. A denser network with stronger global connectivity was observed in the ADHD group compared to the n-ADHD group. The strongest connections were consistent in both networks, i.e., the connections between selective attention and vigilance, and connections between processing speed, fluency, and flexibility. Further centrality estimation revealed attention-related variables to have the highest expected influence in both networks. The observed relationships between neuropsychological functions, and the high centrality of attention, may help identify neuropsychological profiles that are specific to ADHD and optimize neuropsychological assessment and treatment planning of individuals with cognitive impairment.

Keywords: adult ADHD, cognitive functions, network analysis, connections, centrality

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder, characterized by symptoms of inattention, hyperactivity, and impulsivity (American Psychiatric Association, 2013). Up to 50 - 65% of individuals diagnosed with ADHD in childhood still present with ADHD symptoms in adulthood (Ebejer et al., 2012; Faraone, Biederman, & Mick, 2006; Fayyad et al., 2017). Numerous studies showed that adult ADHD, compared to typical development, is associated with a range of adverse outcomes, such as academic failure (Advokat et al., 2011; Arnold et al., 2020; Voigt et al., 2017), occupational underachievement (Fuermaier et al., 2021; Gjervan et al., 2012; Kaiser et al., 2008), problems in social relationships (Bruner et al., 2015; Michielsen et al., 2015; Paulson, Buermeyer, & Nelson-Gray, 2005), sleep problems (Díaz-Román et al., 2018; Hvolby, 2015; Lugo et al., 2020), and lower quality of life (Agarwal et al., 2012; Quintero et al., 2019; Thorell et al., 2019).

Numerous neuropsychological studies demonstrated that adults with ADHD commonly present with impairments in multiple cognitive functions, including processing speed (Shanahan et al., 2006; Woods, Lovejoy, & Ball, 2002), selective attention (Butzbach et al., 2019; Onandia-Hinchado et al., 2021), sustained attention/vigilance (Marchetta, Hurks, De Sonneville, et al., 2008; Salomone et al., 2020), memory (Alderson et al., 2013; Skodzik, Holling, & Pedersen, 2017), planning (Desjardins et al., 2010; Fabio & Caprì, 2017), fluency (Onandia-Hinchado et al., 2021; Tucha et al., 2005), inhibition (Boonstra et al., 2010; Willcutt et al., 2005), and task switching (Cepeda, Cepeda, & Kramer, 2000; King et al., 2007). Impairments in these cognitive functions were still observed in adults with ADHD under stable psychopharmacological treatment (Fuermaier et al., 2017; Müller et al., 2007). However, not all adults with ADHD show impairments in all of these cognitive functions, which is often referred to as heterogeneity of cognitive performance in ADHD (Luo et al., 2019; Mostert et al., 2015; Seidman, 2006). Cognitive heterogeneity refers to the observation that, although individuals with ADHD typically present with impairments in attention and executive functions, not all patients with ADHD share the same type and degree of cognitive dysfunctions. Cognitive profiles of patients with ADHD range from individuals having no impairment in any of the cognitive functions assessed (Coghill et al., 2014; Guo, Fuermaier, Koerts, Mueller, Diers, et al., 2021; Mostert et al., 2015), to patients with ADHD disclosing marked cognitive impairments in all cognitive functions of a neuropsychological test battery (Luo et al., 2019; Seidman, 2006). Several pathway models of cognitive functions were proposed to address the issue of cognitive heterogeneity by suggesting that cognitive deficits of adults with ADHD mainly occur in two to six relatively independent neuropsychological functions (Coghill et al., 2014; Sonuga-Barke et al., 2010; Sonuga-Barke, 2003). For example, the dual pathway model suggests that executive deficits and delay aversion are two independent neuropsychological functions in which patients with ADHD frequently show impairments (Sonuga-Barke, 2003). The triple pathway model suggests that temporal processing may be a third neuropsychological domain (Sonuga-Barke et al., 2010) and the six-pathway model suggests there are six relatively independent neuropsychological functions, including inhibition, working memory, timing, delay aversion, decision making, and response variability (Coghill et al., 2014). These conceptual studies on neuropsychological functions in adult ADHD provide support for the argument that cognitive deficits may exist relatively independently of each other. However, more recent studies provided empirical evidence that performances in the various cognitive functions in adult ADHD are not isolated but closely interrelated. For example, the performance of basic cognitive functions, such as processing speed and distractibility in tasks of basic attention, was shown to have a sizable effect on the performance of complex cognitive functions, such as inhibition, cognitive flexibility, and memory (Boonstra et al., 2010; Butzbach et al., 2019; Guo, Fuermaier, Koerts, Mueller, Diers, et al., 2021; Holst et al., 2017; Mohamed et al., 2021). Additionally, even though Coghill (2014) and colleagues claimed the existence of six relatively independent neuropsychological functions, the authors also reported significant and meaningful associations between these neuropsychological functions. Considering the inconsistency (e.g., independence or interrelatedness of cognitive functions) and limitations (e.g., limited cognitive functions assessed; small clinical samples, lack of replication, etc.) of previous studies, the relationship between the various cognitive functions still needs to be investigated in order to learn about existence and nature of a possible cognitive profile of adult ADHD.

An analytic technique for exploring the relationships between different variables, known as network analysis, may be a suitable approach to provide new insight into the picture of intertwined cognitive functions in adult ADHD. Compared to more traditional statistical approaches, such as univariate or multivariate group comparisons and correlation matrices, network analysis considers all variables for drawing a complex network that visually depicts the interrelations between variables. A network consists of nodes representing any conceivable variables (e.g., symptoms of mental disorders) and edges connecting these nodes which represent any conceivable relationship (e.g., correlation coefficients that indicate the degree of association between symptoms) (Borsboom et al., 2013). Network analysis not only provides information about the correlations of various variables but also offers information about the relative importance of variables in the network by so-called node centrality indices, such as the node expected influence that has been most frequently used in recent studies. Nodes (or variables) with a high centrality may strongly affect other nodes in the network because of their strong connections (Bringmann et al., 2019; Opsahl, Agneessens, & Skvoretz, 2010). Network analysis has gained growing interest in the past decade for presenting complex relations in psychological science (Fonseca-Pedrero, 2017, 2018; Fried et al., 2017; McNally, 2016). A considerable number of studies applied network analysis in different psychological fields and clinical conditions, such as post-traumatic stress disorder (Cao et al., 2019; McNally, Heeren, & Robinaugh, 2017; Peters et al., 2021), depression (Bringmann et al., 2015; Scott et al., 2021), anxiety (Beard et al., 2016; Fisher et al., 2017), and personality (Costantini et al., 2015; Richetin et al., 2017). In the field of ADHD, network analysis has been considered in a number of studies on the interaction between ADHD symptoms (Goh, Martel, & Barkley, 2020; Goh et al., 2021; Martel et al., 2016; Silk et al., 2019). For example, network analysis revealed that the various symptoms of ADHD contribute in different levels of importance to the clinical picture of ADHD, and this structure of symptoms may change in the development over time (Martel et al., 2016; Silk et al., 2019). Considering the advantages of network analysis in examining the relationships as well as the unique roles of a set of variables, we propose network analysis as a suitable approach to exploring the relationship between neuropsychological functions in ADHD, which may advance our understanding of cognitive profiles of adult ADHD.

The present study is, to our knowledge, the first to apply network analysis on neuropsychological functions (performance test variables) of a large sample of clinically referred individuals at an ADHD outpatient clinic. The goal of this study is to examine the potential relationship between various aspects of cognitive functions of individuals diagnosed with or without ADHD. Specifically, the present study aims to (1) explore the potential relationships between different cognitive functions of individuals diagnosed with ADHD as well as individuals who did not meet the diagnostic criteria of ADHD and whether there is a specific network structure for the ADHD group, which may have the potential to define ADHD-specific cognitive profiles. Moreover, this study aims to (2) define the centrality of cognitive functions, which is characterized by strong connections to numerous other cognitive functions. Central cognitive functions have the potential to be the primary targets of treatment to effectively improve the functioning of adults with ADHD.

Methods

Procedure and Participants

Participants were recruited from the ADHD outpatient clinic of the Department of Psychiatry and Psychotherapy, LVR-Hospital Essen, University of Duisburg-Essen, Essen, Germany. Individuals were referred for a diagnostic evaluation of ADHD because of being suspected of suffering from ADHD by their GPs, psychiatrists, or by themselves. All individuals underwent a comprehensive diagnostic evaluation of adult ADHD based on the Diagnostic and Statistical Manual of Mental Disorders (5th Edition, American Psychiatric Association, 2013). The diagnostic criteria for all individuals followed empirical-informed guidelines for the diagnosis of first-time ADHD in adulthood (Sibley, 2021), since information on a formal diagnosis of ADHD in childhood could not be retrieved reliably for all cases. The diagnostic evaluation consisted of a semi-structured interview for the evaluation of ADHD and related psychopathology, self- and informant-report rating scales for symptoms and impairments, significant other reports, and consideration of objective indications of impairment in childhood and adulthood. Additionally, all participants completed a comprehensive neuropsychological assessment. Even though neuropsychological assessments are part of the standard routine examination for all individuals referred to the ADHD outpatient clinic of the LVR-Hospital Essen, the results are not part of the standard diagnostic decision-making. Patients who were included in this study were assessed in 2020 and 2021. All individuals were informed about the scientific use of their data in anonymized form and gave written informed consent. Processing of their data for research purposes did not affect their clinical evaluation and treatment. This study received ethical approval from the ethical review board of the medical faculty of the University of Duisburg-Essen, Germany (20-9380-BO).

A total of 332 participants agreed to take part in the present study, however, 13 of 332 participants were excluded from the data analysis. Eight participants were excluded because they were currently treated with psychostimulants at the time of the assessment. Another five participants were excluded as they were considered as not representative of this population, i.e. individuals with mental disability (i.e. mental retardation, $n = 2$; fetal alcohol syndrome, $n = 1$), a neurological condition (i.e. dementia, $n = 1$), or a condition affecting the ability to perform cognitive tests (i.e. tic disorder, $n = 1$). Finally, a total of 319 participants were included in the data analysis, of which 173 participants received a diagnosis of ADHD after a comprehensive evaluation (ADHD group, $n = 173$) and 146 participants who did not meet the diagnostic criteria of ADHD (n-ADHD group, $n = 146$). In the n-ADHD group, 92 of the 146 participants did not reach diagnostic criteria of any psychiatric disorder, whereas 54 participants showed evidence for one or more other psychiatric disorders other than ADHD, including mood disorders (n = 34), personality disorders (n = 8), addiction disorders (n = 6), anxiety disorders (n = 4), adjustment disorders (n = 2), post-traumatic stress disorders (n = 2), eating disorders (n = 2), autistic disorders (n = 1), schizophrenia (n = 1), and somatization disorder (n = 1). In the ADHD group, 149 individuals were diagnosed with the predominantly combined symptom presentation, 23 individuals with the predominantly inattentive symptom presentation, and one individual with the predominantly hyperactive/impulsive presentation. Further, 46 of the 173 patients with ADHD were additionally diagnosed with one or more comorbid psychiatric disorders (see (Katzman et al., 2017), for a discussion of comorbidity in adult ADHD), including mood disorders (n = 27), addiction disorders (n = 11), personality disorders (n = 8), anxiety disorders (n = 6), adjustment disorders (n = 5), autistic disorders (n = 2), oppositional defiant disorders (n = 1), post-traumatic stress disorders (n = 1). The observation that the distribution of psychiatric conditions other than ADHD was comparable and non-significantly different between the ADHD and the n-ADHD group (see Table 4.1), supports the notion that any potential group differences observed in test performances and network analysis are specific to ADHD. Demographic characteristics of all participants are presented in Table 4.1. No significant group differences were observed in age, t (283) = -1.780, p = 0.076, sex ratio, χ^2 (1) = 3.781, p = 0.052, and education level, χ^2(4) = 8.570, p = 0.073. As expected, patients with ADHD scored significantly higher in both current self-reported ADHD symptoms, t (299) = 3.398, p = 0.001, and retrospective self-reported ADHD symptoms for childhood, t (298) = 7.223, p < 0.001. However, no significant group difference was observed in self-reported cognitive functioning, t (313) = 1.922, p = 0.056.

Table 4.1 Demographic characteristics of all participants

Demographic and clinical characteristics	ADHD (*n*=173)	n-ADHD (*n*=146)	t/χ^2	*p* value	*Cohen's r*[6]
Age (years)	33.2 ± 9.6	35.3 ± 11.2	-1.780	0.076	0.10
Sex (male/female)	111/62	78/68	3.781	0.052	0.11
Education level (% in 1/2/3/4/5)[1]	4.0/17.9/30.1/32.9/15.1	0/16.7/31.9/29.2/22.2[5]	8.570	0.073	0.16
Current ADHD symptoms[2]	32.2 ± 9.5	28.3 ± 10.4	3.398	0.001*	0.19
Childhood ADHD symptoms[3]	40.2 ± 13.3	29.5 ± 12.2	7.223	<0.001*	0.38
Self-report cognitive functions[4]	77.8 ± 20.2	73.4 ± 20.4	1.922	0.056	0.11
Psychiatric disorders other than ADHD (% of individuals with/without)					
Mood disorders	15.6/84.4	23.3/76.7	3.020	0.082	0.10
Addiction disorders	6.4/93.6	4.1/95.9	0.795	0.373	0.05
Personality disorders	4.6/95.4	5.5/94.5	0.122	0.727	0.02
Anxiety disorders	3.5/96.5	2.7/97.3	0.138	0.710	0.02
Adjustment disorders	2.9/97.1	1.4/98.6	0.853	0.356	0.05
Autistic disorders	1.2/98.8	0.7/99.3	0.189	0.664	0.02
Oppositional defiant disorders	0.6/99.4	0/100	0.847	0.358	0.05
Post-traumatic stress disorder	0.6/99.4	1.4/98.6	0.533	0.465	0.04
Eating disorders	0/100	1.4/98.6	2.385	0.123	0.08
Schizophrenia	0/100	0.7/99.3	1.189	0.276	0.06
Somatization disorder	0/100	0.7/99.3	1.189	0.276	0.06

Note: [1] Education level (1/2/3/4/5) = no school-leaving qualification/compulsory school or secondary school completed/completed technical school or vocational training/higher school with university entrance qualification/university or college degree. [2] Current ADHD symptoms were assessed by the German version of the ADHD self-report scale. [3] Childhood ADHD symptoms were assessed by the German version of the Wender Utah rating scale-short version. [4] Self-report cognitive functions were assessed by the Questionnaire on Mental Ability of the Vienna Test System. [5] Education level were not reported in two cases. [6] Based on *Cohen's* criteria for *r*: 0.1 indicates a small effect, 0.3 indicates a medium effect, and 0.5 indicates a large effect. *Statistically significant at $p < 0.01$.

Measures

Self-report scales for ADHD symptoms and cognitive functions

The German short version of the Wender-Utah Rating Scale (WURS-K) was used to retrospectively assess ADHD symptoms in childhood (Retz-Junginger et al., 2003). A total of 25 items scored on a 5-point Likert scale were included in the WURS-K. The German version of the ADHD symptoms self-report scale (ADHD-SR) was administered to check the current ADHD symptoms (Rösler et al., 2004). A total of 18 items scored on a 4-point Likert scale were included in the ADHD-SR. The Questionnaire on Mental Ability (FLEI) of the Vienna Test System (VTS; Schuhfried, 2013) was used to measure self-reported cognitive functions. A total of 35 items assessed on a 5-point Likert scale were included. A sum score was calculated for each scale.

Neuropsychological assessment

A computerized neuropsychological test battery for the assessment of cognitive functions in adult ADHD (CFADHD; Lara Tucha et al. 2013) of the VTS was administered to all participants. The test battery was designed for clinical use to be sensitive to reveal cognitive deficits in adult ADHD and was not composed for research purposes tailored to this study. Because of this naturalistic setting, not all cognitive functions discussed in the literature review were assessed on the present patient samples.

Selective attention

The Perceptual and Attention Functions - selective attention (WAFS; Sturm, 2011) was used to measure selective attention. In this test, a total of 144 geometric stimuli (triangle, circle, and square) that may get darker or lighter or stay the same were presented to the participants. Participants were asked to react to 30 target stimuli (i.e., a circle becomes darker, a circle becomes lighter, a square becomes darker, a square becomes lighter) by pressing the response button as quickly as possible and ignoring distracting stimuli. Recorded outcome measures included reaction time (RT) in milliseconds and dispersion of reaction time (SDRT), as well as the number of omission errors. The internal consistency (Cronbach's α) of the main variables was reported to be 0.95.

Vigilance

Vigilance was assessed with the Perceptual and Attention Functions - vigilance (WAFV; Sturm, 2012). In this test, a total of 900 squares that sometimes get darker were presented to the participants. The participants had to react to 50 target stimuli (square becomes darker) by pressing the response button as fast as possible and ignoring other distracting stimuli. The mean reaction time (RT) in milliseconds and the number of omission errors were registered. The internal consistency (Cronbach's α) of the main variables was reported to be 0.96.

Working memory

Working memory was measured with the 2-back design of the NBV (N-Back Verbal; Schellig & Schuri, 2012) task, which was developed by Kirchner (Kirchner, 1958). In this task, a succession of 100 consonants was presented one by one to the participants who had to press the response button if the consonant currently displayed was identical to the last-but-one consonant and ignored it if it was not. The number of correct responses was recorded. The internal consistency (Cronbach's α) of the main variable correct responses was reported to be 0.85.

Figural fluency

The 5-point test - Langensteinbach Version was administered to measure figure fluency (Rodewald et al. 2014). In this test, participants were presented with five symmetrically arranged dots (like the number five on a dice) and were asked to create as many unique patterns as they can in 2 minutes by connecting at least two dots. The number of unique patterns created in 2 minutes was recorded. The internal consistency (Cronbach's α) of this variable was reported to be 0.86.

Interference control

Interference control was assessed with the Stroop Interference Test (Schuhfried, 2016), which was developed by Stroop (Stroop, 1935). This test form included two baseline conditions and two interference conditions. The first baseline condition was the reading-baseline condition, in which color-words (RED, GREEN, YELLOW, BLUE) printed in gray were presented to participants who were asked to press the button with the same color as the meaning of the presented color-word. The second baseline condition was the naming-baseline condition, in which banners printed with four colors (red, green, yellow, blue) were presented to participants who had to press the button with the same color as the color of banners. The first interference condition was the reading-interference condition, in which color-words printed in mismatching ink (e.g., RED printed with green ink) were presented to participants who were asked to press the button with the same color as the meaning of the color-word while ignoring the ink of it. The second interference condition was the naming-interference condition, which was different from the reading-interference condition in that participants were asked to press the button with the same color as the ink of the color-word while ignoring the meaning of it. Participants were asked to react as fast as possible throughout the test. The variables of interest were reading interference and naming interference. *Reading interference* was calculated by subtracting the time needed for the reading-baseline condition from the time needed for the reading-interference condition. *Naming interference* was calculated by subtracting the time needed for the naming-baseline condition from the time needed for the naming interference condition. The internal consistency (Cronbach's α) of the main variables was reported to be 0.97.

Processing speed and cognitive flexibility

The Trail-Making Test - Langensteinbach Version (TMT-L; Rodewald et al. 2012) was used as a measure of processing speed and cognitive flexibility. In part A, 25 numbers (1-25) were simultaneously presented on the computer screen and participants had to connect the numbers as fast as possible in ascending order. In part B there were 13 numbers (1-13) and 12 letters (A-L) and participants were asked to connect numbers and letters alternately and in ascending order as quickly as possible. The time needed for part A (in seconds) was used as a measure of processing speed and the time needed for part B was used as a measure of cognitive flexibility. The internal consistency (Cronbach's α) of part A and part B was reported to be 0.92 and 0.81, respectively.

Planning

The Tower of London - Freiburg Version (TOL-F; Christoph et al. 2011) was administered to assess planning ability. In this task, there were three rods of different heights, on which three differently colored balls (yellow, red, blue) were placed. The left-hand rod can hold three balls, the central rod can hold two balls and the right-hand rod can hold one ball. Start state and goal state, as well as the minimum number of moves needed to convert the start state into the goal state, were presented on the screen. Participants had to convert the start state into the goal state by the minimum number of moves in 60 seconds. The next item was presented automatically as soon as the current item had been solved in 60 seconds or the current item was not solved after 60 seconds. This test consisted of 28 items, comprising four three-move items and each eight four-move, five-move, and six-move items. These items were presented to participants in the order of an increasing minimum number of moves. The items at the start of the test that can be solved in three moves served as practice items. The number of the four- to six-move items solved in the minimum number of moves was recorded as the measure of planning ability. The internal consistency (Cronbach's α) of this test was reported to be 0.70.

Response inhibition

The Go/No-Go test paradigm (Kaiser et al. 2016) was used to measure response inhibition. In this test, a series of triangles (202) and circles (48) were presented one by one on the computer screen. Participants had to press the response button when triangles (Go trials, 80.8% of all trials) were presented and no response was required to circles (No-Go trials, 19.2% of all trials). The number of commission errors was registered. The internal consistency (Cronbach's α) of this test was reported to be 0.83.

Task switching

Task switching was measured with the SWITCH (Gmehlin et al. 2017). In this test, a series of bivalent stimuli which can be categorized based on form (triangle/circle) and brightness (gray/black) were presented. Participants were asked to react interchangeably based on these two dimensions (triangle/circle or gray/black). After each two items, the dimensions to which participants had to react changed. The items that require a reaction based on the same dimension as the preceding item were defined as repeated items, whereas the items that require a reaction based on the different dimension than the preceding item were defined as switch items. The variable of interest was *task switching accuracy*, which was the difference between the percentage of correct responses for switching and repeated tasks. The internal consistency (greatest lower bound) of this variable was satisfactory and reported to be 0.81.

Statistical analysis

Descriptive statistics and inferential group comparisons were computed using IBM SPSS (Version 25.0 for Windows). Network analyses of neuropsychological functions were performed with RStudio (RStudio Team, 2021).

Descriptive statistics and group comparisons

The Median and interquartile range (IQR) of each test variable, as well as the percentage of individuals showing impairment in each of the neuropsychological functions, are presented in descriptive statistics. The interpretation of test data was based on norm scores provided by the test publisher. Impairment was defined if a test variable indicated a score equal to or below the 16^{th} percentile (i.e., one standard deviation below the mean) of the respective normative group (Schuhfried, 2013). Furthermore, because our data are not normally distributed, test performances of groups were compared using nonparametric statistics (i.e. Mann-Whitney U tests). To control for alpha error growth in multiple testing, a stringent significance level of $p < .01$ was applied. Finally, the magnitude of group differences was indicated by the effect size *Cohen's r,* with $r = 0.1$ indicating a small effect, $r = 0.3$ indicating a medium effect, and $r = 0.5$ indicating a large effect (Cohen, 1988).

Network estimation

The networks of neuropsychological functions were estimated for the ADHD group and the n-ADHD group, using the R packages *bootnet* and *qgraph* (Epskamp, Borsboom, & Fried, 2018; Epskamp et al., 2012). In these networks, 14 variables were depicted as nodes and the partial correlation coefficients between neuropsychological functions were depicted as edges. Partial correlation coefficients represent the correlation between two variables after controlling for all other variables in the network (Borsboom et al., 2013). To avoid spurious connections and make networks more interpretable, the graphical lasso algorithm, which is a variant of the prominent regularization algorithm Least Absolute Shrinkage and Selection Operator (LASSO) was applied to estimate the network (Epskamp & Fried, 2018; Tibshirani, 1996). This graphical lasso algorithm controls the degree of regularization by a tuning parameter (λ), which can be determined using the Extended Bayesian Information Criterion (EBIC) (Chen & Chen, 2008; Friedman et al., 2008). The visualization of these networks was based on the Fruchterman-Reingold algorithm (Fruchterman & Reingold, 1991). In the graph that is plotted based on the Fruchterman-Reingold algorithm, nodes with stronger connections are placed more proximal to each other, and connections between nodes with higher absolute coefficients are represented with thicker and more saturated colored edges. Additionally, identical layouts of nodes were produced for two groups using the *averageLayout* function of *qgraph* package to enable visual comparison between groups (Epskamp et al., 2012). As our data were not normally distributed, a rank transformation (Spearman correlations as input) (Isvoranu & Epskamp, 2021) was performed before estimating network structures.

Node centrality estimation

The relative importance of variables in the network was examined with node expected influence, which is a node centrality index representing the sum of connections for one node. Compared to node strength, which is the previously most used node centrality index representing the sum of the absolute value of connections for one node, node expected influence considers both positive and negative connections (Opsahl et al., 2010; Robinaugh, Millner, & McNally, 2016). The *centrality*, *centralityTable,* and *centralityPlot* function of *qgraph* package was used to compute and plot the expected influence (Epskamp et al., 2012).

Accuracy and Stability estimation

The accuracy of edge weights and the stability of the order of node centrality were examined. The edge weight accuracy was estimated by bootstrapping the 95% confidence intervals (CIs) of the edge weights, with smaller CIs indicating higher accuracy of the order of most edges in the network. Node centrality stability was estimated using the correlation stability coefficient (CS coefficient). Based on the simulation design of Epskamp et al. (2018), CS coefficients > 0.25 indicate moderate stability and > 0.5 indicate strong stability. The R package *bootnet* was used to perform these analyses.

Network comparison

The global connectivity strength of the network, which represents the sum of the weights of all edges within the network, was compared between the ADHD group and the n-ADHD group. The Network Comparison Test (NCT), which is a statistical testing procedure for network comparison, was used to perform these comparisons (van Borkulo et al., 2021). NCT compares the global connectivity strength of different group networks using the permutation test that repeatedly estimates the networks for randomly regrouped individuals and then calculates the accompanying test statistic. The R package *NetworkComparisonTest* was used for these comparisons (van Borkulo, 2018).

Additional network analyses

First, additional network analysis was performed on the individuals with the combined symptom presentation only to examine the potential influence of different symptom presentations of ADHD. Second, to address the possibility that different weights for each test (e.g., more variables were extracted from tests for selective attention and vigilance compared to other tests) may bias our findings, additional network analysis was performed based on averaged Z-scores per neuropsychological function. Finally, considering the nearly significant sex difference between the ADHD and n-ADHD group (p = .052), additional network analyses were carried out to examine the potential influence of sex.

Results

Descriptive statistics and group comparisons

Descriptive statistics and group comparisons of neuropsychological test performance for the ADHD and n-ADHD groups are presented in Table 4.2. Compared to test norms, the number of individuals with an impairment in each test variable ranged from 9.9% to 57.9% in the ADHD group and from 10.4% to 42.4% in the n-ADHD group. Per test variable, the largest impairment rates were found in vigilance - omission errors (57.9% and 42.4% in the ADHD and n-ADHD group, respectively), response inhibition - commission errors (45.9% and 40.3%), and selective attention - SDRT (40.1% and 39.6%). The fact that impairment rates were at or below 16% of several test variables indicates that individuals with ADHD did not show decreased performance compared to normative data in a range of aspects of cognitive functioning. Data analyses indicate that the differences in impairment rates between two groups are small, and only the difference in the number of omissions of the vigilance test turned statistically significant (p = 0.003), as individuals in the ADHD group made significantly more omissions errors than the n-ADHD group as shown in a small effect of *Cohen's r* = 0.16. Per neuropsychological function, the largest impairment rates were found in vigilance (58.5% and 44.4% in the ADHD and n-ADHD group, respectively), selective attention (55.2% and 55.5%), response inhibition (45.9% and 40.3%), and interference control (40.7% and 39.6%). Impairment in a given function is defined if impairment was observed in at least one test variable of this function.

Table 4.2. Neuropsychological test performance of the ADHD and n-ADHD group

Neuropsychological variables	ADHD (n = 173)			n-ADHD (n = 146)			Group comparison		
	Median	IQR [a]	% impaired [b]	Median	IQR [a]	% impaired [b]	*Z*	*P*	*Cohen's r* [c]
Selective attention [d] - RT	347.00	87.25	16.37	355.00	95.75	13.99	-0.419	0.675	0.02
Selective attention [d] - SDRT	1.26	0.11	40.12	1.22	0.12	39.58	-0.065	0.948	0.003
Selective attention [d] - Omissions	0	1.00	32.56	0	1.00	28.67	-1.049	0.294	0.05
Vigilance [e] - RT	446.00	123.00	20.47	443.00	109.50	14.69	-0.212	0.832	0.01
Vigilance [e] - Omissions	2.00	5.00	57.89	1.00	3.00	42.36	-2.953	0.003*	0.16
Working memory [f]	12.00	4.00	17.44	12.00	4.00	14.58	-0.766	0.444	0.04
Figural fluency [g]	28.00	16.00	13.95	24.00	14.50	15.97	-2.226	0.026	0.13
Interference control [h] - reading	0.17	0.15	31.40	0.17	0.15	29.86	-0.883	0.377	0.05
Interference control [h] - naming	0.11	0.14	17.44	0.11	0.11	17.36	-0.773	0.439	0.04
Cognitive flexibility [i]	28.15	12.68	12.28	29.00	11.90	11.80	-0.666	0.505	0.04
Planning [j]	14.00	4.25	10.59	14.00	5.00	11.27	-0.915	0.360	0.05
Response inhibition [k]	14.00	11.25	45.93	13.00	11.00	40.28	-1.572	0.116	0.09
Task switching [l]	3.00	5.25	20.35	3.00	6.00	18.06	-0.032	0.975	0.002
Processing speed [m]	18.40	6.60	9.88	18.80	5.55	10.42	-1.474	0.141	0.08

Note: [a] IQR = Interquartile Range; [b] Impairment defined if percentile rank ≤ 16; [c] Based on *Cohen's* criteria for r: 0.1 indicates a small effect, 0.3 indicates a medium effect, and 0.5 indicates a large effect; [d] Perceptual and Attention Functions - selective attention (WAFS); [e] Perceptual and Attention Functions - vigilance (WAFV); [f] 2-back design of the NBV (verbal); [g] 5-point test; [h] Stroop Interference Test; [i] Trail-Making Test, part B (TMT-B); [j] Tower of London - Freiburg Version (TOL-F); [k] Go/No-Go; [l] SWITCH; [m] Trail-Making Test, part A (TMT-A); [*] Statistically significant at $p < .01$.

Network estimation

The visualized networks of the ADHD and n-ADHD groups are presented in Figure 4.1 and Figure 4.2, respectively. For the ADHD group, a density network is depicted that connects almost all variables in the network. The n-ADHD network has few connections and most of the connections are weak. But the strongest connections appear to be consistent between these two networks, including the connections between two attention tests, i.e. selective attention test and vigilance test (2, 4, and 5), as well as the connection between two variables stemming from the Trail Making Test (10 and 14). Furthermore, connections between all variables of attention (selective attention and vigilance, see 1 to 5) and connections between figural fluency, cognitive flexibility, and processing speed (7, 10, and 14) were also observed in both the ADHD and n-

ADHD networks. Additionally, the connection between selective attention and working memory (3 and 6) as well as the connection between vigilance and response inhibition (4 and 12) was observed in the ADHD network. Compared to other variables, task switching (13) is relatively isolated in the ADHD network.

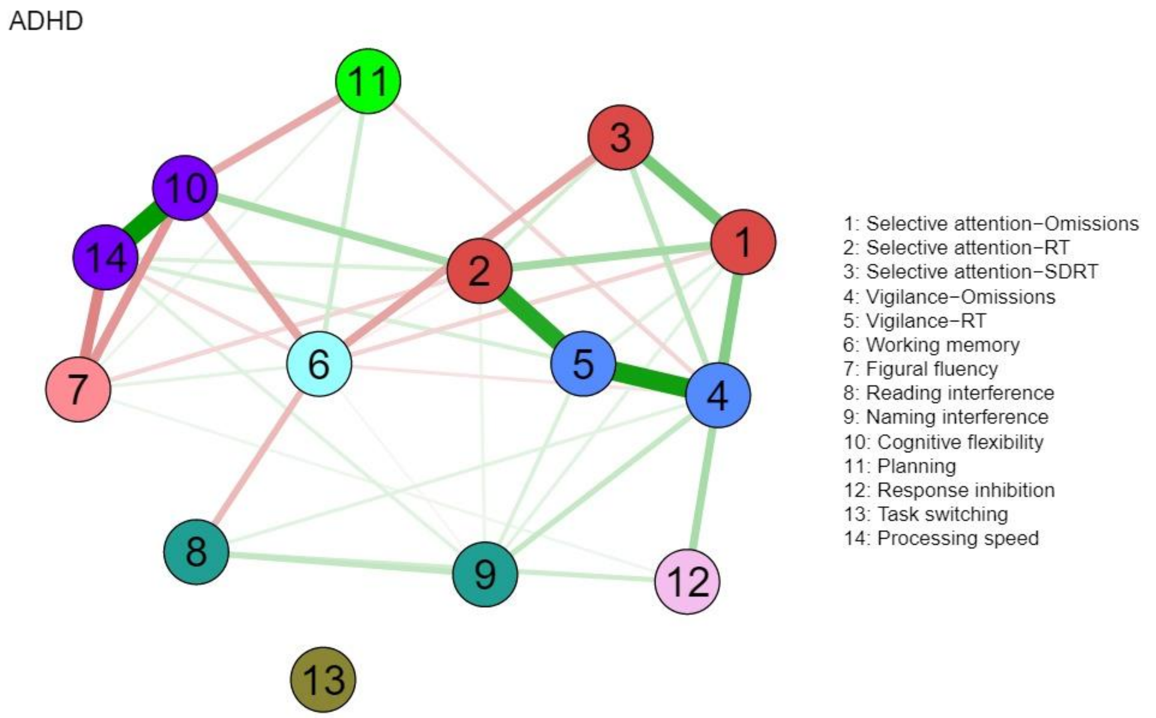

Figure 4.1. Network of neuropsychological functions for the ADHD group (N = 173).

Note. Nodes represent neuropsychological test variables. Neuropsychological test variables stemming from the same test are presented in the same color. Edges connecting nodes represent the regularized partial Spearman correlations. Higher absolute correlations are represented with thicker and more saturated colored edges. Green edges indicate positive correlations, red edges indicate negative correlations.

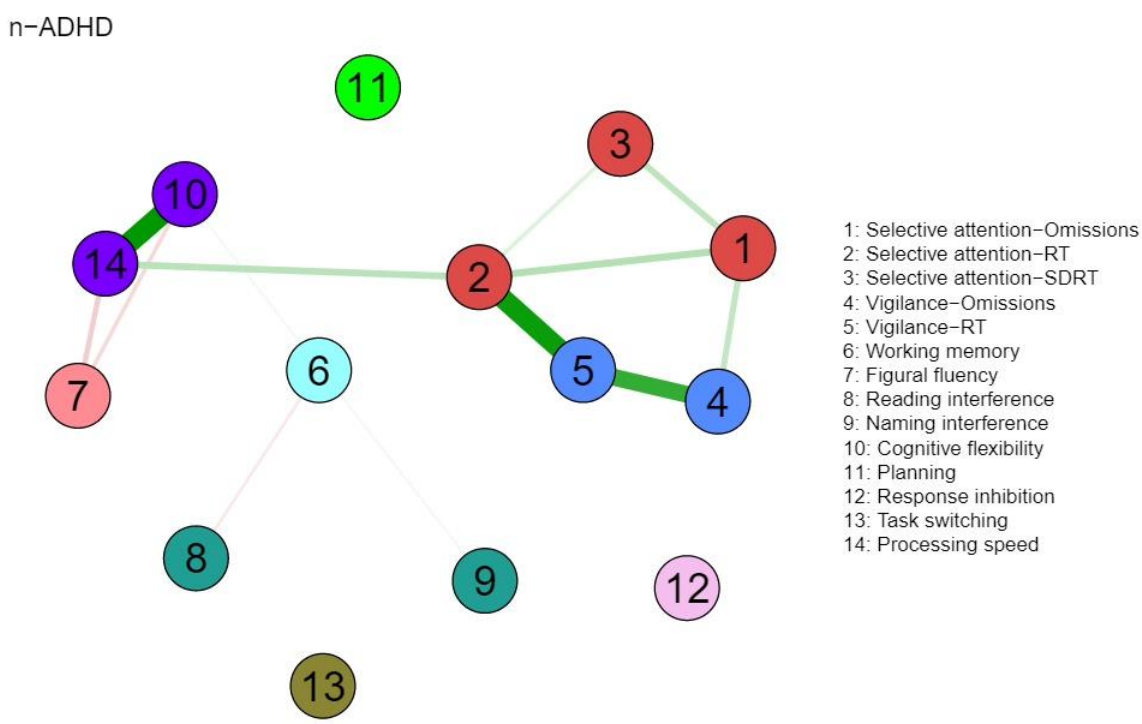

Figure 4.2. Network of neuropsychological functions for the n-ADHD group (N = 146).

Note. Nodes represent neuropsychological test variables. Neuropsychological test variables stemming from the same test are presented in the same color. Edges connecting nodes represent the regularized partial Spearman correlations. Higher absolute correlations are represented with thicker and more saturated colored edges. Green edges indicate positive correlation, red edges indicate negative correlations.

Node centrality estimation

Node centrality estimations are presented in Figure 4.3. In both groups, nodes with high expected influence are mainly attention-related variables, especially the reaction time of these tests. In the ADHD group, the nodes depicting the RT of selective attention, RT of vigilance, and omissions of vigilance task have the highest expected influence. In the n-ADHD group, the RT of selective attention and RT of vigilance have the highest expected influence.

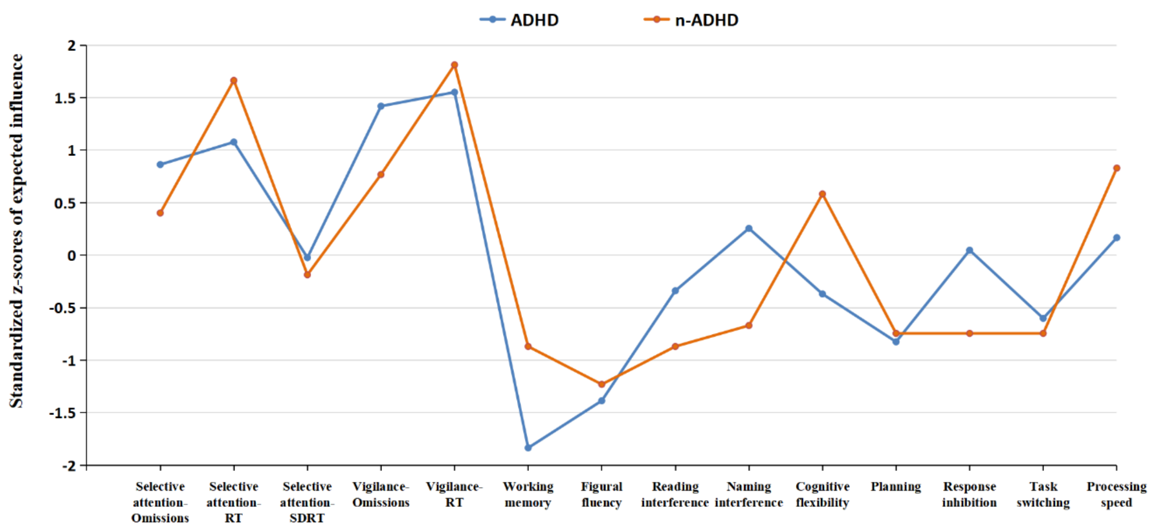

Figure 4.3. Node expected influence for the ADHD and n-ADHD group.

Note. Higher standardized z-scores indicate higher expected influence, and nodes with higher expected impact have closer and stronger relationships with other neuropsychological test variables in the network.

Stability estimation

The edge weight accuracy estimation revealed moderate CIs and indicated that the orders of edge weights were accurately estimated in both the ADHD network and the n-ADHD network (see Figure S4.1 and Figure S4.2 in Supplemental Material). The node centrality estimation revealed that the CS coefficients were 0.36 (ADHD) and 0.44 (n-ADHD), indicating that the orders of node centrality were stable.

Network comparison

The visual comparison suggests denser and stronger connections in the ADHD network than in the n-ADHD network. Further NCT analysis indicates that the global connectivity strength of the ADHD network is significantly stronger than that of the n-ADHD network (4.09 vs. 1.54, $s = 2.55$, $p = 0.026$).

Additional network analyses

First, no meaningful differences were observed between network analysis based on the combined symptom presentation only and the analysis of the entire group of patients with ADHD. Second, the results of network analysis based on averaged Z-scores per neuropsychological function were comparable to our initial analysis. Finally, no significant differences were observed by sex. Please find detailed results in Supplemental Material.

Discussion

The present study analyzed neuropsychological performance data of a large sample of individuals at clinical evaluation of adult ADHD by using both traditional descriptive and inferential statistics as well as network analyses to explore the relationship between neuropsychological functions. Traditional statistics showed neuropsychological impairments in a large proportion of both individuals in the ADHD and n-ADHD groups as compared to test norms, including deficits in vigilance, selective attention, inhibition, and reading interference control. The marked impairments of neuropsychological functions observed in both groups support the earlier argument that neuropsychological assessment plays an important role in acquiring a comprehensive understanding of an individual’s cognitive strengths and weaknesses (Lange et al., 2014; Mapou, 2019; Seidman, 2006). Further, the present data show that neuropsychological functions did not differ significantly between the groups in most of the measures, except for decreased vigilance performance (i.e. more omission errors) in the ADHD group. Pronounced vigilance impairments in the ADHD group underline the prominent role of vigilance and sustained attention tests in the clinical evaluation of ADHD, as it was demonstrated in a large body of empirical research on individuals with ADHD of various age groups (Bijlenga et al., 2019; Hall et al., 2016; Marchetta, Hurks, De Sonneville, et al., 2008; Slobodin, Yahav, & Berger, 2020; Tucha et al., 2017), and advocated in an international consensus report (Fuermaier et al., 2018). Further, the present neuropsychological performance data are also in line with prior research on an independent data set from the same referral context (Guo et al., 2021), stressing that cognitive deficits are not specific to individuals diagnosed with ADHD but occur commonly in individuals of this referral context. These results also corroborate earlier studies indicating that the assessment using neuropsychological tests may have limited value in the discrimination of individuals with ADHD from individuals with other psychiatric conditions (Barkley, 2019; Holst & Thorell, 2017; Pettersson et al., 2018).

A visual inspection of the networks displays an interrelated pattern of neuropsychological test performance in the ADHD group, with the strengths of the connections varying from weak to strong. Few connections were observed in the n-ADHD group, with significantly weaker global connectivity strength compared to the ADHD group. This finding gives an indication that the extensive connections between various neuropsychological functions are not uniform in all individuals in the clinical evaluation of adult ADHD. Most of the neuropsychological functions were connected in the ADHD group but were relatively isolated in the n-ADHD group. The finding that a denser and stronger network of neuropsychological functions was observed in the ADHD group compared to the n-ADHD group may provide further information for the cognitive profiles of adults with ADHD. For example, dense connections observed in the ADHD network indicate close relationships between cognitive functions, forming a holistic cognitive function system in individuals with ADHD (Karyakina & Shmukler, 2021). Further, it could be speculated that the connected cognitive functions observed in the ADHD group may reflect a functional compensatory mechanism as was suggested in functional imaging studies (Abramov et al., 2019; Hale et al., 2014). Compared to individuals who do not meet the diagnostic criteria of ADHD, individuals diagnosed with ADHD may compensate with the involvement of additional cortical areas in order to increase specific cognitive task performance (Fassbender & Schweitzer, 2006). This compensatory mechanism may lead to an inter-related involvement of cognitive functions and may result in close connections of cognitive functions in network analysis. Future studies using functional magnetic resonance imaging would be suited to further explore the relationship between neuropsychological functions and compensatory mechanisms of cortical areas in ADHD. Moreover, combined with previous findings that denser and stronger networks of cognitive functions were also observed in other psychiatric disorders (e.g., schizophrenia, major depression) when compared to healthy controls (Karyakina et al., 2021; Liang et al., 2018), future studies need to explore how the network of cognitive functions of ADHD relates to the networks of a community sample or specific psychiatric disorders other than ADHD.

Even though fewer and weaker connections were observed in the n-ADHD compared to the ADHD network, there are some consistent connections that were observed in both the ADHD and n-ADHD networks, including the connections between measures of selective attention and vigilance (nodes 1 – 5) and connections between measures of processing speed, flexibility, and fluency (nodes 7, 10, 14). The connections between selective attention and vigilance add evidence to the argument that different attention components are related in terms of behavioral performance as well as its neural basis (Angelelli et al., 2020; McDowd, 2007; Stuss & Alexander, 2007; Wilding, 2005). The correlations between processing speed, flexibility, and fluency add evidence to the notion that basic functions (e.g., processing speed) are substantially related to more complex cognitive functions (i.e., fluency and flexibility) and that training of processing speed may also improve performance on executive functions (Butzbach et al., 2019; Guo, Fuermaier, Koerts, Mueller, Diers, et al., 2021; Lin et al., 2016; Mohamed et al., 2021; Sheline et al., 2006; Takeuchi & Kawashima, 2012). Additionally, the correlations between variables of the same test (e.g. TMT, WAFS, WAFV), and strong correlations between related functions (e.g. between selective attention and vigilance), may indicate some redundancy in lengthy test batteries and the possibility to tailor assessment batteries more efficiently to clinical and individual needs. We conclude that the possibility of shortening neuropsychological assessment batteries may be attractive to minimizing or avoiding fatigue (Feltmate, Hurst, & Klein, 2020; Luna et al., 2018; Tucha et al., 2017), increase compliance by examinees, and save valuable clinical resources in unnecessary administration, scoring, and interpretation of test data. Further, shorter test batteries may have the advantages that existing norm data are more valid if applied to individual performance data that may not underly pronounced transfer effects in extensive test batteries.

Other than these consistent connections, most variables in the ADHD network were weakly or moderately correlated with each other, such as working memory, planning, response inhibition, and interference control. The position of these functions in the network is partly consistent with earlier findings that children with ADHD show deficits in several relatively independent neuropsychological functions, including working memory, inhibition, and response variability (Coghill et al., 2014), that have also been assessed in the present study. However, some dependence between neuropsychological functions in weak to moderate size was shown earlier, and is underlined by the fact that individuals with ADHD mostly show deficits in more than one of the functions assessed, e.g. 46% of children with ADHD show impairments in at least two of six functions assessed by Coghill (2014), and 81% of adults with ADHD show deficits in at least two of the ten functions assessed by Guo and colleagues (Guo et al., 2021). In a study on self-reported neuropsychological functioning, 80% of adults with ADHD reported deficits in at least two of eight aspects of functioning (Fuermaier et al., 2014). The differences in occurrence rates of neuropsychological impairments can be explained by various factors, as this may depend on the functions assessed in the respective test battery, the test characteristics, and the referral context. Moreover, the observed association between working memory and the variability of reaction time in the ADHD network extends the argument that slowed processing speed may be a cause for working memory deficits in ADHD (Karalunas & Huang-Pollock, 2013; Weigard & Huang-Pollock, 2017), by suggesting that it may be the variability of reaction time that causes impairments in working memory, not the slowed down responses. It may also serve as an explanation for why an earlier meta-analytic review revealed that slow reaction times in ADHD may disappear after controlling for reaction time variability (Kofler et al., 2013). For clinical practice, we may conclude that task switching should be assessed separately in a comprehensive neuropsychological investigation because of the weak and few connections of this function with other functions that are commonly assessed.

Moreover, the highest expected influence of attention-related variables (e.g., reaction time of selective attention, reaction time of vigilance, and omissions of vigilance) in both the ADHD and the n-ADHD network stresses the central role of attention for a broad range of other neuropsychological functions. High expected influence of attention observed in the present study provides new empirical evidence to the argument that basic cognitive functions are significantly associated with and contribute to the higher-order cognitive functions as suggested in numerous studies (Adams et al., 2011; Arciniegas, Held, & Wagner, 2002; Butzbach et al., 2019; Felmingham, Baguley, & Green, 2004; Guo, Fuermaier, Koerts, Mueller, Diers, et al., 2021; Mohamed et al., 2021). On the basis of the central role of attention in relation to other cognitive functions, clinicians may be advised to consider attention-related tests as the first choice when composing an assessment battery for the clinical evaluation of adult ADHD. Also, it could be speculated that improving attention abilities in the treatment of ADHD may secondarily also improve other cognitive functions that build upon attention. For example, methylphenidate (MPH) has been shown to be effective in improving attention abilities in patients with ADHD (Hadar et al., 2021; Pievsky & McGrath, 2018; Spencer et al., 2009; Tamminga et al., 2016; Tucha et al., 2006), and was also shown to be effective in improving the ability of higher-order cognitive functions, such as planning, memory, fluency, inhibition, and interference control (Abikoff et al., 2009; Fuermaier et al., 2017; Kobel et al., 2009; Rubio Morell & Hernández Expósito, 2019; Tamminga et al., 2016; Yang et al., 2012; Yildiz et al., 2011). Even though these studies do not provide evidence to the treatment mechanisms, the network structure of the present study gives support to the notion that MPH may improve primarily attention functions which may positively affect a broad range of other cognitive functions secondarily. In this vein, other types of treatment for ADHD may show a similar mechanism in improving neuropsychological functions, such as cognitive training or biofeedback (Cortese et al., 2015; Monastra, 2005; Sonuga-Barke et al., 2014; Stern et al., 2016).

Further, in order to address the possibility that different weights for each test (e.g., more variables were extracted from tests for selective attention and vigilance compared to other tests) may bias the findings of centrality estimation, additional network analysis was performed based on averaged Z-scores per neuropsychological function. Results were comparable to our initial analysis, such as the strong connection between selective attention and vigilance, the strong connection between processing speed/flexibility and fluency, and the highest expected influence of selective attention and vigilance. These results support the reliability of our initial analysis based on multiple test scores per function (see Figure S4.3-S4.5 of the Supplemental Material). Finally, considering the nearly significant sex difference between the ADHD and n-

ADHD group (p = .052), additional network analyses were carried out to examine the potential influence of sex (see Figure S4.6-S4.8 of the Supplemental Material). These additional analyses revealed no significant differences in global connectivity strength by sex, neither in the ADHD nor the n-ADHD group. Selective attention and vigilance still have the highest expected influence in the male and female networks within both the ADHD and n-ADHD groups. However, we noted that variables of selective attention (i.e., omissions and SDRT) have a seemingly higher expected influence in the male n-ADHD network compared to the female n-ADHD network, which needs replication on larger samples in future studies.

Limitations and future directions

Several limitations of the present study should be taken into account. First, effect sizes of network analyses cannot be calculated based on current statistical methodology. The magnitude of the findings, e.g. to compare global connectivity or expected influence, would benefit the interpretation of the findings and their clinical implications. Second, it must be stressed that networks do not indicate causal relationships between functions. Even though 'expected influence' may appear like directional paths, no such causal relationships can be inferred from networks (Bringmann et al., 2019; Dablander & Hinne, 2019). Third, the majority of individuals in the ADHD group (149 of 173) were diagnosed with the predominantly combined symptom presentation, leading to an unbalanced sample and potentially biased network estimation because of the potential different cognitive profiles across different subtypes of ADHD (LeRoy, Jacova, & Young, 2019). Additional network analysis was performed on the individuals with the combined symptom presentation only (for details see Figures S4.9 and S4.10 of the Supplemental Material), and revealed no meaningful differences compared to the analysis of the entire group of patients with ADHD. Even though the present study gives no indication for bias by ADHD subtype, future studies are needed on large samples of ADHD with sufficiently large numbers of the various ADHD symptom presentations in order to address this issue properly. Fourth, potential cognitive subtypes proposed in previous research (e.g., Roberts, Martel, & Nigg, 2017) may also affect the representativeness of our sample, which may require more thorough consideration on large samples in future studies. Fifth, future studies using network analysis should consider including a more comprehensive battery of neuropsychological functions that may be relevant in the assessment of ADHD. For example, timing, delay aversion, decision-making, and more memory functions (e.g., retrospective memory, prospective memory) have been included in many previous studies but were not included in this study because all assessments in the present study were from a routine battery as part of the clinical protocol.

Conclusions

This study is the first using network analysis to investigate the relationship between various neuropsychological functions in a large sample of clinically referred individuals at an ADHD outpatient clinic. Further strengths of this study are that it uses a naturalistic design, using data derived from the routine clinical practice of an ADHD clinic, as well as a clinical comparison group with similar characteristics in key clinical features which increases ecological validity. Network estimations and comparison revealed a denser and significantly stronger network of neuropsychological functions in the ADHD group compared to the n-ADHD group. The stronger and more interrelated network of neuropsychological functions observed in individuals with ADHD may be a starting point to identifying intertwined neuropsychological characteristics that are typical for ADHD. Further, among the broad range of neuropsychological functions assessed, attention performance displayed the highest expected influence on other neuropsychological functions in both the ADHD and the n-ADHD network, which provides clinically relevant implications for the clinical assessment, treatment planning, and treatment evaluation of individuals with cognitive impairment.

Supplemental Material

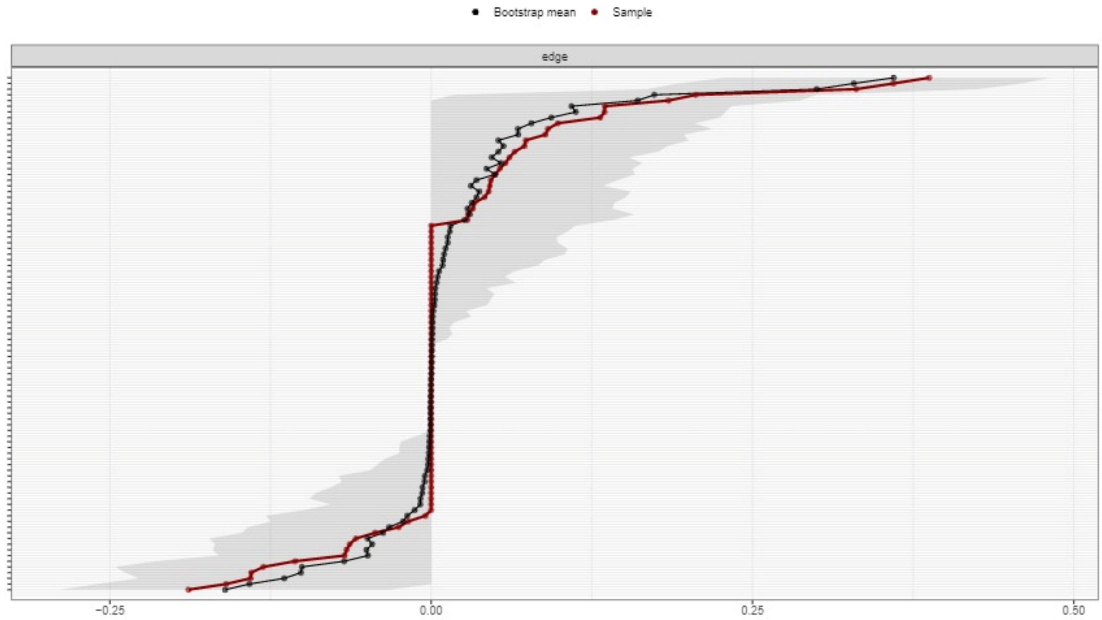

Figure S4.1. Bootstrapped CIs of estimated edge-weights for the estimated network of the ADHD group. *Note*. Each horizontal line represents one edge of the network, ordered from the edge with the highest edge-weight to the edge with the lowest edge-weight. The red line indicates the sample values of edge weights and the black line indicates the Bootstrap mean values of edge weights. The gray area indicates the bootstrapped CIs. The y-axis labels have been removed to avoid cluttering.

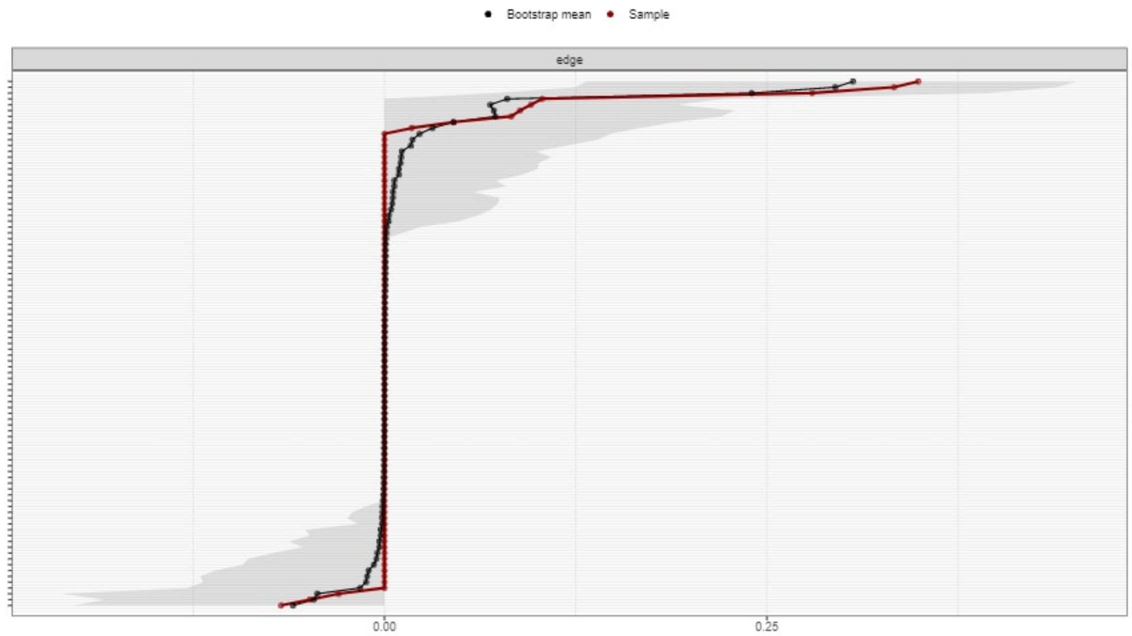

Figure S4.2. Bootstrapped CIs of estimated edge-weights for the estimated network of the n-ADHD group. *Note*. The gray area indicates the bootstrapped CIs. Each horizontal line represents one edge of the network, ordered from the edge with the highest edge-weight to the edge with the lowest edge-weight. The y-axis labels have been removed to avoid cluttering.

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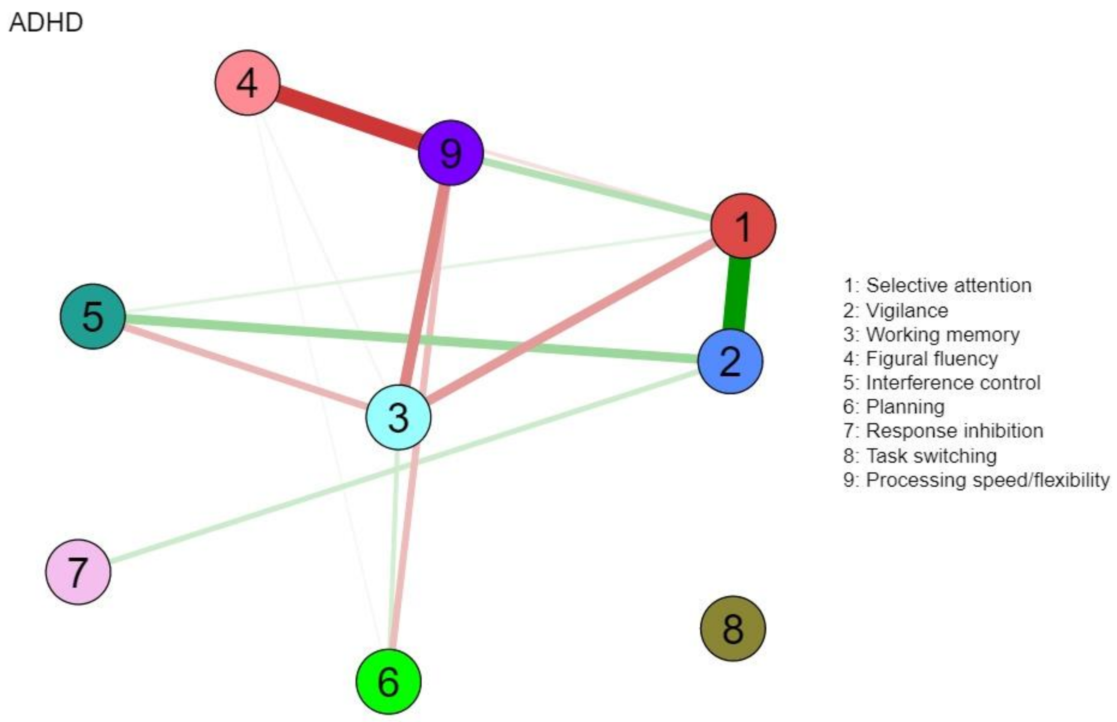

Figure S4.3. Network of neuropsychological functions for the ADHD group based on (averaged) Z-scores (N = 173).

Note. Nodes represent neuropsychological functions. Each neuropsychological function is presented in a different color. Edges connecting nodes represent the regularized partial Spearman correlations. Higher absolute correlations are represented with thicker and more saturated colored edges. Green edges indicate positive correlations, red edges indicate negative correlations.

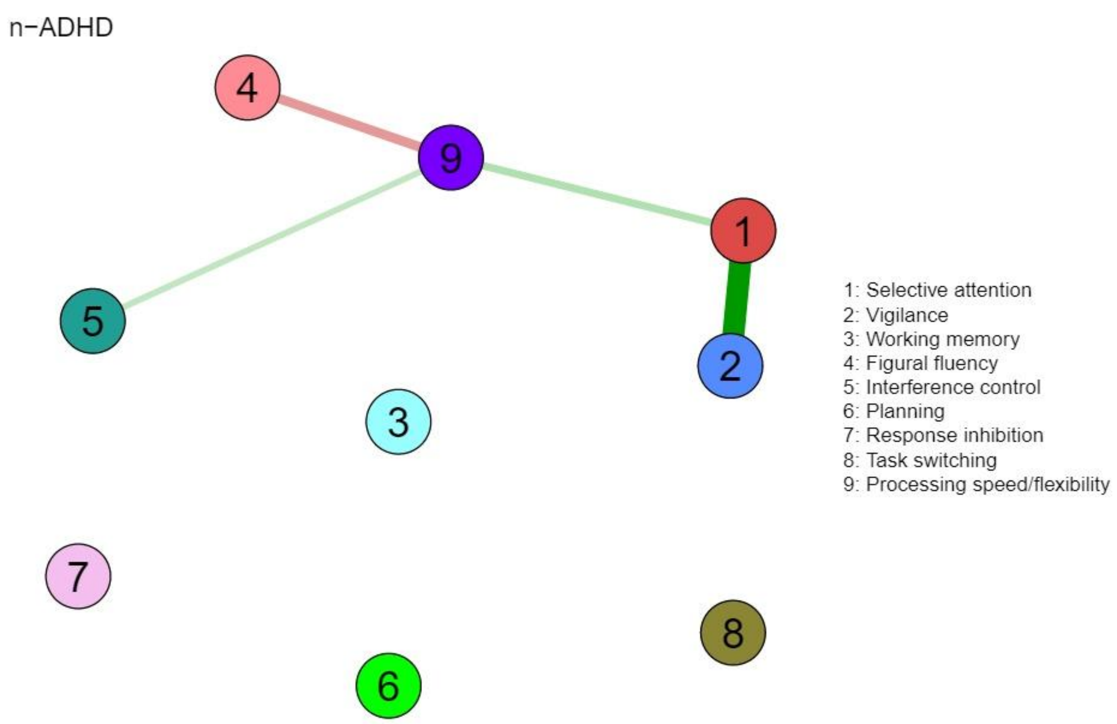

Figure S4.4. Network of neuropsychological functions for the n-ADHD group based on (averaged) Z-scores (N = 146).

Note. Nodes represent neuropsychological functions. Each neuropsychological function is presented in a different color. Edges connecting nodes represent the regularized partial Spearman correlations. Higher absolute correlations are represented with thicker and more saturated colored edges. Green edges indicate positive correlations, red edges indicate negative correlations.

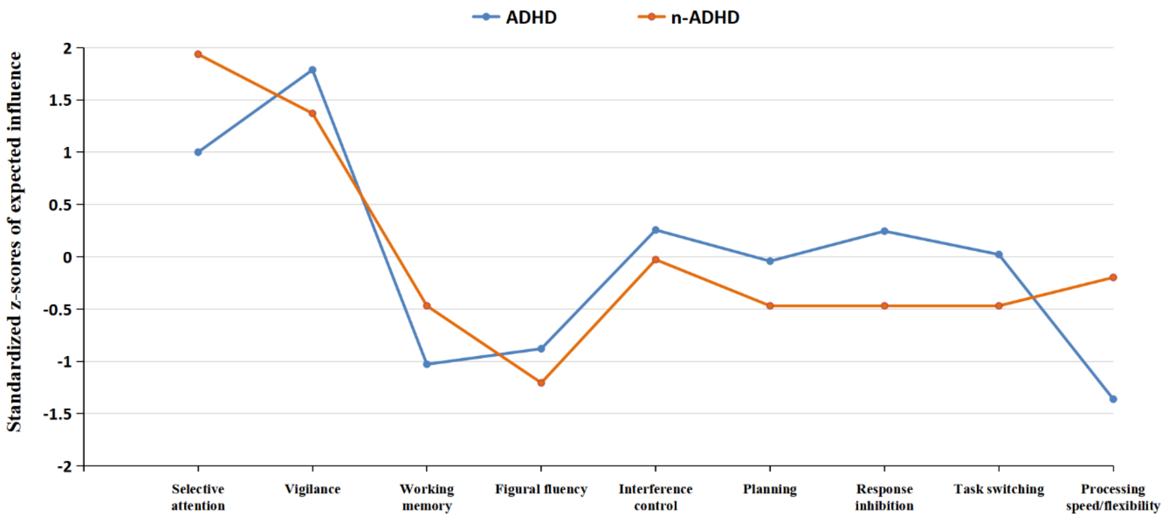

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Figure S4.5. Node expected influence for the ADHD and n-ADHD networks based on (averaged) Z-scores. *Note*. Higher standardized Z-scores indicate higher expected influence, and nodes with higher expected impact have closer and stronger relationships with other neuropsychological functions in the network.

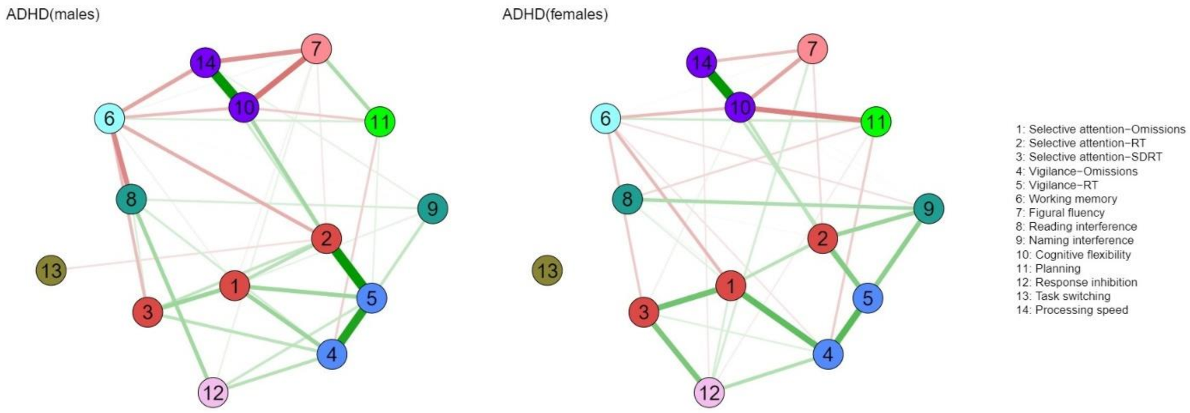

Figure S4.6. Networks of neuropsychological functions of individuals with ADHD, separately for males and females.

Note. Nodes represent neuropsychological test variables. Neuropsychological test variables stemming from the same test are presented in the same color. Edges connecting nodes represent the regularized partial Spearman correlations. Higher absolute correlations are represented with thicker and more saturated colored edges. Green edges indicate positive correlations, red edges indicate negative correlations.

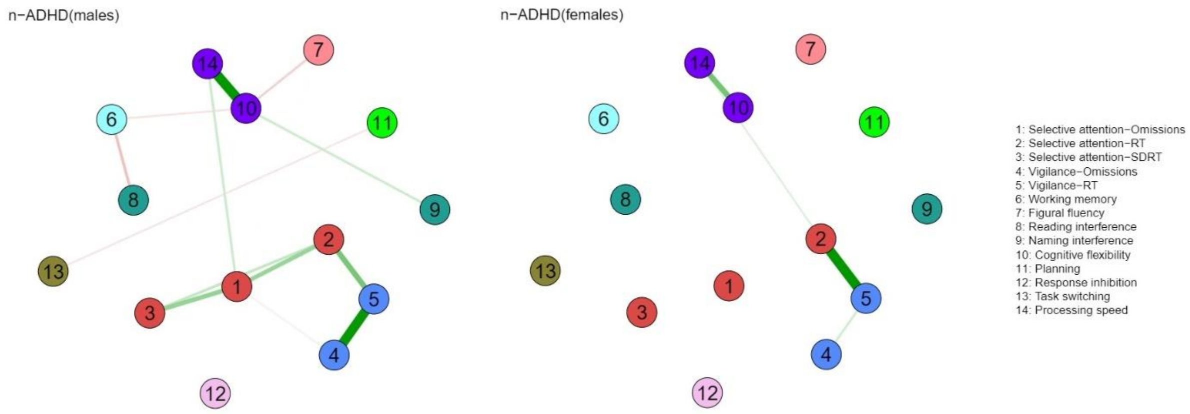

Figure S4.7. Networks of neuropsychological functions of individuals not diagnosed with ADHD, separately for males and females.

Note. Nodes represent neuropsychological test variables. Neuropsychological test variables stemming from the same test are presented in the same color. Edges connecting nodes represent the regularized partial Spearman correlations. Higher absolute correlations are represented with thicker and more saturated colored edges. Green edges indicate positive correlations, red edges indicate negative correlations.

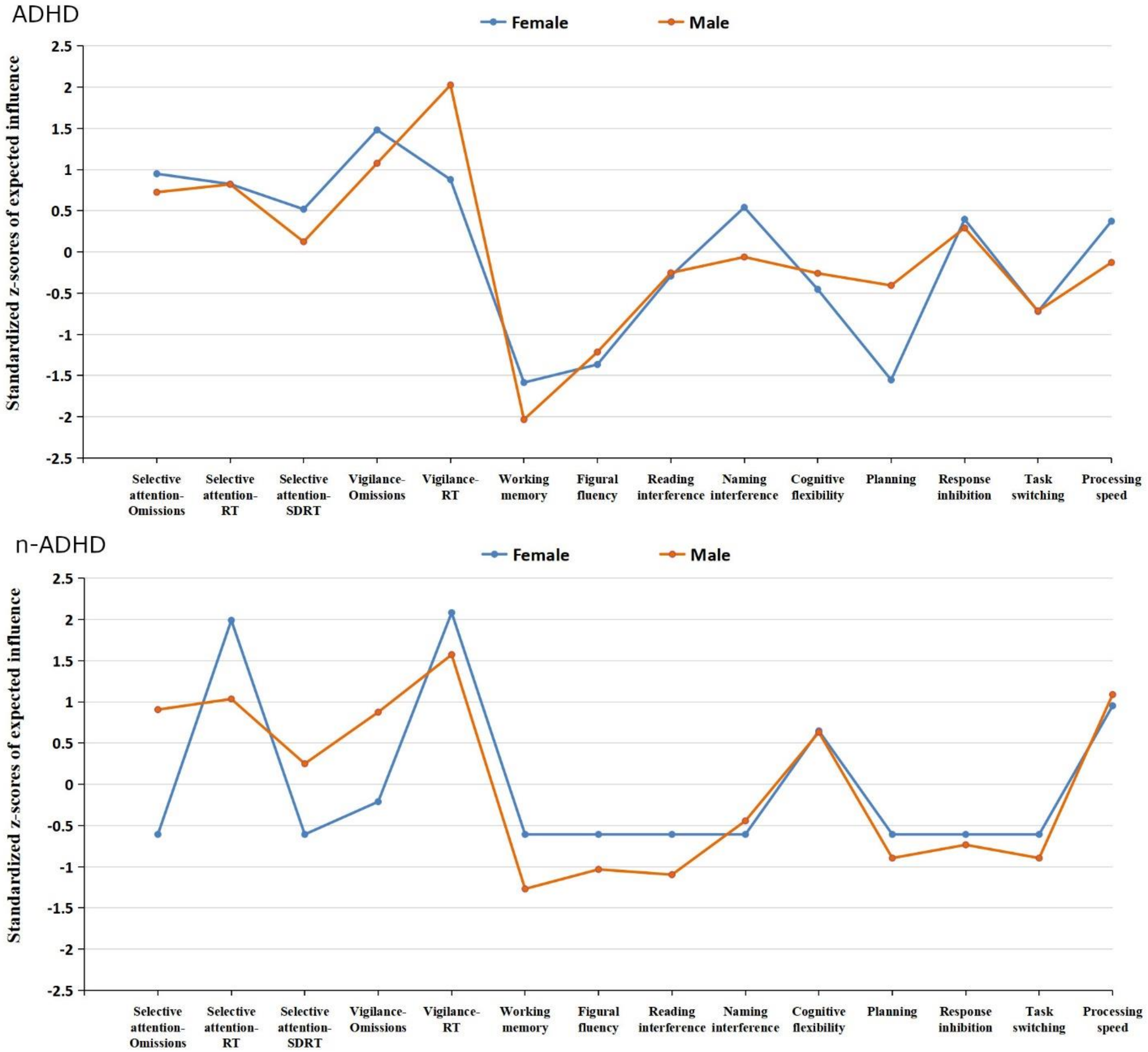

Figure S4.8. Node expected influence for the male and female networks in two groups.

Note. Higher standardized z-scores indicate higher expected influence, and nodes with higher expected impact have closer and stronger relationships with other neuropsychological test variables in the network.

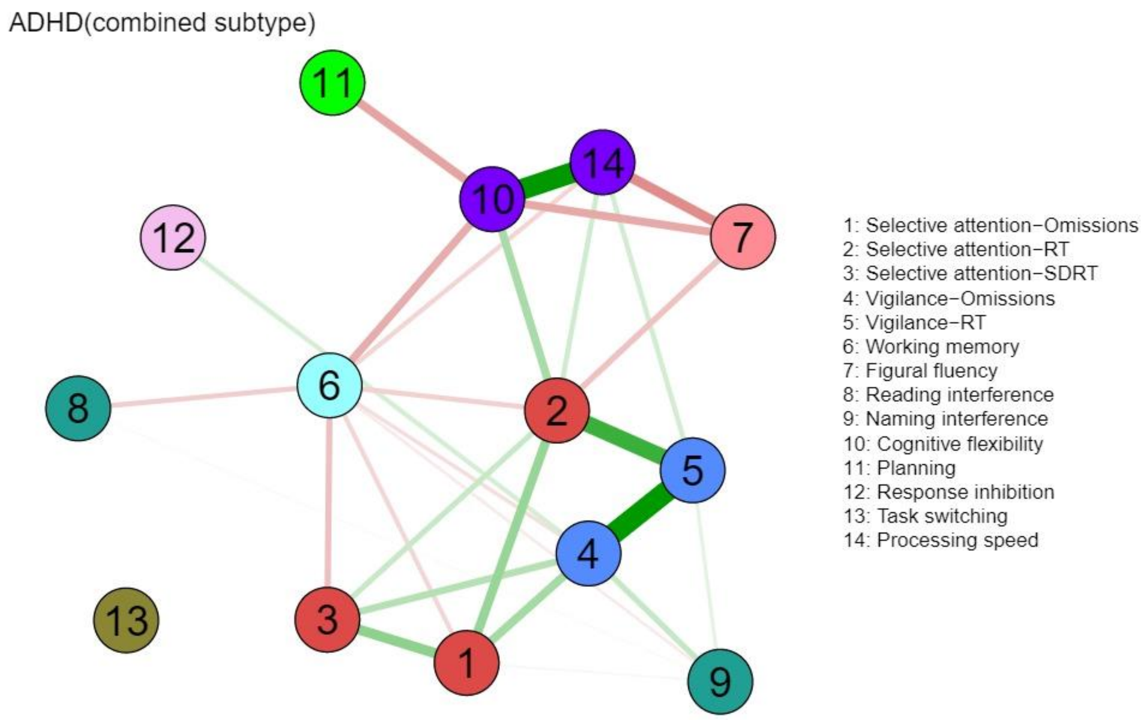

Figure S4.9. Network of neuropsychological functions for individuals with the combined symptom presentation of ADHD (N = 149).

Note. Nodes represent neuropsychological test variables. Neuropsychological test variables stemming from the same test are presented in the same color. Edges connecting nodes represent the regularized partial Spearman correlations. Higher absolute correlations are represented with thicker and more saturated colored edges. Green edges indicate positive correlations, red edges indicate negative correlations.

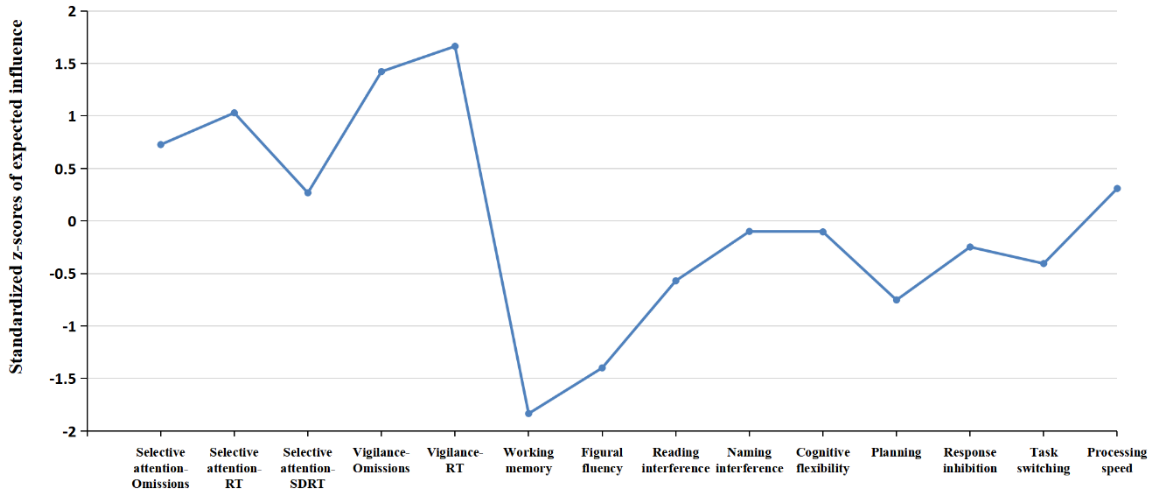

Figure S4.10. Node expected influence of the network of individuals with the combined symptom presentation of ADHD.

Note. Higher standardized Z-scores indicate higher expected influence, and nodes with higher expected impact have closer and stronger relationships with other neuropsychological test variables in the network.

Chapter 5

Stability of attention performance of adults with ADHD over time: Evidence from repeated neuropsychological assessments in one-month intervals

This chapter has been published as:

Guo, N., Koerts, J., Tucha, L., Fetter, I., Biela, C., König, M., ... & Fuermaier, A. B. M. (2022). Stability of Attention Performance of Adults with ADHD over Time: Evidence from Repeated Neuropsychological Assessments in One-Month Intervals. *International Journal of Environmental Research and Public Health*, 19(22), 15234. https://doi.org/10.3390/ijerph192215234

Abstract: Neuropsychological assessments of attention are valuable sources of information in the clinical evaluation of adults with attention-deficit/hyperactivity disorder (ADHD). However, it is unclear whether the attention performance of adults with ADHD is stable or fluctuates over time, which is of great importance in the interpretation of clinical assessments. This study aimed to explore the stability of attention performance of adults with ADHD in repeated assessments at one-month intervals. Twenty-one adults diagnosed with ADHD took part in this study by completing selective attention and vigilance tests three times, each one month apart. Test scores of participants were compared with and interpreted based on test norms. A considerable proportion of 'below average' performance scores were observed in most of the variables of selective attention and vigilance in all three assessments. Further, selective attention and vigilance performance scores did not differ significantly between the three repeated assessments. Finally, the majority of participants received consistent test score interpretations across the three repeated assessments. This study confirms previous research and highlights abnormal selective attention and vigilance performance in adults with ADHD. Further, this study preliminarily demonstrates relatively stable attention performance across repeated assessments, which has the potential to support clinical assessment, treatment planning, and evaluation.

Keywords: adult ADHD; selective attention; vigilance; assessment; stability; fluctuation; variability

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a childhood-onset neurodevelopmental disorder that lasts into adulthood in the majority of cases and affects about 6% of adults worldwide (American Psychiatric Association, 2013; Song et al., 2021). Deficits in attention are, by definition, a core feature of adult ADHD, and empirical evidence has been presented for deficits in various aspects of attention, including alertness, selective and focused attention, divided attention, sustained attention, and vigilance (Fuermaier et al., 2015; Gmehlin et al., 2016; Onandia-Hinchado et al., 2021; Schoechlin et al., 2005; Tucha et al., 2017; Tucha et al., 2006). Below-average levels of performance were also observed in various higher-order cognitive functions in adults with ADHD, including response inhibition (Coghill et al., 2014; Fabio et al., 2017), planning (Fabio et al., 2017; Tucha et al., 2011), memory (Alderson et al., 2013; Fuermaier et al., 2013; Skodzik et al., 2017), and decision-making (Bangma et al., 2019; Mowinckel et al., 2015). Cognitive dysfunction may interfere with multiple aspects of daily life functioning and may contribute to, for example, poor performance in education and academic settings, poor financial situation, problems at work, traffic accidents and traffic violations, drug abuse, relationship breakup, and problems in socializing (Arnold et al., 2020; Beauchaine et al., 2020; Brunkhorst-Kanaan et al., 2021; Fuermaier et al., 2021; Kalbag et al., 2005; Michielsen et al., 2015).

The close relationship between attention and higher-order cognitive functions has been observed in both clinical samples (Barkley, 1997; Butzbach et al., 2019; Mangels et al., 2002; Spikman, Zomeren, & Deelman, 1996) and non-clinical samples (Hüttermann, Memmert, & Nerb, 2019; Kreitz et al., 2015; Posner & Rothbart, 1998; Posner, Snyder, & Solso, 2004) by numerous studies, suggesting that the development of higher-order cognitive functions may be based on the development of basic attention. More recently, the hierarchical relationship between attention and higher-order cognitive functions was reported in patients with ADHD, which underlines the relevance of attention in ADHD (Butzbach et al., 2019; Guo, Fuermaier, Koerts, Mueller, Diers, et al., 2021; Mohamed et al., 2021). In this context, research showed that attention might be the foundation of more complex cognitive functions that build upon attention, such as response inhibition, planning, memory, and task-switching. Thus, deficits in attention are significantly associated with and may result in deficits in complex cognitive functions. Further, a network study of cognitive functions on a large sample of adults with ADHD demonstrated that selective attention and vigilance have a central role and high expected influence on other cognitive functions, underscoring the strong interrelation between attention and various other cognitive functions (Guo et al., 2022).

Considering the fundamental and central role of attention in the clinical neuropsychology of adults with ADHD, an accurate assessment of attention is of great importance for clinical practice, as it may contribute to developing individualized treatment plans and improving the accuracy of treatment evaluation. Neuropsychological performance tests are the mainstay in the assessment of attention functions within the clinical evaluation of adult ADHD. A broad variety of neuropsychological tests are available for neuropsychological practice and research, which have been shown to be sensitive in assessing abnormal attention in both children and adults with ADHD (Fuermaier et al., 2018; Hall et al., 2016; Mapou, 2019; Nikolas, Marshall, & Hoelzle, 2019). However, a thorough examination of the evidence provides a more inconsistent picture for application in practice, as most studies derive their conclusion from group comparisons, in which groups of adults with ADHD perform significantly lower than their comparison groups, which does not indicate that all individuals of the respective ADHD group have lower scores than their controls (Fuermaier et al., 2015; Guo et al., 2022; Mostert et al., 2015). Further, while the majority of studies report lower attention scores in adults with ADHD compared to controls in at least some of the attention tests applied, a considerable number of studies also showed intact attention performance in adults with ADHD in other performance measures of attention (Booth et al., 2005; Manly et al., 2001; Marchetta, Hurks, De Sonneville, et al., 2008; Salomone et al., 2020; Tucha et al., 2008). Finally, the vast majority of attention tests provide several output measures, mostly including indications of both speed and accuracy; however, no consistent picture can be identified whether patients with ADHD typically show deficits in speed, accuracy, or both.

One possible explanation for the consistently inconsistent findings of attention performance in adults with ADHD may be the instability of individuals' attention performance over time. Intra-individual variability in attention task performance over a period of seconds or milliseconds has been observed repeatedly in individuals with ADHD within the course of a single, one-time assessment (Gmehlin et al., 2016; Johnson et al., 2007; Kofler et al., 2013; Lundervold et al., 2011). Further, a number of studies demonstrated intra-individual variability over a period of seconds or milliseconds in cognitive functions other than attention in individuals with ADHD, such as working memory (Buzy, Medoff, & Schweitzer, 2009; Friedman, Rapport, & Fabrikant-Abzug, 2022; Klein et al., 2006) and inhibitory control (Gmehlin et al., 2014; Klein et al., 2006; Vaurio et al., 2009). These findings suggest that intra-individual variability may be a ubiquitous and characteristic feature of ADHD and may, at least in part, account for the cognitive heterogeneity observed in adults with ADHD (Karalunas et al., 2014; Kofler et al., 2013; Tamm et al., 2012). Moreover, intra-individual variability in adults with ADHD was not only observed over a period of seconds or milliseconds but was shown more recently also over a period of days and weeks in ADHD symptoms (Pedersen et al., 2020; Schmid et al., 2020). However, compared to time spans of seconds or milliseconds, which have been extensively studied, fewer studies were dedicated to exploring fluctuations in behavior and cognition of adults with ADHD over longer time intervals (e.g., over days, weeks, or months).

Considering that neuropsychological evaluations in clinical practice are usually based on a single, one-time assessment and assume the stability of their findings without repeated assessment, an examination of intra-individual neuropsychological performance fluctuations in adults with ADHD appears relevant and of clinical importance. Thus, the present study aimed to explore the stability of attention performance in adults with ADHD over time through three repeated assessments in one-month intervals. More specifically, a sample of adults diagnosed with ADHD completed a neuropsychological assessment of selective attention and vigilance three times under stable conditions within a time interval of about one month on average. We expected, first, that a substantial number of adults with ADHD perform in the below-average range ($T \leq 36$, Guilmette et al., 2020) of the respective age-representative norm group in the first assessment. Second, we hypothesized that the performances of selective attention and vigilance within each individual were not stable over time but fluctuated from one assessment to the other, which also resulted in different test score interpretations. However, third, we expected that, on a group level, also in the second and third assessment test scores of a considerable proportion of patients with ADHD fall in the below-average range as compared to test norms.

Materials and Methods

Participants

A total of 21 adults diagnosed with ADHD took part in the present study. All participants were recruited from the Department of Psychiatry and Psychotherapy of the SRH Clinic Karlsbad-Langensteinbach, Germany. Participants were self-referred or referred by local psychiatrists or neurologists to the clinic for a comprehensive ADHD diagnostic because of suspected ADHD in adulthood. The diagnosis of adult ADHD was made jointly by at least two experienced clinicians after a thorough diagnostic assessment. Both clinicians were clinical (neuro)psychologists of the Department of Psychiatry and Psychotherapy of the SRH Clinic

Karlsbad-Langensteinbach and mutually agreed upon the diagnostic decision. The diagnostic assessment procedure followed the guidelines for a first-time adult ADHD diagnosis (Sibley, 2021). Specifically, the diagnostic assessment was based on a clinical psychiatric interview enquiring about symptoms and impairments of ADHD and possible comorbidities as outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013). The diagnostic assessment further included various types and sources of information, such as reports from schools, and information from partners, parents, and/or employers. An objective indication of impairment was incorporated whenever accessible, e.g., academic failure, unemployment, traffic accidents, drug use, relationship breakups, divorces, etc. To assess the severity of ADHD symptoms, participants completed 2 self-report scales that were developed to quantify retrospective and current ADHD symptoms, i.e., the short version of the Wender Utah Rating Scale (WURS-K; Retz-Junginger et al., 2003) and the Conners' Adult ADHD Rating Scales—Self-Report: Long Version (CAARS-S:L; Christiansen et al., 2012). Among those 21 individuals diagnosed with ADHD, 2 met the diagnostic criteria of the predominantly inattentive presentation of ADHD, 18 met the diagnostic criteria of the combined symptom presentation, while the symptom presentation of one individual was not reported. Moreover, seven of the 21 individuals were additionally diagnosed with one or more comorbid psychiatric disorders, including mood disorders (*n* = 6), addiction disorders (*n* = 1), anxiety disorders (*n* = 1), and post-traumatic stress disorder (*n* = 1). Twelve of the 21 individuals were currently treated with stimulant medication under stable conditions on all three assessment days. The remaining 9 participants did not take stimulant medication on any of the assessment days. Descriptive information and ADHD symptom scores are presented in Table 5.1.

Table 5.1. Descriptive information and ADHD symptoms of all participants

			Adults with ADHD (*n* = 21)		
Sex (male/female)			**8/13**		
Education (1/2/3/4/5/6) [a]			**0/1/8/6/5/1**		
	Min	Max	Median	Mean	SD
Age (in years) [b]	20	65	47.5	46.1	11.6
Childhood ADHD symptoms [c]	11	57	41	39.3	13.1
Current ADHD symptoms [d]					
Inattention	1	22	13	13.2	6.2
Hyperactivity/Impulsivity	3	24	13	12.2	6.0
Total symptoms	6	46	25	25.5	10.7

Note: [a] Education (1/2/3/4/5/6) = Basic schooling with no formal degree (less than 9 years of schooling)/ Secondary school (usually 9 - 10 years of schooling)/ Secondary school with additional vocational training (usually 10 - 12 years of schooling)/ Secondary school with university entrance qualification (usually 12–13 years of schooling)/ University degree (usually 16–17 years of schooling)/Not reported. [b] Data was missing for one participant. [c] Measured with the short version of the Wender Utah Rating scale (WURS-K); data were missing for eight participants. [d] Measured with the Conners' Adult ADHD Rating Scales—Self-Report: Long Version (CAARS-S:L); data were missing for eight participants.

Materials

This study is part of a larger project which comprises an extensive battery of measures for the assessment of symptoms, impairments, and cognitive functioning of adults with ADHD. In the following sections, only the measures relevant to this study are described.

Self-Report Scales of ADHD Symptoms

The German short version of the WURS-K was administered to assess ADHD symptoms in childhood (Retz-Junginger et al., 2003). This scale consisted of a total of 25 items (21 items assessing symptoms, 4 control items), each scored on a 5-point Likert scale ranging from 0 (not at all or very slightly) to 4 (very much). Participants rated each item based on the recall of their childhood experiences. The sum score of 21 items (except for the 4 control items) was calculated to assess the severity of retrospective ADHD symptoms.

The German version of CAARS-S:L was applied to assess the severity of current ADHD symptoms (Christiansen et al., 2012). The CAARS-S:L includes 66 items, each scored on a 4-point Likert scale ranging from 0 (not at all/never) to 3 (very much/very frequently). A number of subscales can be derived from the CAARS-S:L. For the present study, the sum scores of three subscales that assess ADHD symptoms as listed in the DSM-IV (American Psychiatric Association, 1994) were calculated and reported, i.e., the DSM-IV subscales for inattentive symptoms, hyperactive/impulsive symptoms, and total symptoms.

Assessment of selective attention and vigilance

Selective attention and vigilance were assessed with two computerized tests of the Vienna Test System (VTS; Schuhfried, 2013), including the test perception and attention functions: selective attention (WAFS) and the test perception and attention functions: vigilance (WAFV). These two tests have been shown valid and sensitive in revealing attention deficits in various clinical populations and are commonly applied in the clinical neuropsychological evaluation of adult ADHD and related disorders (Fuermaier et al., 2022; Ramm et al., 2019; Ramm et al., 2018).

Selective Attention

The test WAFS was used to assess selective attention. In this test, three kinds of geometric stimuli (circles, squares, and triangles) that may get lighter or darker or stay the same were presented on the screen. Participants were asked to respond as quickly as possible to changes in circles and squares (a circle gets lighter or darker, a square gets lighter or darker) by pressing the response button. No response is needed when a triangle gets lighter or darker. Each stimulus was presented for 1500 ms, and a change may take place after 500 ms. The interstimulus interval was 1000 ms. A total of 144 stimuli were presented, 30 of which were targets. The test duration is about 8 min. The mean reaction time (RT), the logarithmic standard deviation of the reaction times (SDRT), and the number of missed reactions (omission errors) were recorded. Adult norms are accessible consisting of 295 individuals representing the general population (46.4% men; 53.6% women) aged between 16 and 77 (median = 39; sd = 15.1). All individuals in the normative group performed tests in the German language. The internal consistency (Cronbach's α) of this test is excellent, with 0.95 in the normative sample.

Vigilance

The test WAFV was administered to assess vigilance. In this test, squares that may get darker or stay the same were presented one by one on the screen. Participants were asked to press the response button as quickly as possible whenever a square got darker. The frequency of targets (squares getting darker) is 5%. Each stimulus was presented for 1500 ms, and a change may take place after 500 ms. The interstimulus interval was 500 ms. A total of 900 stimuli were presented, 50 of which were targets. The test duration is 30 min. The mean RT, the logarithmic SDRT, and the number of omission errors were recorded. The WAFV and the WAFS are evaluated based on the same normative group, consisting of 295 individuals representing the general population (46.4% men; 53.6% women) aged between 16 and 77 (median = 39; sd = 15.1). All individuals in the normative group performed tests in the German language. The internal consistency (Cronbach's α) of this test is excellent, with 0.96 in the normative sample.

Procedure

All participants were invited to take part in the study on a voluntary basis. It was stressed to all participants that the study was for research purposes only and will not affect their clinical evaluation and treatment. All participants signed the written informed consent before taking part in the study. The neuropsychological assessment of selective attention and vigilance was performed three times on three different assessment days. The time interval between the different assessments was, on average, 1 month from each other, ranging from 21 to 49 days, and in 90% of the cases ranging from 21 to 35 days. The assessments per person took place, as much as possible, on the same day of the week and at the same time of the day. All assessments were performed in a quiet environment at the Department of Psychiatry and Psychotherapy of the SRH Clinic Karlsbad-Langensteinbach, Germany. The order of the administration of all tests (including measures of selective attention and vigilance) was randomized across participants but kept constant for each individual across all three assessment days. Self-report symptom scales were completed only once, i.e., prior to the first attention assessment. Participants were rewarded with 60 euros upon completion of all three assessments. Participants who were included in the present study were assessed between January 2019 and June 2021. The study was approved by the ethical review board of the medical faculty of the University of Heidelberg, Germany (protocol code: S-588/2018, date: 1 October 2018).

Statistical Analysis

Missing values occurred in 2.7%, 4.7%, and 13.8% of the data for the first, second, and third assessments, respectively, and the missing values were not replaced. Descriptive statistics of attention performance scores are presented for all participants. Moreover, T-scores based on representative normative data as provided by the test publisher are computed (Schuhfried, 2013). T-scores equal to or lower than 36 are defined as ‘below average’ performance (Guilmette et al., 2020). The percentages of participants scoring in the below-average range ($T \leq 36$) are calculated per test variable for each of the three assessments. Further, attention performance scores are compared between the three assessments using nonparametric statistics (i.e., Friedman test). Post hoc pairwise comparisons are computed using Wilcoxon signed-rank tests. To control the alpha inflation in multiple testing, a Bonferroni adjusted significance level of $p < 0.017$ ($p = 0.05/3$) was applied. The magnitude of pairwise differences is indicated using effect size Cohen’s r, with $r = 0.1$ indicating a small effect, $r = 0.3$ indicating a medium effect, and $r = 0.5$ indicating a large effect (Cohen, 1988).

Moreover, the absolute values of individual T-score differences between any two of the three assessments are calculated for each test variable. Further, to examine whether test score interpretations differed from one assessment to another, the percentage of consistent test score interpretations is indicated for each comparison. Consistent test score interpretation is considered if both test scores indicate below-average performance ($T \leq 36$) or both test scores indicate no below-average performance ($T > 36$). The percentage of consistent test score interpretation is calculated by the number of participants who received consistent test score interpretation divided by the total number of participants. The percentage of consistent test score interpretations across three assessments is also calculated for each variable. Finally, Spearman correlation coefficients are calculated to indicate the association between test scores at any two of the three assessments and a Bonferroni adjusted significance level of $p < 0.017$ ($p = 0.05/3$) was applied.

Results

Descriptive statistics of attention performance for the three assessments and the percentages of participants who scored below average (T ≤ 36) are presented in Table 5.2. A comparison to test norms indicates a higher percentage of participants scoring in the below-average range, in particular in the selective attention task. Figures 5.1 and 5.2 illustrate mean T-scores below 50 for most of the variables of the selective attention and vigilance task and mean T-scores slightly above 50 for SDRT of the vigilance task. Figures 5.1 and 5.2 visually depict that no meaningful changes occurred from one time point to another on a group level. Furthermore, comparing attention performance over time (T1, T2, and T3) revealed no significant differences. Pairwise comparisons confirmed non-significant differences, with effect sizes ranging from negligible to small size (Table 5.2).

Table 5.2. Attention performance of individuals with ADHD (n = 21) across the three assessments T1, T2, and T3.

Attention Performance Test Scores	T1			T2			T3			Friedman Test		Pairwise Comparisons [a]		
												T1 vs. T2	T1 vs. T3	T2 vs. T3
	Median	IQR	% below Average [b]	Median	IQR	% below Average [b]	Median	IQR	% below Average [b]	χ^2	p	*Cohen's r* [c]	*Cohen's r* [c]	*Cohen's r* [c]
Selective attention [d]—RT	394.00	158.00	23.8	354.00	136.00	14.29	339.00	166.50	21.05	0.12	0.94	0.15	0.02	0.12
Selective attention [d]—SDRT	1.24	0.12	19.05	1.20	0.07	10.53	1.25	0.10	17.65	0.92	0.63	0.09	0.09	0.25
Selective attention [d]—Omissions	0	1.00	19.05	0	0.75	15.00	0	0.25	16.67	0.26	0.88	0.08	0.09	0.11
Selective attention [e]			33.33			19.04			36.84					
Vigilance [f]—RT	440.00	109.50	15.00	421.00	150.00	23.81	434.00	163.00	21.05	3.35	0.19	0.13	0.09	0.05
Vigilance [f]—SDRT	1.24	0.08	5.26	1.24	0.09	5.26	1.21	0.06	0	0.52	0.77	0.13	0.25	0.08
Vigilance [f]—Omissions	0	1.00	15.00	1.00	1.00	9.52	1.00	1.00	0	0.35	0.84	0.09	0.06	0.05
Vigilance [e]			20.00			38.10			21.05					

Note: T1 = First assessment, T2 = Second assessment, T3 = Third assessment. IQR = Interquartile range. [a] Post hoc tests were performed using Wilcoxon signed-rank tests. None of the comparisons indicated significance on a Bonferroni-adjusted significance level of p = 0.017. [b] Percentage of participants who scored in the below-average range (T score ≤ 36). [c] Based on Cohen's criteria for r: r = 0.1 indicates a small effect, r = 0.3 indicates a medium effect, and r = 0.5 indicates a large effect. [d] Selective attention was assessed using the Perceptual and Attention Functions—Selective attention (WAFS). [e] Below average performance in selective attention/vigilance is defined by below average performance in at least one variable of its test variables. [f] Vigilance was assessed using the Perceptual and Attention Functions—Vigilance (WAFV).

5

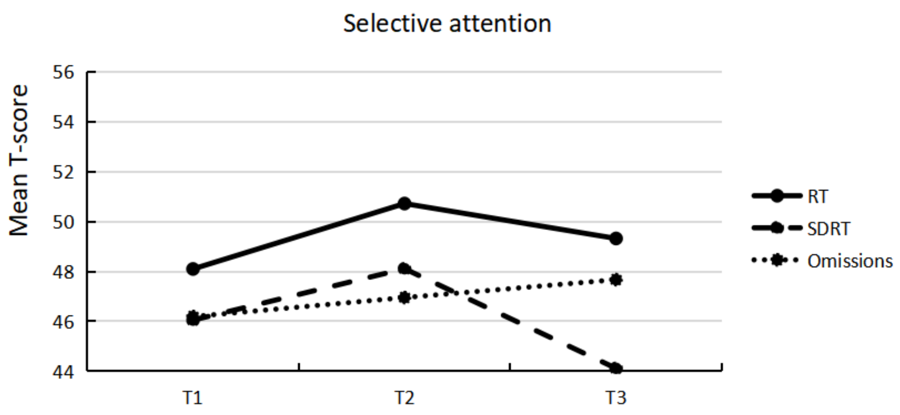

Figure 5.1. Mean T-score of variables of selective attention at each of the three assessments.

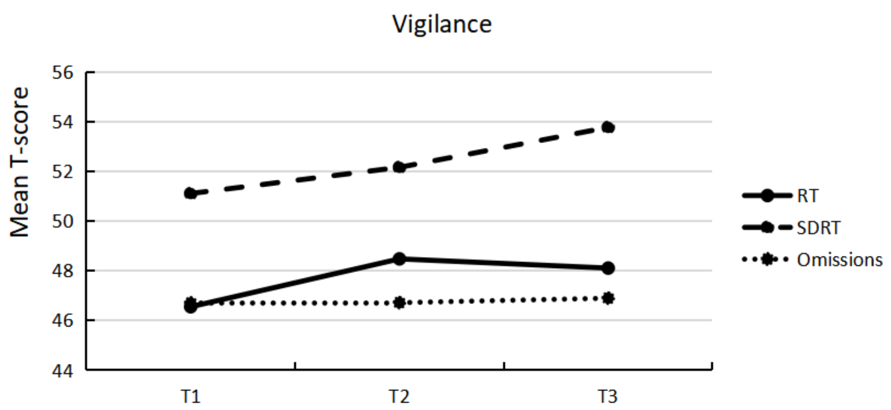

Figure 5.2. Mean T-score of variables of vigilance at each of the three assessments.

Further, individual changes are indicated by absolute T-score differences from one time point to another. Descriptive statistics of absolute T-score differences between assessments are presented in Table 5.3. Results indicate that the mean T-score difference ranges from 3.2 to 8.9, with the smallest difference observed between the second and the third (T2–T3) assessment in the omissions of the selective attention task and the largest difference observed between the second and the third (T2–T3) assessment in the SDRT of the vigilance task. In addition, the majority of participants received the same test score interpretation as below average ($T \leq 36$) or no below average ($T > 36$), with at least 74% of participants being consistent in their test score interpretation across all three assessments (see Table 5.3). When comparing test score interpretations between any two assessments, the consistency rate is above 80% for the majority of measures and comparisons (Table 5.3). In total, 20–25% of participants received inconsistent test score interpretations. Finally, correlation analyses revealed that the RTs of both selective attention and vigilance are significantly correlated (large effect size) between any two of the three assessments ($p < 0.01$). However, for SDRT, a significant correlation is observed only between the first and the third assessment of selective attention ($p < 0.05$; large effect). For omission errors, significant correlations are observed between any two of the three assessments of selective attention (medium to large effect size) but only between the first and the second assessment in the vigilance task (medium effect size).

Table 5.3. Stability of attention performance and correlations between attention scores of the three assessments of individuals with ADHD (*n* = 21).

Attention Performance Test Scores	T1–T2 [a]				T1–T3 [a]				T2–T3 [a]				% Consistent Test Score Interpretations across the Three Assessments
	Range	M	% Consistent Test Score Interpretations [b]	*r* [c]	Range	M	% Consistent Test Score Interpretations [b]	*r* [c]	Range	M	% Consistent Test Score Interpretations [b]	*r* [c]	
Selective attention [d]—RT	2–17	5.86	81	0.828*	0–19	4.95	79	0.833*	0–9	4.58	95	0.927*	79
Selective attention [d]—SDRT	1–23	8.79	89	0.369	1–22	7.82	76	0.556	0–21	8.00	88	0.265	75
Selective attention [d]—Omissions	0–23	4.10	80	0.569*	0–23	4.78	83	0.489	0–14	3.24	100	0.592*	82
Vigilance [e]—RT	0–17	4.35	80	0.779*	0–29	6.05	84	0.591*	0–13	5.53	84	0.784*	74
Vigilance [e]—SDRT	1–24	8.59	88	0.379	2–19	6.65	95	0.441	1–33	8.88	94	0.238	88
Vigilance [e]—Omissions	0–23	5.85	75	0.465	0–23	5.95	85	0.221	0–23	5.05	89	0.290	74

Note: T1 = First assessment; T2 = Second assessment; T3 = Third assessment. [a] T1–T2 = Mean of absolute values of T-score differences between the first and the second assessment; T1–T3 = Mean of absolute values of T-score differences between the first and the third assessment; T2–T3 = Mean of absolute values of T-score differences between the second and the third assessment. [b] Percentage of participants who received consistent test score interpretations across two assessments. [c] *r* indicates the Spearman correlation between the two assessments. [d] Selective attention was assessed using the Perceptual and Attention Functions—Selective attention (WAFS). [e] Vigilance was assessed using the Perceptual and Attention Functions—Vigilance (WAFV). * Correlation is significant at the Bonferroni adjusted level, $p < 0.017$

Discussion

This study aimed to explore the stability of attention performance over time in adults diagnosed with ADHD by repeatedly assessing selective attention and vigilance three times with a one-month time interval between each assessment. Results confirmed previous research showing that a considerable proportion of individuals with ADHD score in the below-average range in both selective attention and vigilance. Furthermore, both performance scores and test score interpretations (below average or not) remained relatively stable over time.

Inspecting the attention performance of adults with ADHD revealed that the percentage of participants who scored in the below-average range was higher than expected from a representative norm group (≥ 8%, Guilmette et al., 2020) in most of the attention measures assessed, in particular in selective attention. Mean T-scores were below 50 for most variables (except for the SDRT of the vigilance task with mean T-scores slightly higher than 50), although the percentage of participants scoring in the below-average range in the variability of reaction times and omission errors of the vigilance tests was not as high as in the reaction times of the vigilance task. These results, thus, confirm previous findings that selective attention and vigilance deficits may be characteristic of adult ADHD (Fuermaier et al., 2015; Huang-Pollock et al., 2012; Onandia-Hinchado et al., 2021; Tucha et al., 2009) and that neuropsychological performance tests are sensitive instruments to demonstrate attention deficits in the clinical evaluation of adults with ADHD (Fuermaier et al., 2018; Fuermaier et al., 2022; Mapou, 2019; Nikolas et al., 2019).

Different from our expectations, the comparisons of attention performance between the three assessments revealed relatively stable scores with nonsignificant group differences of negligible to small size. Moreover, most individuals deviated only slightly in the performance scores, as shown by individual T-score differences of about 5 points (ranging from 3.2 to 8.9) from one assessment to another, which further supports the notion of stable selective attention and vigilance dysfunction over time. Prior to data analysis, we expected selective attention and vigilance performance to fluctuate from one assessment to another based on research showing cognitive performance fluctuations in tasks over seconds and milliseconds in individuals with ADHD (Buzy et al., 2009; Friedman et al., 2022; Gmehlin et al., 2014; Johnson et al., 2007; Kofler et al., 2013; Vaurio et al., 2009), as well as inconsistent findings on attention performance in individuals with ADHD (Booth et al., 2005; Marchetta, Hurks, De Sonneville, et al., 2008; Mostert et al., 2015; Onandia-Hinchado et al., 2021; Salomone et al., 2020). The relatively stable attention performance over time observed in the present study suggests that inconsistent findings across previous studies in adults with ADHD may more likely be related to external factors, such as differences in test selection, sample composition, or clinical characteristics, rather than reflecting unstable cognitive abilities. Further, preliminary conclusions could be drawn that attention performance may fluctuate over seconds or milliseconds in individuals with ADHD within the course of a single, one-time assessment (Gmehlin et al., 2016; Johnson et al., 2007; Kofler et al., 2013; Lundervold et al., 2011), but overall attention performances may be stable across assessments with longer time intervals. A neural basis for performance fluctuations within tasks in adults with ADHD was suggested in imaging research by showing a link between greater reaction time variability in adults with ADHD and reduced activation in frontoparietal brain regions and anterior cingulate gyrus (Cao et al., 2008; Karalunas et al., 2014; Konrad et al., 2006; Rubia et al., 2007). However, this activation pattern may be similar when repeatedly performing the same tasks at different time points, resulting in relatively stable performance scores, as observed in this study. Further, this study provides implications regarding the test-retest reliability of the applied instruments on clinical samples of adults with ADHD. Although good reliability estimates of the applied tests were provided by the test publisher, most of the reliability analyses stem from non-clinical samples. Thus, evidence of test-retest reliability of these tests on clinical samples is scarce. Consistent and stable attention performance across three repeated assessments as observed in the present study, thus, support the test-retest reliability of these attention tests in clinical samples. Moreover, correlation analyses demonstrated the largest associations between variables of reaction time, whereas considerably smaller and mostly non-significant associations were found between variables representing SDRT and omissions. Although previous research in this field failed to identify a specific variable type (including RT, SDRT, omissions and commissions) that stands out to be most sensitive in detecting vigilance deficits in adult ADHD (Fuermaier et al., 2022), current data indicate that measures of reaction time seem to be most stable across time.

More importantly for clinical practice, test score interpretations were consistent across the three assessments for the majority of participants. Specifically, more than 74% of participants received consistent test score interpretations (below or no below-average performance) across all three assessments, and more than 80% of participants received consistent test score interpretations between any two assessments for most variables. Consistent test score interpretations are encouraging for clinicians by providing an evidence base that the results of a one-time neuropsychological attention assessment may be well suited as a basis for clinical evaluation, treatment planning, and treatment evaluation. Of note, there are still about 20-25% of participants who received inconsistent test score interpretations across the different assessments, which may indicate unstable attention performance over time. For these cases, a one-time attention assessment may bias or distort the interpretation of cognitive performance scores, and it is advisable to integrate results from neuropsychological performance assessment with other clinical measures (of attention) in order to receive a comprehensive and valid understanding of the individual's functioning (Kooij et al., 2019; Marshall et al., 2021; Pettersson et al., 2018). However, also for those participants receiving inconsistent test score interpretations, it must be stressed that T-score differences remained rather small (maximum difference of 8.9 points), and inconsistent test score interpretations mainly resulted from the dichotomous nature of test score interpretations as applied in this study. In addition, another possible explanation for the inconsistent test score interpretations observed in 20-25% of participants could be the occurrence of regression towards the mean (Bland & Altman, 1994), which is shown by participants yielding an extremely low or high score in the first assessment, but a score closer to the mean in a reassessment (i.e., extreme scores get less extreme in a reassessment). The occurrence of such effects of regression towards the mean may also lead to inconsistent test score interpretations across three assessments. Finally, the majority of participants (12 of the 21) were currently treated with stimulant medication, so it could be speculated that the stability of attention performance observed in most cases reflects the cognitive ability status of individuals who are already diagnosed and treated for ADHD, but not individuals who are still seeking a clinical diagnostic check-up.

Limitations and Future Directions

Of note, the data of this study need to be interpreted in the context of several limitations. Most importantly, the sample size of this study is relatively small and may lead to low statistical power. Thus, the conclusions of this study should be taken as preliminary and require replication on larger and more homogenous samples. Larger samples would yield more robust findings and may allow the investigation of moderating factors, such as symptom presentation, comorbidities, or medication status. Support for the robustness of our results is given by the good psychometric properties of our instruments and a similar distribution of scores in one-time assessments on independent and large clinical samples (Guo, Fuermaier, Koerts, Mueller, Diers, et al., 2021; Guo et al., 2022). Second, some of the participants (7 of 21) were additionally diagnosed with one or more comorbid psychiatric disorders other than ADHD, which may confound our findings. However, it must be noted that our sample represents a naturalistic sample of patients with ADHD and how it commonly occurs in clinical settings, in which comorbid psychiatric disorders are the rule rather than the exception. Thus, controlling or removing comorbidity would result in unrealistic samples. Additionally, as symptoms of inattention and hyperactivity also occur in many other disorders than ADHD, the findings of this study may also hold for other related conditions with overlapping symptoms, which need to be addressed in future research. Third, administrative difficulties in implementing the repeated assessment design in clinical practice resulted in non-identical time intervals between assessments. Even though differences were kept as minimal as possible, it must be noted that variation in time intervals may confound results on performance stability. Forth, implications on test-retest reliability of tests used in this study in clinical samples should also be taken into consideration while interpreting results. Future studies on independent and larger clinical samples could benefit us in getting a more accurate understanding of test-retest reliability in clinical populations. Fifth, the findings of this study are restricted in a way that they are based on selective attention and vigilance performance as assessed by the Vienna Test System. Future replication studies would benefit from including also other measures to gain information on the specificity/generalization of the findings. Finally, test score interpretations contrasted ‘below average’ performance with all other performance scores, which neglects more nuanced and fine-grained performance evaluations that are possible on larger samples, e.g., also considering cognitive strengths in above-average scores.

Conclusions

This study confirms previous research that a considerable proportion of adults with ADHD show below-average selective attention and vigilance performance. Moreover, this study highlights that selective attention and vigilance performance did not differ significantly between three repeated assessments in one-month intervals. In this context, the majority of individuals showed only minor T-score differences between the three assessments and received consistent test score interpretations. Pending future replication on larger samples, this study forms an empirical evidence base relevant for clinical practice as it suggests that the results of a one-time attention assessment may be sensitive in revealing attention deficits and may be stable over time for the majority of individuals, thus being useful to guide individual treatment planning and evaluation.

Chapter 6

General discussion

General conclusions of this thesis

This thesis examined a broad range of neuropsychological functions of individuals in the clinical evaluation of adult ADHD and further defined the role of performance tests, self-reports, and informant reports in the clinical evaluation. This thesis also addressed the inter-relations of neuropsychological functions in adult ADHD and whether particular functions stand out and may play a more central role. Moreover, this thesis examined whether the core neuropsychological functions of adults with ADHD are stable or fluctuate over time in repeated clinical assessments. We demonstrated that neuropsychological deficits are prominent features in the majority of individuals seeking a clinical evaluation of adult ADHD, but are not specific for individuals who meet the diagnostic criteria of ADHD (chapter 2), suggesting that neuropsychological assessments using cognitive tests may not provide the clinician with incremental information for the differential diagnostic process of adult ADHD. Additionally, the study described in chapter 2 extends previous findings by revealing that significant relationships between basic and complex cognitive functions were observed not only in individuals with ADHD, but also in individuals with other psychiatric disorders, such as mood disorders, addiction disorders, and anxiety disorders, which may provide implications for the assessment and treatment of cognitive deficits of patients with psychiatric conditions. Further (chapter 3), by examining the role of subjective reports on ADHD symptoms and impairments in the clinical evaluation of adults with ADHD, we concluded that self-reported ADHD symptoms, particularly retrospectively assessed ADHD symptoms in childhood, have the strongest potential to contribute to the differential diagnosis of adult ADHD. Also, we observed that subjective reports of symptoms and impairments have no meaningful predictive value for objective neuropsychological test performances, indicating that subjective reports and objective test performances seem to be distinct and nonredundant sources of information and should not be treated interchangeably. In chapter 4, we replicated the observation that neuropsychological deficits are prominent features in individuals seeking a clinical evaluation of adult ADHD and demonstrated that neuropsychological performance indicators are not isolated but rather interrelated with each other in a complex network in both individuals with and without ADHD. Although connections were observed in both networks, stronger and denser connections were observed in the ADHD group compared to the clinical comparison group. Moreover, attention functions were found to have a central role among various neuropsychological functions in both groups. The final study (chapter 5) examined the stability of attention performance of adults with ADHD over time in repeated assessments. We revealed that selective attention and vigilance performance did not differ significantly between three repeated assessments in one-month intervals, suggesting that the results of a one-time attention assessment may be sensitive in revealing attention deficits and may be stable over time for the majority of adults with ADHD.

Implications for future research and clinical practice

The results from this thesis help us to further define the role of a neuropsychological assessment in the clinical evaluation of adult ADHD. We conclude from this thesis that neuropsychological tests are sensitive tools in revealing cognitive deficits of patients in this referral context and have the potential to help clinicians gain a comprehensive understanding of the individual's functioning in this context. This finding supports previous arguments that the use of neuropsychological tests is helpful in determining whether significant and meaningful cognitive deficits are present, whether accommodations are necessary to apply, or whether the cognitive level of functioning improves after treatment (Gallagher et al., 2001; Mapou, 2019). Moreover, a deeper understanding of individual cognitive strengths and weaknesses has the potential to guide treatment planning, such as the administration of cognitive remediation programs or acquiring compensation strategies to overcome the consequences of cognitive deficits (Guo, Fuermaier, Koerts, Mueller, Diers, et al., 2021; Lange et al., 2014; Pineda et al., 2007). However, our findings also suggest that neuropsychological tests have limited value in the differential diagnosis of adult ADHD. These findings are in line with a recent review on the use of neuropsychological tests in ADHD evaluations (Rosso et al., 2023), and empirically-informed diagnostic guidelines as outlined by Sibley (2021) promoting accurate adult ADHD diagnoses, in which neuropsychological tests are not mandatory to use (Sibley, 2021). The differential diagnosis between ADHD and other psychiatric conditions is complex. Many clinical manifestations, such as problems with attention, are shared by individuals with ADHD and other psychiatric conditions (e.g., depression, anxiety, conduct disorders), and individuals with ADHD are also commonly diagnosed with one or more co-occurring psychiatric disorders (Antshel & Russo, 2019; Gillberg et al., 2004; Panagiotidi, Overton, & Stafford, 2019; Pritchard et al., 2012). An accurate diagnosis of ADHD in differentiation from other psychiatric disorders is important, not only for the prescription of safe and effective treatment, but also to save costs for ineffective (and unjustified) treatments (Katzman et al., 2017; Young et al., 2021). For example, stimulant medication was shown to be effective in the treatment of ADHD but not in depression or anxiety, notwithstanding the large overlap in symptoms and impairments (Biederman et al., 2009; Gillberg et al., 2004; Strawn, Dobson, & Giles, 2017). While seemingly not suited for differential diagnostic purposes (see Rosso et al., 2023, a review including research of this thesis), a large body of research advocates the use of neuropsychological performance tests in the clinical evaluation of adult ADHD in order to provide a comprehensive functional assessment of individuals with ADHD, which has the potential to reduce the risk of adverse outcomes in academic, occupational, and relationship and improve the quality of life of individuals with ADHD (Planton et al., 2021; Pritchard et al., 2012). For example, a neuropsychological assessment could be useful to understand the problems experienced in daily life and explain a patient's cognitive strengths and weaknesses. Further, a neuropsychological assessment could help to follow an individual's trajectory, monitor potential changes in cognition, and further evaluate the patient's response to treatment (Cox, 2011; Harvey, 2022). In this context, longitudinal studies could be a direction for future research to examine the utility of neuropsychological assessments in following a patient's course and monitoring treatment effects. While long-term follow-up studies may be challenging and difficult to carry out, they would be a worthwhile addition to the majority of the cross-sectional work of this thesis (Coghill et al., 2014; Lin & Gau, 2019; Seidman, 2006).

In addition to neuropsychological assessments using cognitive tests, more research is needed to further define the role of patients' subjective reports on symptoms and impairments in the clinical evaluation of adult ADHD. Even though both self- and informant-reported symptoms are recommended use in the diagnostic guidelines outlined by Sibley (Sibley, 2021), our results of Chapter 3 indicated that retrospectively assessed self-reported ADHD symptoms in childhood were the only measure that meaningfully differentiated between individuals with ADHD and other clinical groups. One possible reason for this finding is that all participants of our study stem from the same referral context and were all suspected of having ADHD, thus, a large overlap in symptoms and impairments of individuals with and without ADHD can be assumed. The finding of this chapter stresses that self-reported ADHD symptoms in childhood have the strongest potential to improve the accuracy of differential diagnoses of adult ADHD and other clinical groups, such as mood disorders and anxiety disorders, and should be included in the clinical assessment of individuals in this referral context. While the majority of self- and other report rating scales seem not to be specific for adult ADHD but are sensitive for detecting ADHD-related symptoms and impairments of all individuals in this referral context, future research is needed to define their role in a clinical assessment in more detail (De Los Reyes & Makol, 2021; Fuermaier et al., 2014). For example, reports from narrowly defined significant others, e.g., parents or spouses, close friends, teachers, or co-workers, could provide clinicians with further information spanning various important domains of daily living, including educational functioning, work performance, or peer and intimate relationships. This information has the potential to improve the accuracy of differential diagnoses of adult ADHD as it provides domain specific aspects of functioning (Pritchard et al., 2012). Moreover, although neither neuropsychological assessments using tests nor subjective reports administered alone were able to distinguish individuals with ADHD from individuals with other clinical conditions, it was suggested that a combined application of neuropsychological tests and subjective reports may enhance the classification accuracy of adult ADHD (Nikolas et al., 2019; Söderström, Pettersson, & Nilsson, 2014; Rosso et al., 2023). Large scaled and systematic clinical studies are needed that address the question of which and how clinical instruments can be applied in conjunction to improve diagnostic accuracy between related and overlapping clinical syndromes.

In contrast to focusing on how neuropsychological instruments may improve the differential diagnostic accuracy of adult ADHD, another perspective for research and clinical practice is to move away from diagnostic entities and drift towards a transdiagnostic approach in neuropsychological syndromes. The observation of reliable findings of neuropsychological deficits across conditions, with an absence of disorder-specific neuropsychological profiles, has already been made in the late 20th century (Zakzanis, Leach, & Kaplan, 1999), and was supported in a steadily growing number of studies ever since (Castaneda et al., 2008; Doyle et al., 2018; Snyder, Miyake, & Hankin, 2015; Wright et al., 2014). More recent research supported the view of neuropsychological deficits as a transdiagnostic dimension that may be an indication of general psychopathology but may not be specific to a particular disorder (Abramovitch, Short, & Schweiger, 2021; East-Richard et al., 2020). Findings of this thesis that neuropsychological deficits were observed in the majority of individuals in the clinical evaluation of ADHD, independent of their diagnostic status, may give support for the view of a neuropsychological deficit as a transdiagnostic dimension across disorders, including overlapping clinical conditions of the same referral context.

While chapters 2 and 3 may suggest future research on longer, more comprehensive, and exhaustive clinical assessment batteries that may improve diagnostic accuracy (Kim et al., 2017; Laske et al., 2015), indications to shorten existing batteries can be derived from chapter 4. The results of this study revealed a denser and stronger network of neuropsychological functions in the ADHD group compared to the clinical comparison group, suggesting neuropsychological functions were highly interrelated in individuals with ADHD. Further, it must be underlined that attention performance has the most intensive and strongest links with other functions, suggesting a central role of attention in the neuropsychological network. The central role of attention in the neuropsychological network provides more evidence to the argument that there is a hierarchical relationship between basic (e.g., processing speed and attention focus) and complex cognitive functions (e.g., executive functions) (Butzbach et al., 2019; Guo, Fuermaier, Koerts, Mueller, Diers, et al., 2021; Holst et al., 2017). Because of the interrelatedness and central role of attention functions, one could explore how to shorten and streamline the clinical assessment without losing valuable clinical information. For example, basic attention functions, such as accuracy and response speed in short and long lasting neuropsychological tasks may be promising candidates which carry most clinical information because of their large expected influence on a range of other cognitive operations. In addition, the central role of attention performance in the network of neuropsychological functions gives implications for the treatment of ADHD, for example, medications targeted at improving attention performance could be the primary choice in the treatment of ADHD and attentional performance could also be the first choice when evaluating the effectiveness of treatment. Moreover, network analysis may also provide a new avenue for studying the relationship between subjective and objective measures. Other than the interrelations observed between various neuropsychological functions derived from performance tests in this thesis, earlier studies showed that also self-reported ADHD symptoms can be depicted in an inter-related network (Goh et al., 2020; Goh et al., 2021; Martel et al., 2016; Silk et al., 2019). Considering that both neuropsychological performance indicators and ADHD symptoms contribute to the comprehensive understanding of individuals with ADHD, we believe that, other than exploring the relationships of neuropsychological functions and ADHD symptoms separately, network analyses on larger samples, including a wide range of functions and sets of instruments, are needed to further understand the roles and relationships between subjective and objective clinical instruments in this assessment context. Although the relationships between objective and subjective assessments have been examined in a substantial body of research (Butzbach et al., 2021; Fuermaier et al., 2015; Guo, Fuermaier, Koerts, Mueller, Mette, et al., 2021; Potvin et al., 2016; Slobodin & Davidovitch, 2019), network analysis may have the potential to gain new insights into this issue. For example, network analysis does not only provide information about whether objectively assessed neuropsychological functions and subjectively reported ADHD symptoms are interrelated or isolated, but has the potential to also provide information about whether there are particular functions or symptoms which play a "bridge" role by connecting cognitive functions and symptoms well (Borsboom, 2017).

Further, the observation that the network of neuropsychological functions was denser and the global connectivity was significantly stronger in the ADHD group compared to the clinical comparison group suggests that an ADHD-specific neuropsychological network may exist and could be a subject for future research. In this way, more research exploring the neuropsychological network characteristics of ADHD is needed, such as, whether a denser and stronger neuropsychological network can still be observed in the ADHD group when compared to other psychiatric conditions specifically. For this purpose, it would be relevant to derive a statistical parameter describing the individual person's fit to the respective network, indicating the fit of one's person network to the network of the respective group. A deeper understanding of the neuropsychological network characteristics of ADHD may be helpful in the clinical evaluation as, for example, the network connections may underline the relevance of the performance pattern over the individual test score. Further, an ADHD-specific neuropsychological network with a corresponding 'network parameter' has the potential to aid the differential diagnostic process in the clinical evaluation of adult ADHD and should be subject of further research.

However, although the network of neuropsychological functions was denser and stronger in the ADHD group compared to the clinical comparison group, a central role of attention functions was observed in both the ADHD and clinical control networks. This indicates that attention may not only play a central role in the clinical syndrome of individuals with ADHD, but also in individuals with other psychiatric conditions. Previous studies showed consistent findings that attention deficits were not specific for ADHD but occur across multiple psychiatric disorders, including major depressive disorder, anxiety disorders, obsessive-compulsive disorder, and schizophrenia (Carter et al., 2010; Grant & Chamberlain, 2022; Tetik et al., 2022; Wang, Zhou, & Zhu, 2020). These findings indicate that attention deficits may be in the center of neuropsychological syndromes and a core clinical feature in a wide range of psychiatric disorders other than ADHD, which further complicates differential diagnosis. In addition, the finding of the central role of attention in both the ADHD and clinical comparisons' neuropsychological networks may have implications for the treatment recommendation and evaluation. For example, clinicians may consider improving attention performance as a primary goal when developing treatment plans for not only ADHD but also other psychiatric disorders. This may apply for both pharmacological and non-pharmacological approaches, such as remedial and compensatory techniques. Improvement in attention performance may thus be a primary indicator of treatment success.

Chapter 5 examined the stability of attention performance in individuals with ADHD over time and revealed that attention performance did not differ significantly between three repeated assessments, suggesting rather stable attention performance over a one-month interval in the majority of individuals. The stable attention performance observed in this study, together with the central role of attention in the neuropsychological function networks, further support the notion that attention performance may be well suited as a basis for clinical evaluation, treatment planning, and treatment evaluation. However, given the relatively small sample size and mixed medication status of participants of chapter 5, the results remain preliminary and require more research including larger samples on homogenous clinical groups to conclude on the stability of attention performance. Moreover, in addition to assessing the stability of attentional performance using a repeated neuropsychological test in clinical practice, another direction for future research is to assess attentional performance in-the-moment during daily life activities. In this regard, ecological momentary assessment (EMA), or e-diaries, may be a good option for future research. EMA is a research method for collecting data that is based on a repeated assessment of participants' behaviors and experiences in the daily environment, with the advantages of increasing ecological validity, minimizing recall biases, and allowing the examination of processes and functions that influence behavior in real-world contexts (Degroote et al., 2020; Koch et al., 2021; Shiffman, Stone, & Hufford, 2008). With modern technology (e.g., apps for smartphones or tablets), EMA has the potential to include both self-reported experiences of cognitive functioning in the moment, and objective indicators of cognition (e.g., speed of responses, variability of responses) in short performance tests. Applying EMA to repeatedly assess attention of individuals with ADHD at different times of the day and week, and during different tasks, has the potential to better understand stability or possible performance fluctuations, determining factors, as well as the role of attention in real-life functioning.

Limitations

The strength of our conclusions may be restricted by several limitations. First, the recruitment and assessment settings were similar across the studies of this thesis by representing adult first-time diagnoses of ADHD from outpatient referral contexts. It would be of interest to examine whether the cognitive characteristics and profiles of those individuals match the profiles of individuals with formal childhood ADHD diagnoses in the past, or diagnoses established in psychoeducational settings on young (emerging) adults. Related to this point, a longitudinal perspective would allow the exploration of the stability of the described cognitive networks in the same individuals across developmental phases or treatment statuses (Campbell, Halperin, & Sonuga-Barke, 2014). Second, it must be noted that data were collected from naturalistic settings and not from controlled (experimental) designs. The naturalistic design, for example, caused the neuropsychological data and diagnostic status to be intertwined as the results of the assessments were accessible to clinicians when establishing diagnoses and may have influenced diagnostic decisions. Third, also related to the naturalistic character of this thesis, the expectations and beliefs of participants may have biased their performance in the assessment. The majority of participants included in this thesis were seeking a diagnostic check-up for adult ADHD when presenting to the outpatient clinic. Help-seeking behavior and expectations towards the clinical assessment may have influenced their response and test performance. Fourth, related to the point of patient characteristics and inter-individual heterogeneity, ADHD symptom presentation, comorbid disorders, and pharmacological treatment status, may be further moderating factors on the presented findings and is worth exploring in more detail (Mckenzie et al., 2022; Sobanski, 2006). Finally, it must be assumed that test performance and inter-relations between tests also depend on the test material and test selection. While test characteristics and demands resemble each other on the computerized test battery of this thesis, it could be speculated that the derived cognitive network may look different on less coherent (paper-pencil) test batteries.

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Summary

This thesis aimed to explore and further define the neuropsychological characteristics of adults with ADHD in order to improve the differential diagnosis, optimize the neuropsychological evaluation, and give the foundation for more targeted and efficient treatment plans. To achieve these goals, the first study (chapter 2) examined a broad range of neuropsychological functions of individuals in the clinical evaluation of adult ADHD and made a thorough comparison of these functions between individuals diagnosed with ADHD and clinical comparison individuals. The second study (chapter 3) further examined the role of performance tests, self-reports, and informant reports in the clinical evaluation of adult ADHD. The relationship between neuropsychological test performances and subjective reports on symptoms and impairments was also examined in this study. Moreover, the third study (chapter 4) addressed the inter-relations of neuropsychological functions in adult ADHD and determines whether particular functions stand out and may play a more central role. Finally, the fourth study (chapter 5) examined whether core neuropsychological functions of adults with ADHD are stable or fluctuate over time in repeated clinical assessments.

Chapter 2 examined the neuropsychological functions of individuals in the clinical evaluation of adult ADHD and revealed that the majority of adults diagnosed with ADHD show impairments in multiple neuropsychological functions, including selective attention, vigilance, interference control, inhibition, and working memory. However, these neuropsychological impairments were not specific to ADHD but occur commonly in individuals from this referral context. This finding suggests neuropsychological assessments using cognitive tests may have limited value in the differential diagnosis of ADHD. Moreover, the relationship between basic and complex cognitive functions was examined and revealed that basic cognitive functions were significantly associated with complex cognitive functions. We concluded and supported earlier research that basic functions may be the foundation of complex cognition and may affect all cognitive operations that build upon it.

Moreover, by examining the role of subjective reports on symptoms and impairments in the clinical evaluation of adult ADHD, chapter 3 highlighted the role of retrospectively self-reported ADHD symptoms in the clinical evaluation of adult ADHD in an outpatient referral context. This study demonstrates that retrospectively self-reported ADHD symptoms have the potential to make a meaningful contribution to the differential diagnosis of ADHD. Additionally, this study revealed that subjective reports of symptoms and impairments have no pronounced predictive value for objective neuropsychological test performances, suggesting that subjective reports of symptoms and impairments and objective neuropsychological test performances

seem to be distinct and nonredundant sources of information and should not be treated interchangeably.

The inter-relations of different neuropsychological functions in adult ADHD were examined in chapter 4. This chapter revealed a denser neuropsychological network with stronger global connectivity in the ADHD group compared to the clinical comparison group, which may be a starting point to identifying intertwined neuropsychological characteristics that are typical for ADHD. Further, centrality estimation underlined the central role of attention-related variables in both the ADHD and the clinical comparison network, which gives implications for the clinical assessment, treatment planning, and treatment evaluation of individuals with cognitive impairment. For example, medications targeted at improving attention performance could be the primary choice in the treatment of ADHD and attentional performance could also be the first choice when evaluating the effectiveness of treatment.

Considering the central role of attention performance among different neuropsychological functions, the final study (chapter 5) further examined the stability of attention performance over time in adults with ADHD by repeatedly assessing attention performance three times in one-month intervals. This study highlights that selective attention and vigilance performance did not differ significantly between three repeated assessments. This study forms an empirical evidence base relevant for clinical practice as it suggests that the results of a one-time attention assessment may be sensitive in revealing attention deficits and may be stable over time for the majority of individuals, thus being useful to guide individual treatment planning and evaluation.

In conclusion, this thesis explored the neuropsychological characteristics of adults with ADHD from various perspectives, starting with a thorough assessment of neuropsychological test performances of individuals in the clinical evaluation of adult ADHD and ending with the stability of central neuropsychological functions in repeated assessments. The main findings of this thesis include, first, that most of the individuals in the clinical evaluation of adult ADHD showed deficits in a range of neuropsychological functions, but no meaningful differences in neuropsychological test performance seem to exist between individuals diagnosed with ADHD and individuals who did not meet the diagnostic criteria of ADHD. Findings demonstrate that neuropsychological deficits were not specific to individuals with ADHD but occur commonly in individuals of this referral context (chapter 2). Chapter 3 underlined the potential of self-reported ADHD symptoms in childhood to differentiate adult ADHD from other clinical conditions. This chapter also stressed that subjective reports on symptoms and impairments and objective neuropsychological test performances should not be treated interchangeably as self- and informant reports failed to predict cognitive dysfunctions as indicated by

neuropsychological test performance. The third study (chapter 4) revealed that various neuropsychological functions were more strongly connected in adults with ADHD than in the clinical comparison group. This study also reveals that attention seems to play a central role in both the ADHD and clinical comparisons' neuropsychological networks. Finally, the fourth study stressed the stability of attention performance in adults with ADHD over three repeated assessments in one-month intervals.

Dutch Summary

Dit proefschrift beoogde de neuropsychologische kenmerken van volwassenen met ADHD te onderzoeken en verder te definiëren om de differentiële diagnose te verbeteren, de neuropsychologische evaluatie te optimaliseren en de basis te leggen voor meer gerichte en efficiënte behandelplannen. Om deze doelen te bereiken, onderzocht de eerste studie (hoofdstuk 2) een breed scala aan neuropsychologische functies van volwassenen die werden gezien voor de klinische evaluatie van ADHD en werd met betrekking tot deze functies een vergelijking gemaakt tussen volwassenen met de diagnose ADHD en zogenaamde klinische vergelijkingspersonen. De tweede studie (hoofdstuk 3) onderzocht de rol van prestatietests, zelfrapportages en rapportages van informanten in de klinische evaluatie van ADHD bij volwassenen. De relatie tussen neuropsychologische testprestaties en subjectieve rapportages over symptomen en beperkingen werd ook in deze studie onderzocht. Vervolgens werd in de derde studie (hoofdstuk 4) gekeken naar de onderlinge samenhang van neuropsychologische functies bij volwassenen met ADHD en werd onderzocht of bepaalde functies mogelijk een meer centrale rol speelden. Ten slotte werd in de vierde studie (hoofdstuk 5) onderzocht of neuropsychologische kernfuncties van volwassenen met ADHD stabiel zijn of fluctueren over de tijd bij herhaalde klinische beoordelingen.

Hoofdstuk 2 onderzocht de neuropsychologische functies van volwassenen die werden gezien voor de klinische evaluatie van ADHD en liet zien dat de meerderheid van de volwassenen met de diagnose ADHD beperkingen vertoonden in meerdere neuropsychologische functies, waaronder selectieve aandacht, vigilantie, interferentiecontrole, inhibitie en werkgeheugen. Deze neuropsychologische beperkingen waren echter niet specifiek voor ADHD, maar komen vaak voor bij volwassenen in deze verwijssituatie. Deze bevinding suggereert dat neuropsychologische beoordelingen met behulp van cognitieve tests van beperkte waarde kunnen zijn bij de differentiële diagnose van ADHD. Verder werd de relatie tussen basale en complexe cognitieve functies onderzocht en bleek dat basale cognitieve functies significant geassocieerd waren met complexe cognitieve functies. Wij concludeerden, in aansluiting op eerder onderzoek, dat basale functies het fundament lijken te zijn van complexe cognitieve functies en van invloed kunnen zijn op alle cognitieve operaties die voortbouwen op deze basale functies.

Door de rol van subjectieve rapportages over symptomen en beperkingen in de klinische evaluatie van ADHD bij volwassenen te onderzoeken, werd in hoofdstuk 3 de rol van retrospectief zelfgerapporteerde ADHD-symptomen in de klinische evaluatie van ADHD bij volwassenen in een ambulante verwijscontext bepaald. Deze studie toonde aan dat retrospectief zelfgerapporteerde ADHD-symptomen een zinvolle bijdrage kunnen leveren aan de differentiële diagnose van ADHD. Bovendien bleek uit dit onderzoek dat subjectieve rapportages van symptomen en beperkingen geen uitgesproken voorspellende waarde hebben voor objectieve neuropsychologische testprestaties, hetgeen suggereert dat subjectieve rapportages van symptomen en beperkingen en objectieve neuropsychologische testprestaties afzonderlijke en niet-overlappende bronnen van informatie lijken te zijn en niet uitwisselbaar zijn.

De onderlinge relaties van verschillende neuropsychologische functies bij volwassenen die werden gezien voor de klinische evaluatie van ADHD werden onderzocht in hoofdstuk 4. Dit hoofdstuk toonde een compacter neuropsychologisch netwerk met sterkere globale connectiviteit in de ADHD groep vergeleken met de klinische vergelijkingsgroep, wat een aanknopingspunt kan zijn voor het identificeren van aan elkaar verbonden neuropsychologische kenmerken die typisch zijn voor ADHD. Verder onderstreepte de centraliteitsschatting de centrale rol van aandachtsgerelateerde variabelen in zowel het ADHD- als het klinische vergelijkingsnetwerk, wat implicaties heeft voor de klinische beoordeling, de planning van de behandeling en de evaluatie van de behandeling van volwassenen met cognitieve beperkingen. Zo zou medicatie gericht op het verbeteren van de aandachtsprestatie de eerste keuze kunnen zijn bij de behandeling van ADHD en zouden aandachtsprestaties ook de eerste keuze kunnen zijn bij het evalueren van de effectiviteit van behandeling.

Gezien de centrale rol van aandachtsprestaties, werd in de laatste studie (hoofdstuk 5) de stabiliteit van aandachtsprestaties over de tijd bij volwassenen met ADHD verder onderzocht door aandachtsprestaties driemaal, met tussenpozen van een maand, te beoordelen. Uit deze studie blijkt dat selectieve aandacht en vigilantie prestaties niet significant verschilden tussen drie herhaalde beoordelingen. Deze studie vormt een empirische basis voor de klinische praktijk, omdat het suggereert dat de resultaten van een eenmalige beoordeling van aandachtsfuncties voldoende kan zijn voor het bepalen van aandachtstekorten, aangezien deze stabiel lijken te zijn over de tijd voor de meerderheid van de personen, en dus kunnen dienen als leidraad voor individuele behandelplanning en evaluatie.

Concluderend, dit proefschrift onderzocht de neuropsychologische kenmerken van volwassenen met ADHD vanuit verschillende perspectieven, te beginnen met een zorgvuldige beoordeling van neuropsychologische testprestaties van volwassenen die werden gezien voor de klinische evaluatie van ADHD en eindigend met de stabiliteit van centrale neuropsychologische functies in herhaalde beoordelingen. De belangrijkste bevindingen van dit proefschrift zijn, ten eerste, dat de meeste volwassenen die worden gezien voor de klinische evaluatie van ADHD tekorten vertoonden in een reeks van neuropsychologische functies, maar dat er geen betekenisvolle verschillen in neuropsychologische testprestaties lijken te bestaan tussen volwassenen met de diagnose ADHD en volwassenen die niet voldeden aan de diagnostische criteria van ADHD. De bevindingen tonen aan dat neuropsychologische tekorten niet specifiek zijn voor volwassenen met ADHD, maar veel voorkomen bij mensen in deze verwijzingscontext (hoofdstuk 2). Hoofdstuk 3 onderstreepte het potentieel van zelfgerapporteerde ADHD-symptomen in de kindertijd om ADHD bij volwassenen te onderscheiden van andere klinische aandoeningen. Dit hoofdstuk benadrukte ook dat subjectieve rapportages over symptomen en beperkingen en objectieve neuropsychologische testprestaties niet uitwisselbaar zijn, aangezien zelf- en informantrapportages prestaties op neuropsychologische tests niet konden voorspellen. De derde studie (hoofdstuk 4) liet zien dat verschillende neuropsychologische functies sterker verbonden waren bij volwassenen met ADHD dan bij de klinische vergelijkingsgroep. Deze studie laat ook zien dat aandacht een centrale rol lijkt te spelen in de neuropsychologische netwerken van zowel de ADHD- als de klinische vergelijkingsgroep. De vierde studie tenslotte benadrukte de stabiliteit van de aandachtsprestaties bij volwassenen met ADHD over drie herhaalde beoordelingen met tussenpozen van een maand.

List of Publications

2022

Guo, N., Koerts, J., Tucha, L., Fetter, I., Biela, C., König, M., ... & Fuermaier, A. B. M. (2022). Stability of Attention Performance of Adults with ADHD over Time: Evidence from Repeated Neuropsychological Assessments in One-Month Intervals. *International Journal of Environmental Research and Public Health*, *19*(22), 15234. DOI: https://doi.org/10.3390/ijerph192215234

Guo, N., Fuermaier, A. B. M., Koerts, J., Tucha, O., Scherbaum, N., & Müller, B. W. (2022). Networks of Neuropsychological Functions in the Clinical Evaluation of Adult ADHD. *Assessment*. DOI: https://doi.org/10.1177/10731911221118673

Fuermaier, A. B. M., Tucha, L., **Guo, N.**, Mette, C., Müller, B. W., Scherbaum, N., & Tucha, O. (2022). It takes time: Vigilance and sustained attention assessment in adults with ADHD. *International Journal of Environmental Research and Public Health, 19*(9), 5216. DOI: https://doi.org/10.3390/ijerph19095216

2021

Guo, N., Fuermaier, A. B. M., Koerts, J., Mueller, B. W., Mette, C., Tucha, L., ... & Tucha, O. (2021). The Role of Self-and Informant-Reports on Symptoms and Impairments in the Clinical Evaluation of Adult ADHD. *Sustainability*, *13*(8), 4564. DOI: https://doi.org/10.3390/su13084564

Guo, N., Fuermaier, A. B. M., Koerts, J., Mueller, B. W., Diers, K., Mroß, A., ... & Tucha, O. (2021). Neuropsychological functioning of individuals at clinical evaluation of adult ADHD. *Journal of Neural Transmission*, *128*, 877-891. DOI: https://doi.org/10.1007/s00702-020-02281-0

P

2019

Wei, L., **Guo, N.*,** Baeken, C., Bi, M., Wang, X., Qiu, J., & Wu, G. R. (2019). Grey matter volumes in the executive attention system predict individual differences in effortful control in

young adults. *Brain topography*, *32,* 111-117. DOI: https://doi.org/10.1007/s10548-018-0676-1

2017

Wang, Y., **Guo, N.*,** Zhao, L., Huang, H., Yao, X., Sang, N., ... & Qiu, J. (2017). The structural and functional correlates of the efficiency in fearful face detection. *Neuropsychologia*, *100*, 1-9. DOI: https://doi.org/10.1016/j.neuropsychologia.2017.04.004

* Shared first authorship

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Curriculum Vitae

Curriculum Vitae

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2011 – 2015	B.Sc. in the Faculty of Psychology, Xinxiang Medical University, China

Publications

Guo, N., Koerts, J., Tucha, L., Fetter, I., Biela, C., König, M., ... & Fuermaier, A. B. M. (2022). Stability of Attention Performance of Adults with ADHD over Time: Evidence from Repeated Neuropsychological Assessments in One-Month Intervals. *International Journal of Environmental Research and Public Health*, *19*(22), 15234. DOI: https://doi.org/10.3390/ijerph192215234

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Fuermaier, A. B. M., Tucha, L., **Guo, N.**, Mette, C., Müller, B. W., Scherbaum, N., & Tucha, O. (2022). It takes time: Vigilance and sustained attention assessment in adults with ADHD. *International Journal of Environmental Research and Public Health, 19*(9), 5216. DOI: https://doi.org/10.3390/ijerph19095216

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C

Guo, N., Fuermaier, A. B. M., Koerts, J., Mueller, B. W., Diers, K., Mroß, A., ... & Tucha, O. (2021). Neuropsychological functioning of individuals at clinical evaluation of adult ADHD. *Journal of Neural Transmission*, *128*, 877-891. DOI: https://doi.org/10.1007/s00702-020-02281-0

Wei, L., **Guo, N.*,** Baeken, C., Bi, M., Wang, X., Qiu, J., & Wu, G. R. (2019). Grey matter volumes in the executive attention system predict individual differences in effortful control in young adults. *Brain topography*, *32,* 111-117. DOI: https://doi.org/10.1007/s10548-018-0676-1

Wang, Y., **Guo, N.*,** Zhao, L., Huang, H., Yao, X., Sang, N., ... & Qiu, J. (2017). The structural and functional correlates of the efficiency in fearful face detection. *Neuropsychologia*, *100*, 1-9. DOI: https://doi.org/10.1016/j.neuropsychologia.2017.04.004

* Shared first authorship

Scientific conferences, Symposium

2021	8th World Congress on ADHD, online. Poster presentation
2023	9th World Congress on ADHD, Amsterdam, The Netherlands. Poster presentation
2021, 2023	Heymans Symposium, Groningen, the Netherland. Poster presentation

Awards

2021	Snijders-Kouwer Award

C

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