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Long-term Outcome of Cognitive and Emotional Functioning in Young People with ADHD

PIA TALLBERG

CLINICAL SCIENCES, LUND | FACULTY OF MEDICINE | LUND UNIVERSITY





PIA TALLBERG is a licensed clinical psychologist, specialized in neuropsychology with an interest in pediatric mental disorders, especially neurodevelopmental disorders. This is a dissertation on the three-year outcome of cognitive, executive and emotional functioning in treatment seeking children and adolescents with ADHD.



Long-term Outcome of Cognitive and Emotional Functioning in Young People with ADHD

Pia Tallberg



LUND
UNIVERSITY

DOCTORAL DISSERTATION

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Abstract Clarification on how cognitive, executive and emotional functioning contribute to symptom reduction or improved function in childhood attention deficit hyperactivity disorder (ADHD) is needed to find additional treatment methods. The clinical utility of continuous performance test (CPT) (Conners' CPT-II, QbTest) to complement rating scales in diagnostic assessments and treatment evaluations (QbTest) was examined using one dataset from clinical records of 118 treatment-seeking youth (ADHD, n = 80; non-ADHD, n = 38) (diagnostic) and one dataset of 56 youth treated for ADHD (treatment evaluation) (Paper I). The course of cognitive, executive, emotional functioning and their relationship with ADHD outcome was investigated in a clinical study group of 137 treatment-seeking youth with ADHD (Papers II, III, and IV). A control group (n = 59) participated in parts of papers II and IV. The youth completed the Wechsler Intelligence Scales, the Conners' CPT II, and the Beck Youth Inventories at baseline and follow-up after three years. Their parents completed the Swanson-Nolan-Pelham Scale, fourth edition (SNAP-IV), the Behavior Rating of Executive Function (BRIEF) at baseline and follow-up, the Five To Fifteen scale at baseline, and the Strengths and Difficulties Questionnaire at follow-up. The Conners' CPT II was useful in diagnostic assessments of ADHD in cases with ambiguous parental/teacher ratings, and the QbTest was useful in identifying patients with a positive response to medical treatment (Paper I). Cognitive, executive, and emotional functioning were largely stable across measuring points in youth with ADHD when using standardized scores, except for worsening verbal functioning and improved reaction time variability (Papers II, III, and IV). Worsened BRIEF scores between baseline and follow-up were associated with ADHD symptom severity and overall functional impairment at follow-up. Self- and parent-rated internalizing symptoms were related to BRIEF composite scores. Verbal functioning predicted whether ADHD children at follow-up attained passing grades. In clinical practice, it is important to monitor cognitive, executive, and emotional functioning in youth with ADHD. Reducing stress and failure in daily life may decrease internalizing symptoms and enable youth with ADHD to manage better in school.			
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MADE IN SWEDEN 

*Till mina kära
Magnus, Disa och Molly*

*”Du har tappat ditt ord och din papperslapp,
du barfotabarn i livet.
Så sitter du åter på handlarns trapp och gråter så övergivet.
Vad var det för ord - var det långt eller kort,
var det väl eller illa skrivet?
Tänk efter nu - förrn vi föser dej bort, du barfotabarn i livet”.*
Nils Ferlin, "Barfotabarn", Bonniers förlag, 1933

Förord

Utan alla er som på något sätt varit delaktiga i arbetet med avhandlingen, hade det faktiskt inte gått. Jag vill särskilt rikta min tacksamhet till:

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Lund, augusti 2021

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Populärvetenskaplig sammanfattning

Den här avhandlingen har som syfte att bidra till att täcka kunskapsluckor om hur tilläggssvårigheter vid attention deficit hyperactivity disorder (ADHD) hos barn förändras och om dessa har ett samband med hur ADHD-problematiken utvecklas under 3 års tid. ADHD är en utvecklingsrelaterad kognitiv funktionsnedsättning som debuterar hos barn och unga, 12 år eller yngre, genom höga nivåer av uppmärksamhet och/eller hyperaktivitet-impulsivitet som orsakar svårigheter att hantera vardagen. Hur funktionsnedsättningen yttrar sig är också avhängigt sociala faktorer som familjen, hem- och skolmiljön. Skolbarn förväntas kunna sitta still, ha impuls kontroll, vara uppmärksamma och koncentrerade samt att samspela med barn i en stor grupp. Det är svårt för barn med förhöjda ADHD-symtom att leva upp till dessa förväntningar och de har därför ofta en försämrad skolfunktion. Andelen personer som uppfyller kriterierna för ADHD i befolkningen är ca 6%, varav ca 2/3 är pojkar. Så ser det ut i hela världen sedan många år tillbaka. Ungefär hälften så många vuxna uppfyller kriterierna för ADHD jämfört med skolbarn, alltså verkar ADHD klinga av hos en stor andel av barnen.

Unga personer med ADHD är en heterogen grupp med samsjuklighet på många olika sätt. Vanliga samtida tillstånd är inlärningssvårigheter, utagerande beteendestörningar och internaliserade svårigheter såsom depression och ångesttillstånd. För att spegla barnets styrkor och svårigheter på ett heltäckande sätt baseras ADHD-utredningar på flera olika metoder: omfattande diagnostiska intervjuer om barnets symtom på ADHD och andra barnpsykiatriska tillstånd samt om barnets fungerande i olika miljöer; breda skattningsformulär som lärare, föräldrar och barnet själv fyller i; intervju om barnets utveckling och sjukdomshistoria (anamnes); observationer och eventuellt neuropsykologiska test. I regel är föräldrarna den huvudsakliga rapportören i ADHD-utredningar för barn och unga.

Unga personer med ADHD får i stor utsträckning behandling för sina ADHD-symtom, oftast läkemedelsbehandling i kombination med utbildning om ADHD och stödåtgärder. Trots det har barn och ungdomar med ADHD sämre förutsättningar för att etablera en fungerande vardag som leder till godkända skolbetyg, utbildning och ett framtida arbete. För att minska de negativa konsekvenserna av ADHD-problematiken, behöver man hitta nya behandlingsmetoder och komplement till de metoder som redan är etablerade. Man behöver ta reda på vilka psykologiska mekanismer som bidrar till symtomminskning eller bättre funktion för barn med ADHD. Det kan exempelvis handla om kognitiva (begåvningsrelaterade) funktioner och exekutiva funktioner (hjärnans styr- och regleringsfunktioner) och emotionella

symtom (ångest, depressivitet). Det finns en kunskapslucka om hur dessa funktioner utvecklas hos unga som behandlats för ADHD samt om dessa påverkar prognosen vid ADHD.

Internaliserade Symtom

Det är vanligt att barn och unga med ADHD har tankar om att känna sig misslyckade, bli orättvist behandlade eller felaktigt uppfattade. Att ha dessa tankar under lång tid har kunnat kopplas till depression och självmordstankar. När barn och unga söker hjälp för sina svårigheter är det lätt att missa symtom på internaliserad ilska, ångest och depressivitet, då dessa kan skymmas av de uppenbara beteendesvårigheterna. Studier har visat att personer med ADHD har en ökad risk för att utveckla internaliserad problematik samt att dessa symtom kan debutera tidigare och ha allvarigare konsekvenser än för personer utan ADHD.

Kognitiva och Exekutiva Funktioner

Barn och unga med ADHD har som grupp en måttlig funktionsnedsättning gällande kognitiva och exekutiva funktioner i jämförelse med kontrollgrupper av barn i allmänhet. Detta är viktigt att beakta, eftersom låg begåvning är en känd riskfaktor för bristfällig yrkesutbildning och arbetslöshet, vilket i förlängningen kan leda till socialt utanförskap. Däremot är det fortfarande oklart huruvida kognitiva och exekutiva funktioner påverkar det kliniska förloppet hos barn med ADHD.

Grovt indelat kan exekutiva funktioner mätas på två olika och kompletterande sätt. Psykologiska test bedömer barnets optimala prestation gällande uppmärksamhet, impulshämning, arbetsminne, planeringsförmåga, i en standardiserad och kontrollerad miljö. Psykologiska test har god förmåga att identifiera barn och unga med kognitiva svårigheter men har en begränsning i att identifiera svårigheter med vardagsfunktioner (funktioner som behövs för att exempelvis klara skolan, ta hand om sig själv och utöva sina intressen). Ett annat sätt att bedöma exekutiva funktioner är genom att barnets omgivning (föräldrar och lärare) skattar barnets beteendemässiga exekutiva funktioner i vardagslivet. Fördelen med dessa är att de har god förmåga att mäta vardagsfunktioner och dessa kan därför utgöra ett bra underlag för behandlingsplanering. Skattningarna verkar också vara mer användbara för att skilja ut barn med ADHD från barn i kontrollgrupper än psykometriska test. Nackdelen är att resultaten påverkas av personerna som skattar samt barnets omgivande miljö.

För att minska subjektiva inslag i ADHD-utredningar har kliniker och forskare haft förhoppningar att objektiva psykologiska test som mäter exekutiva funktioner skulle

kunna användas i diagnostiskt syfte. Datoriserade continuous performance test (CPT) har undersökts i detta syfte. Dessa test fångar barnets kärnsvarigheter i att prestera jämnt och korrekt under en lång tid på en tråkig uppgift, vilket främst speglas av hur barnets reaktionstid varierar. Eftersom man inte kunnat bevisa att exekutiva test, inklusive CPT, kan skilja barn med ADHD från barn med andra utvecklingsrelaterade funktionsnedsättningar, har de bedömts vara otillräckligt tillförlitliga som diagnostiska instrument. Det är oklart om CPT kan fungera som ett komplement när bilden av barnet är otydlig och motsägelsefull.

Artikel I

Artikel I handlar om den kliniska nyttan av att använda CPT som ett komplement i kliniska bedömningar. Den första delen utvärderade Conners CPT-II hos 118 barn som utretts för ADHD. Åttio barn som diagnostiserats med ADHD jämfördes med 38 barn som inte bedömts uppfylla kriterierna för ADHD. Det framkom att Conners CPT-II var till klinisk nytta som ett komplement till skattningsformulär för att bekräfta eller avfärda diagnosen ADHD när resultatet från skattningsformulär av föräldrar och lärare var tvetydiga. Den andra delen utvärderade behandlingsuppföljningar hos 56 unga personer med ADHD som behandlades med centralstimulerande medicin. Resultatet visade att ett annat CPT, QbTest, var till nytta i behandlingsutvärderingar för att fånga upp fler patienter som drog nytta av medicinsk behandling vid ADHD. Detta kan vara viktigt i underbehandlade grupper.

Artikel II, III och IV

Artikel II, III och IV handlar om hur kognitiva, exekutiva och emotionella funktioner förändrades under tre år hos en grupp unga personer som behandlades för sin ADHD-problematik. Vi undersökte också om dessa kognitiva och exekutiva funktioner bidrog till symtomminskning, bättre funktion och internaliserade symtom hos barn med ADHD. 137 barn och ungdomar med ADHD undersöktes neuropsykologiskt när de utreddes för sin ADHD-problematik. De undersöktes med samma metoder tre år senare. I artikel II och IV deltog en kontrollgrupp bestående av 59 skolbarn i samma ålder som ADHD-gruppen. I undersökningen användes vedertagna psykologiska utredningsmetoder som mäter ADHD-symtom (Swanson-Nolan-Pelham scale, fourth edition, SNAP-IV), begåvning och kognitiva funktioner (Wechsler Intelligence Scales for Children, WISC), exekutiva funktioner (Conners CPT-II och Behavior Rating of Executive functions, BRIEF) och internaliserade symtom (Beck ungdomsskalor, Fem Till Femton, FTF, och Strengths and Difficulties Questionnaire, SDQ). Alla instrument utom SNAP-IV är

standardiserade och normerade. Det betyder att råpoängen omvandlats till en standardiserad poäng som genererats från en representativ normgrupp med flickor och pojkar i olika åldrar i befolkningen. Den standardiserade poängen gör att barn i olika åldrar och med olika kön kan jämföras med varandra.

I artikel II rapporteras att ADHD-gruppens kognitiva funktioner låg lägre än kontrollgruppens och att dessa i stort sett var stabila mellan baseline (första mättillfället) och treårsuppföljningen. Undantaget var den verbala funktionen, vars åldersnormerade resultat försämrades i ADHD-gruppen. Arbetsminnet, men ingen annan kognitiv funktion, var associerad med ADHD-symtom longitudinellt. Verbal funktion vid baseline och uppföljning predicerade godkända skolbetyg vid treårsuppföljningen.

I artikel III tydliggörs att alla funktioner som mättes med standardiserade psykometriska test (Conners CPT-II) och föräldraskattning (BRIEF) var i stort sett stabila över tid i ADHD-gruppen. Undantaget var reaktionstidsvariabiliteten, som förbättrades, liksom ADHD-symtomen (SNAP-IV). Försämrade föräldraskattade exekutiva funktioner mellan baseline och treårsuppföljningen var kopplade till högre nivåer av ADHD-symtom och en uttalad funktionsnedsättning vid treårsuppföljningen.

I artikel IV redogörs för hur internaliserade symtom förändrades under tre års tid hos barn med ADHD och huruvida exekutiva funktioner och ADHD-symtom påverkade utvecklingen. ADHD-gruppen hade högre grad av ångest, depression och ilska i jämförelse med kontrollgruppen. Symtomnivån var i stort sett bestående mellan baseline och treårsuppföljningen. Inga statistiskt säkerställda (signifikanta) samband noterades mellan psykologiska test av exekutiva funktioner och internaliserade symtom. Det fanns däremot statistiskt signifikanta samband mellan föräldraskattade exekutiva funktioner och internaliserade symtom hos ADHD-gruppen. Exekutiva vardagsfunktioner, som har med kognitiva funktioner att göra som igångsättning, arbetsminne, planeringsförmåga samt förmåga att hålla ordning på sina saker, var kopplade till internaliserade symtom som skattats av barnen själva och deras föräldrar. Beteendereglering, såsom att hejda impulser, reglera känslor, flexibilitet, övervaka sitt eget beteende, var kopplade till föräldraskattade internaliserade symtom och självskattade symtom av ilska. Alla samband var longitudinella, vilket betyder att alla skattningsformulär och test som ingick i analyserna hade gjorts vid både baseline och treårsuppföljningarna.

Sammanfattning och kliniska konsekvenser av avhandlingens resultat

Avhandlingsresultatet pekar på att beteendemässiga exekutiva funktioner är involverade i det kliniska förloppet vid ADHD gällande symtomutveckling, funktionsnedsättning och graden av internaliserade symtom. Genom att ge barn med ADHD mer och bättre stödinsatser gällande exekutiva vardagsfunktioner kan stress och misslyckanden i vardagen minska, vilket kan öka livskvaliteten och barnens möjligheter att klara skolan.

Övriga slutsatser är att:

- Skolor och BUP-mottagningar bör använda exekutiva beteendeskattningar i det kliniska arbetet.
- Det är viktigt att följa begåvningen hos barn med ADHD för att kunna stödja deras utveckling. Barn med ADHD har ofta svårt att tillägna sig lika mycket skolkunskap som jämnåriga på grund av sin ADHD-problematik. Även om de tidigare legat genomsnittligt gällande den verbala begåvningen, kanske de inte följer den förväntade utvecklingen.
- Det är viktigt att följa upp emotionella svårigheter hos barn med ADHD, även om dessa inte är tydliga för omgivningen.
- Vid otydliga resultat av skattningsformulär kan CPT vara till klinisk nytta i diagnostiska utredningar samt i behandlingsutvärderingar.

List of papers

Paper I. Tallberg, P., Rastam, M., Wenhov, L., Eliasson, G., & Gustafsson, P. Incremental Clinical Utility of Continuous Performance Tests in Childhood ADHD - an Evidence-Based Assessment Approach. *Scand J Psychol.* 2019; 60:1, 26-35.

Paper II. Tallberg, P., Rastam, M., Perrin, S., Hallin, A. L., & Gustafsson, P. A longitudinal Investigation of Cognitive Functioning and Its Relationship to Symptom Severity and Academic Functioning in Treatment Seeking Youth with ADHD. *Scand J Child Adolesc Psychiatr Psychol.* 2015; 9, 52-63.

Paper III. Tallberg, P., Rastam, M., Hallin, A. L., Perrin, S., Gustafsson, P. A Longitudinal Investigation of Executive Functions, Symptom Severity, and Functional Impairment in Clinically Referred Youth with ADHD. *Submitted.*

Paper IV. Tallberg, P., Svanberg, K., Hallin, A-L., Gustafsson, P., Rastam, M., Perrin, S. The Three-Year Outcome of Internalizing Symptoms in Clinically Referred Youth with ADHD and their Relationship to Executive Functioning. *Submitted.*

Abbreviations

ADHD	Attention Deficit Hyperactivity Disorder
BCFPI	Brief Child and Family Phone Interview
BRI	Behavior Regulation Index
BRIEF	Behavior Rating of Executive Function
BYI	Beck Youth Inventories
CI	Confidence Interval
CPT	Continuous Performance Test
DSM	Diagnostic and Statistical Manual of Mental Disorders
EF	Executive Functioning
FSIQ	Full Scale Intelligence Quotient
FTF	Five to Fifteen scale
GEC	Global Executive Composite
Hit RT	Hit Reaction Time
Hit RT SE	Hit Reaction Time Standard Error
MI	Metacognitive Index
MTA	Multimodal Treatment of Attention Deficit Hyperactivity Disorder
m	Mean
NICE	National Institute for Health and Care Excellence
RT	Reaction Time
RTV	Reaction Time Variability
SNAP-IV	Swanson-Nolan-Pelham Scale, fourth edition
SD	Standard Deviation
SDQ	Strengths and Difficulties Questionnaire
WAIS-IV	Wechsler Adult Intelligence Scales, fourth edition
WISC-IV	Wechsler Intelligence Scales for Children, fourth edition

Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental condition with onset in children and adolescents at the age of 12 years or younger, manifesting as inattentiveness and/or as hyperactivity-impulsivity (American Psychiatric Association, 2013). The cause of ADHD is primarily genetic. Genome-wide association studies (GWAS) have shown that ADHD is caused by many common genes, each of which contributes to a small degree. The genetic deviations involved are not unique to ADHD, since they are involved in other psychiatric and somatic conditions as well (Demontis et al., 2019). Both genetic and environmental factors (i.e., psychosocial, and biological) interact causally through complex mechanisms that have not yet been adequately studied (Anttila et al., 2018; Demontis et al., 2019; Keilow et al., 2020; Kim et al., 2020).

Diagnostic Assessments

In Sweden, it is recommended that children who manifest symptoms of inattention, hyperactivity, and impulsivity should be offered educational and behavioral interventions to improve both symptoms and function (SKR Uppdrag Psykisk Hälsa, 2021). In cases when interventions fail to adequately improve function, an assessment for ADHD should be offered. Children with ADHD comprise a heterogeneous group with a high degree of comorbidity relating to various contexts, including learning disorders as well as externalized and internalized impairments (DuPaul et al., 2013; Jensen & Steinhausen, 2015). This heterogeneity is why assessment for ADHD is based on global diagnostic interviews concerning symptoms and function in different settings, broadly validated self-assessment questionnaires, developmental history, observations, and, if necessary, neuropsychological testing aimed at providing a comprehensive overview of the child's problems (NICE, 2021; Pelham et al., 2005).

Factors Complicating Diagnosis

In the 1960s, ADHD was defined based on symptoms and cause, for example, as the hyperkinetic reaction of childhood (American Psychiatric Association, 1968), or as minimal brain dysfunction (MBD) (Taylor, 2009). In 1980, the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition (DSM-III) coined the diagnosis attention deficit disorder (ADD), with or without hyperactivity, based on behavioral criteria, which continued to apply in the subsequent editions, DSM-III-R, DSM-IV,

and DSM-5 (American Psychiatric Association, 1980, 1987, 1994, 2013). In general, parents are the principal source of information relating to ADHD assessments of children and adolescents (Seixas et al., 2012). School is a particularly vulnerable environment for children with ADHD since schoolchildren are expected to be able to sit still, control impulsive behavior, pay attention, concentrate, and interact with other children in a large group. The school environment is where ADHD symptomatology reveals the presence of functional impairment (DuPaul et al., 2018). This may pose a diagnostic dilemma, since reported behavior in one context cannot always be generalized to another, for example, the family environment versus the school environment (Achenbach et al., 1987; De Los Reyes et al., 2015). Consequently, assessments from different respondents display only low to moderate correlation and these opinions may differ even more from the functional image the young person has of him/herself (Bussing et al., 2008; De Los Reyes et al., 2011). Moreover, parents and teachers may have limited ability to judge the child's non-observable problems (Hemmingsson et al., 2017). The historical link between ADHD and brain functioning raised hopes that objective tests, *i.e.*, psychometric testing to measure executive functioning (EF), the brain's control and regulatory functions), which approximates the symptoms of ADHD, could be used for diagnostic purposes (Bloch et al., 2012; Hall et al., 2016; McGee et al., 2000; Vogt & Shameli, 2011).

Executive and Cognitive Functioning in ADHD

Many, though not all, children with ADHD have some degree of functional impairment related to cognitive and executive functioning. As a group, they demonstrate a moderate degree of impairment compared with normative development (Frazier et al., 2004; Pievsky & McGrath, 2018; Willcutt et al., 2005). The common clinical use of cognitive and EF evaluation is to assess functional impairment in children as a basis for a treatment plan. Performance-based testing is important to assess function in the child without the influence of environmental factors that may affect the outcome since the environment is standardized and controlled (Toplak et al., 2013). As a group, children with ADHD demonstrate greater impairment of working memory, attention, inhibition, and planning skills compared with other executive functions (Frazier et al., 2004; Ramos et al., 2020; Willcutt et al., 2005). Continuous performance testing (CPT) measures reaction time (RT) and reaction time variability (RTV) while the child is tasked with responding to certain stimuli (targets) and inhibiting the impulse to respond to other stimuli (non-targets). These tests were developed in the 1950s to assess patients with epilepsy (Beck et al., 1956). Meta-analyses have shown that CPT results show the largest differences between children with ADHD and their non-ADHD counterparts in the control group (Frazier et al., 2004; Pievsky & McGrath, 2018), especially concerning a high degree of RTV (Kofler et al., 2013). Executive tests, including

CPT, are insufficiently reliable as diagnostic instruments since there is no evidence that they can discriminate between ADHD and other developmental impairments (Kofler et al., 2013; Lipszyc & Schachar, 2010; Munkvold et al., 2014; Nichols & Waschbusch, 2004; Preston et al., 2005; Schatz et al., 2001). Instead, executive dysfunction occurs in many psychiatric conditions besides ADHD and has been characterized as a transdiagnostic psychological mechanism (Bloemen et al., 2018; Chang et al., 2020; Martel et al., 2017; Rock et al., 2014). However, it has been suggested that CPT can complement diagnostic assessments in cases in which other information about the child is ambiguous (Jarrett et al., 2016).

Another complementary approach to assessing EF is by employing behavioral ratings of the child's behavioral EF (Gioia et al., 2008; Gioia et al., 2002). These have high ecological validity (measuring everyday EF) and appear to discern the presence of ADHD compared with control groups better than does performance-based EF testing (Biederman, Petty, et al., 2008; Dehili et al., 2017; Tan et al., 2018; Toplak et al., 2009). However, behavioral ratings are not independent of the child's context and environment. Performance-based EF and behavioral ratings of EF are considered to provide complementary information and display only a low degree of correlation (Barkley & Fischer, 2011; Biederman, Petty, et al., 2008; Gerst et al., 2017; Häger et al., 2020; Krieger & Amador-Campos, 2018; Soto et al., 2020; Tan et al., 2018; Toplak et al., 2009; Toplak et al., 2013).

Prevalence

According to meta-analytic studies, the prevalence of ADHD in school children is 5.9%, 2/3 of whom are boys; these figures have remained relatively consistent worldwide and over time (Polanczyk et al., 2007; Polanczyk et al., 2014). The prevalence of ADHD among adults is about half that among schoolchildren (Simon et al., 2009). Despite the stability of symptom burden over time, the incidence of clinically diagnosed ADHD has increased in Sweden, attributable to increased awareness of ADHD in society, as well as other social phenomena (Rydell et al., 2018; Socialstyrelsen, 2021). Diagnostic changes have also contributed to the increase in ADHD diagnoses since more recent DSM editions have less stringent criteria or have included ADHD with a greater number of co-morbid diagnoses (Fabiano & Haslam, 2020).

Clinical Course and Predictors of ADHD Outcome

During normative development, hyperactivity and impulsivity generally decline between childhood and adulthood (Holbrook et al., 2014). Similarly, hyperactivity and impulsivity tend to decrease in children with ADHD, while studies have found that inattention remains more constant across different age groups (Larsson et al., 2011; Sasser et al., 2016; Vergunst et al., 2019). Several studies have addressed how many children with ADHD still have this diagnosis as adults and have reached diverse conclusions, depending on how the studies were conducted and how ADHD was defined (Faraone et al., 2006). A meta-analytic study showed that 15% of children with ADHD still met the full criteria for this diagnosis (based on DSM-IV) as adults, while 65% had persistent subclinical ADHD. The DSM-IV symptom criteria for meeting a full diagnosis of adult ADHD are more stringent than those in DSM-5 (Faraone et al., 2006). More recent follow-up studies of clinical ADHD groups show that 50–85% have persistent ADHD (Langley et al., 2010; McAuley et al., 2014; Murray et al., 2017; Roy, Hechtman, et al., 2017; van Lieshout et al., 2016). Although symptoms subside during childhood, individuals with “remittent” ADHD may retain a vestige of abnormality compared with individuals who undergo normative development (Molina et al., 2009; Ramtekkar et al., 2010) and/or retain some functional impairment in everyday life (Copeland et al., 2015; Hechtman et al., 2016).

The symptoms of ADHD are associated with impairment in several areas of life, including learning, school performance (DuPaul et al., 2018; Frazier et al., 2007), and establishing and maintaining social relationships (Ros & Graziano, 2018). Manifestations of impairment do not depend exclusively on the symptomatic spectrum of the child but also relate to the social class of the family (Roy, Hechtman, et al., 2017) as well as to the support the child receives at home (Mazursky-Horowitz et al., 2018) and in school (DuPaul et al., 2011). Early symptoms of combined-type ADHD along with easily precipitated aggression affect the child’s prognosis (Lahey et al., 2016; Roy, Hechtman, et al., 2017; Sasser et al., 2017). People diagnosed with ADHD during childhood in whom the condition persists into adulthood have been found to have greater problems as adults than their counterparts with a history of ADHD but whose symptoms have subsided (Brook et al., 2013; Hechtman et al., 2016; Kirova et al., 2019; Yoshimasu et al., 2012).

Cognitive Functioning as Predictors

Low intelligence is a known risk factor for poor prognosis in ADHD, especially for education and working life (Cheung et al., 2015; Ramos-Olazagasti et al., 2018; Roy, Hechtman, et al., 2017). This is an important factor since the level of

intelligence within this group is significantly lower than in control groups with normative development (Frazier et al., 2004). A handful of prospective longitudinal studies have explored whether the development of intelligence and other cognitive functions could be involved in the clinical course of ADHD. These studies have certain limitations, however, such as using an older version of the Wechsler Intelligence Scale for Children, third edition (WISC-III), small study groups (Murray et al., 2017; Nyden et al., 2001), or estimated values for the various indices (Agnew-Blais et al., 2019; Biederman et al., 2009; Faraone et al., 2021; van Lieshout et al., 2019). On a group level, impairment in cognitive function remained essentially stable over time in the ADHD group in comparison with normative development, and no association with ADHD outcome was seen (Agnew-Blais et al., 2019; Biederman et al., 2007; Murray et al., 2017; Nyden et al., 2001).

Executive Functioning as Predictors

Several studies have investigated how changes in performance-based EF may be linked with the development of symptoms in ADHD, without being able to ascertain any such associations (Biederman et al., 2009; Gordon & Hinshaw, 2019; Karalunas et al., 2017; Lin & Gau, 2019; Murray et al., 2017; van Lieshout et al., 2019; Vaughn et al., 2011; Wang et al., 2015). Impairment in performance-based EF, just like intelligence and other cognitive functions, remained essentially stable over time in the ADHD group in comparison with normative development (Agnew-Blais et al., 2019; Biederman et al., 2007; Gordon & Hinshaw, 2019; Karalunas et al., 2017; Lin & Gau, 2019; Murray et al., 2017; Vaughn et al., 2011; Wang et al., 2015). There appears to be a paucity of studies that have carried out multiple measurements with behavioral ratings of EF. Two longitudinal studies found that childhood ADHD was associated with self-rated EF in adulthood (Barkley & Fischer, 2011; Schiavone et al., 2019).

To my knowledge, only two longitudinal prospective studies have investigated the association between performance-based EF and functional impairment in ADHD over time, however, these studies failed to prove such a connection (Gordon & Hinshaw, 2019; van Lieshout et al., 2019). One study found that behavioral ratings of EF were associated with school performance in college students in a one-year follow-up study (Dvorsky & Langberg, 2014).

Internalizing Symptoms as Predictors

ADHD associated with externalizing and internalizing psychiatric and developmental problems poses a significant risk of a negative prognosis concerning severe psychosocial impairment and premature death (Cheung et al., 2015; Copeland et al., 2015; Lahey et al., 2016; Ramos-Olazagasti et al., 2018; Sun et al., 2019). Externalizing problems such as oppositional defiant disorder (ODD) and

conduct disorder (CD) are more common in children with ADHD than internalizing problems (Jensen & Steinhausen, 2015). Still, ADHD is a risk factor for developing internalizing problems and the consequences of which are often more serious, and debut earlier when presented with comorbid ADHD (Barbarese et al., 2013; Biederman, Ball, et al., 2008; Daviss, 2008; Sun et al., 2019). Therefore, it is important to understand the mechanisms related to internalizing problems among children with ADHD.

Negative feelings such as anger and irritability at being treated unfairly or misunderstood are common in ADHD (Benarous et al., 2019; Eyre et al., 2017). Helping these children to cope with these negative emotions is important since irritability in children with ADHD is associated with later depression and suicidal ideation (Bauer et al., 2018; Eyre et al., 2019; Roy et al., 2014). When children and adolescents seek help for their problems, it is easy to overlook their elevated levels of internalized anger as well as their symptoms of anxiety and depression, due to the far more obvious functional impairment caused by the behavioral symptoms (Al Ghriwati et al., 2017). How these symptoms evolve and whether there may be any modifying mechanisms remains unclear. A few studies have found that internalizing symptoms improve or remain stable over time (Biederman et al., 2012; Eyre et al., 2019; Hechtman et al., 2004; Hinshaw et al., 2012; Schweren et al., 2019; van Lieshout et al., 2016).

To explore whether there is a potential link between EF and the modification of internalizing symptoms in young people with ADHD, a small number of dedicated studies were carried out, with mixed results. Some studies found no cross-sectional or longitudinal association between performance-based EF and depression (Roy et al., 2014; Schweren et al., 2019; Øie et al., 2018), while other studies did find a negative correlation between performance-based EF and internalizing symptoms (Fenesy & Lee, 2019; Maric et al., 2018; Roy et al., 2014). One meta-analysis found that children with anxiety and ADHD displayed better response inhibition than did children with ADHD alone (Maric et al., 2018). The few studies examining behavioral assessments of EF dysfunction have consistently shown a correlation with internalizing symptoms in adolescents with ADHD (Jarrett, 2016; Knouse et al., 2013; Sorensen et al., 2012; Sorensen et al., 2011).

Treatment

In Europe, a holistic, multimodal approach is recommended for the treatment of ADHD, in which medical treatment should be neither the first nor only intervention. Initial intervention should be to offer the child and family psychoeducation, parenting support programs with elements of behavioral modification, and educational support in school (NICE, 2021). Central nervous system (CNS)

stimulant medications are a well-proven treatment method for alleviating symptoms of ADHD and should be used along with non-pharmacological interventions. They are highly efficacious for reducing symptoms and improving function (Cortese et al., 2018; Ghirardi et al., 2020; Jangmo et al., 2019). Their long-term efficacy in reducing ADHD symptoms remains unclear, however, since the large The Multimodal Treatment of Attention Deficit Hyperactivity Disorder Study (MTA) (NIMH, 2021) has shown that, on a group level, their efficacy tends to taper off after three years (Molina et al., 2009; Swanson et al., 2017). Their long-term benefit in terms of improving school performance appears to be more promising (Lu et al., 2017). Non-pharmacological treatment interventions have displayed mixed benefits. Interventions, such as mindfulness, planning/organization training, or increased physical activity aimed at children and adolescents, have proven efficacious for ADHD symptoms, EF functioning, and psychological well-being (Bikic et al., 2017; Cerrillo-Urbina et al., 2015; Xue et al., 2019; Zang, 2019). School interventions are important for most children with ADHD, even those who do not have learning disabilities in addition to their ADHD (DuPaul & Jimerson, 2014). Although effective treatments for ADHD are available, a great many difficulties often persist in managing symptoms and daily life. The World Federation of ADHD (2021) is addressing a knowledge gap by seeking the causal biological or psychological mechanisms that contribute to symptom reduction or improved function in children with ADHD. Such research is necessary in order to find new treatment methods, or optimize current methods, to achieve better treatment effect (Faraone et al., 2021).

Rationale

ADHD represents an extensive presence in child and adolescent psychiatry. Although most children with ADHD receive treatment for their symptoms, their prospects for success in school, education, and other aspects of daily living remain worse than those of their peers. There is a need to find new or complementary treatment methods to combat the negative consequences of ADHD-related problems. There is a knowledge gap when it comes to uncovering the psychological mechanisms that contribute to symptom reduction or improved function in children with ADHD. Cognitive and executive functioning, and internalizing symptoms have all received inadequate study in relation to their proposed impact on the development among adolescents treated for ADHD and ADHD outcome.

Aims

Paper I

The specific objectives were to investigate the clinical utility of executive testing as a complement to clinical assessments, in part to identify clinical ADHD in a group of youth who sought treatment for suspected ADHD (Study group I) and in part to monitor the treatment outcome of the use of CNS stimulants in adolescents with ADHD (Study group II).

Paper II

The first aim was to investigate how measurements of cognitive functions change over three years in a group of youth in treatment for ADHD compared with a control group of the same age (Study group III). The second aim was to investigate whether cognitive functioning is linked to ADHD symptoms from a longitudinal perspective. The third aim was to investigate whether ADHD symptoms and/or cognitive function can predict whether the child received passing grades in school at follow-up.

Paper III

The primary aim was to investigate the progress of parental-rated EF over three years in a group of youth treated for ADHD and whether this predicts ADHD outcome (Study group III). We also examined the progress in performance-based EF and whether it was predictive of ADHD outcome in the same group.

Paper IV

One aim was to investigate whether self-rated and parent-rated internalizing symptoms were related to ADHD symptoms and/or EF from a longitudinal perspective. Another aim was to examine the changes in self-rated internalizing symptoms of anxiety, depression, and anger over three years in a group of children and adolescents in treatment for ADHD compared with a control group of similar age (Study group III).

Method

Study Group I (diagnostic), Paper I

Clinical retrospective data from ADHD assessments were collected from Child and Adolescent Psychiatry (CAP) clinical records to examine the clinical diagnostic utility of two continuous performance tests, Conners' CPT-II and QbTest. One hundred and eighteen treatment-seeking youth were assessed for ADHD from 1 November 2009 to 31 December 2010 in a CAP clinic in southern Sweden. In the study, children diagnosed with ADHD (the ADHD group = 80: male = 57, female = 23; age, median = 12.5 years, percentile 25–75 [9.6–14.4]) were compared with children who were deemed not to have ADHD (the non-ADHD group = 38: male = 24, female = 14; age, median = 11.2 years, percentile 25–75 [9.6–13.0]) (see flow chart, Figure 1). All children were diagnosed according to DSM-IV (American Psychiatric Association, 1994). The distribution of ADHD subtypes in the ADHD group was: ADHD combined subtype, $n = 56$; ADHD inattentive subtype, $n = 22$; and ADHD hyperactive/impulsive subtype, $n = 2$. In the non-ADHD group, altogether 24 children were diagnosed with either one or more conditions (autism, $n = 5$; tic disorder, $n = 3$; language impairments or learning disorders, $n = 12$, and internalizing problems such as mood disorder or anxiety disorder, $n = 12$). Fourteen children did not fulfill any diagnostic criteria.

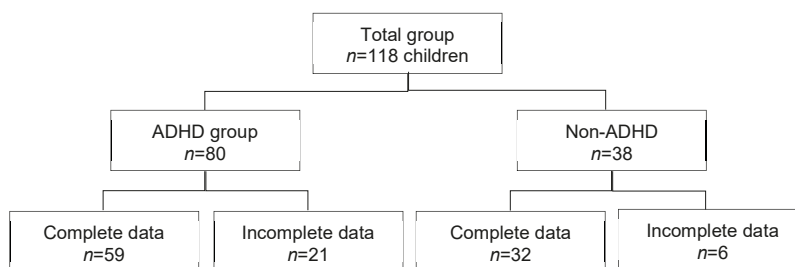


Figure 1 Flow-chart study group I.

Note: ADHD = Attention Deficit Hyperactivity Disorder.

Study Group II (medication), Paper I

Clinical retrospective data from 186 youth with ADHD were collected from clinical records from another CAP clinic in southern Sweden, to evaluate the clinical utility of the QbTest in medical titration. The clinical ADHD diagnoses according to DSM-IV criteria (American Psychiatric Association, 1994) were based on consensus team meetings with licensed CAP clinicians. A total of 186 children with an ADHD diagnosis were assessed using the Swanson-Nolan-Pelham Scale, fourth edition (SNAP-IV) and the QbTest by the team nurses between January 2007 and June 2011 before starting treatment with methylphenidate (see flow chart, Figure 2). They were all followed up and evaluated 1 year later. In 130 children the data were incomplete, leaving 56 patients (male = 45, female = 11; aged 7.1–17.8 years, mean age = 12.3, standard deviation (SD) = 2.4 years) for evaluation and follow-up.

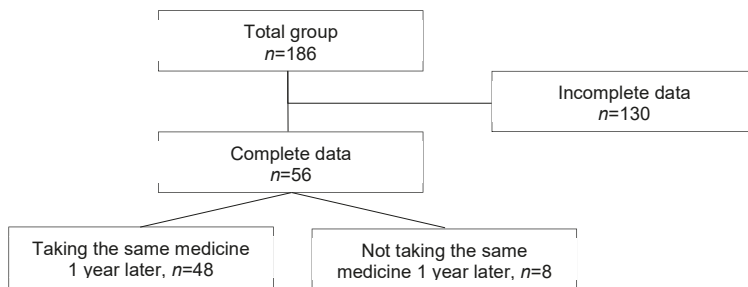


Figure 2 Flow-chart study group II.

Study Group III, Papers II, III, and IV

The participants were recruited between 1 January 2011 and 31 December 2012 from consecutive diagnostic assessments carried out at the Neuropsychiatric Unit of the CAP clinic in Lund, Sweden: $n = 137$ (males = 96, females = 41), mean age = 12.4 years (SD = 3.1; range = 6.7–17.9). The inclusion criteria were: 1) a current diagnosis of ADHD according to the criteria outlined in DSM-IV (American Psychiatric Association, 1994); 2) fluency in Swedish; and 3) absence of a known intellectual disability. In Paper II only, children assessed using the WISC-IV or the WAIS-IV at baseline were included, ADHD group, $n = 125$: male = 87, female = 38, mean age = 11.4 years (SD = 3.3; range = 6.1 years–17.8). Controls, $n = 59$ (male = 31, female = 28) were similarly aged (mean age = 12.0 years; SD = 2.2; range = 8.8–14.9). youths recruited from schools in the same region as the CAP clinic.

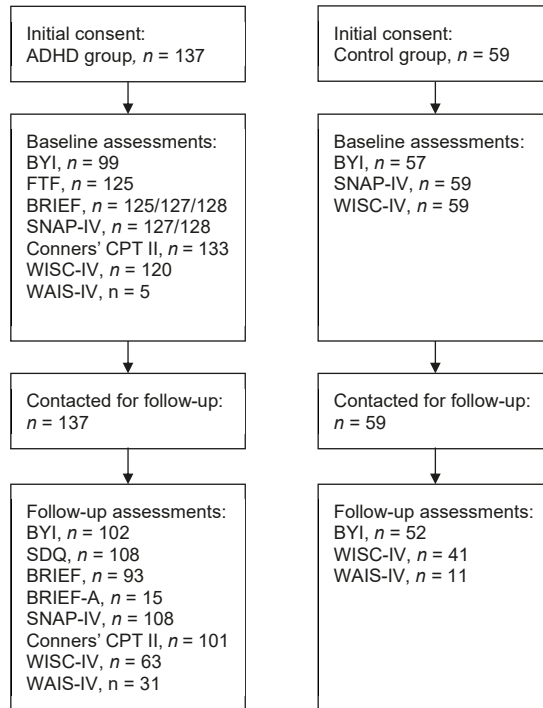


Figure 3 Flow-chart study group III.

Note: ADHD = Attention Deficit Hyperactivity Disorder; BRI = Behavioral Regulation Index; BRIEF = Behavior Rating Inventory of Executive Function; BYI = Beck Youth Inventories; CPT = Continuous Performance Test; FSIQ = Full-Scale Intelligence Quotient; MI = Metacognition Index; RT = reaction time; SNAP-IV = Swanson-Nolan-Pelham scale, fourth edition; Wechsler = Wechsler Adult Intelligence Scales, fourth edition; Wechsler = Wechsler Intelligence Scales for Children, fourth edition. The number of observations in the ADHD group varied due to partial attrition.

Design

For information about measures and variables of the thesis, see Table 1. Paper I is based on cross-sectional historical data of patient records from two CAP clinics in southern Sweden (Study Groups I and II). Papers II, III, and IV are based on a prospective longitudinal study (Study Group III). Baseline data were collected from patient records of clinical ADHD diagnostic assessments from one CAP clinic in LUND. The prospective follow-up assessments mainly used the same assessment methods as the baseline clinical neuropsychological examinations.

Table 1. Outcomes, Independent Variables, Measures, and Controlling Variables used in the Papers.

Variables/Measures	Paper I	Paper II	Paper III	Paper IV
Outcome 1	Clinical ADHD diagnoses	Changes in Cognitive Functions	ADHD Symptoms at baseline and follow-up	Internalizing Symptoms at baseline and follow-up
Measures		Wechsler composites	SNAP-IV	BYI Anxiety, Depression, Anger FTF internalizing subscale SDQ emotional disorder
Independent Variables/ Measures	SNAP-IV	SNAP-IV	BRIEF	BRIEF
	Conners CPT II	Follow-up years	Conners CPT II	Conners' CPT II
	QbTest			SNAP-IV Wechsler Working Memory, Processing Speed
Outcome 2	Treatment outcome	School functioning	ADHD Outcome	Change in Internalizing Symptoms
Measures		Questions on approved grades	SNAP-IV SDQ Impact Score	BYI Anxiety, Depression, Anger
Independent Variables/ Measures	SNAP-IV	Wechsler composites	BRIEF	Follow-up years
	QbTest	SNAP-IV	Conners CPT II	
Outcome 3			Change in EF and ADHD symptoms	
Measures			BRIEF Conners CPT II SNAP-IV	
Independent Variables/ Measures			Follow-up years	
Controlling variables		Gender	Gender	Gender
		ADHD medication	ADHD medication	ADHD medication
		Parents' education level	Parents' education level	Parents' education level
		Wechsler version	Age	Age
		School support		
		FTF		

Note: ADHD = Attention Deficit Hyperactivity Disorder; BRIEF = Behavior Rating Inventory of Executive Function; BYI = Beck Youth Inventories; CPT = Continuous Performance Test; FTF = Five to Fifteen scale; SDQ = Strengths and Difficulties Questionnaire; SNAP-IV = Swanson-Nolan-Pelham scale, fourth edition; Wechsler = Wechsler intelligence scales.

Measures

Self-Rated Internalizing Symptoms

The youth completed the Anxiety, Depression, and Anger Inventories of a validated Swedish-language version of the Beck Youth Inventories (BYI) at baseline and follow-up (Paper IV, Study group III) (Beck et al., 2001, 2004). The BYI also

includes disruptive behaviors and self-concept inventories and was constructed for youth aged 9–18 years. Each subscale covers 20 items rated on a four-point frequency scale (0 = never, 1 = sometimes, 2 = often, 3 = always). The Anxiety Inventory is based on specific worries about school performance, the future, negative reactions of others, and physiological symptoms associated with anxiety. The Depression Inventory consists of items related to negative beliefs about self, life, and the future, feelings of sadness, and sleep disturbance. The Anger Inventory primarily assesses internalizing aspects of anger, for example, thoughts about mistreatment, negative conclusions about others, and physical arousal. Raw scores were standardized according to sex based on a normative sample ($n = 2358$). Higher T scores on all subscales indicate greater symptom severity, in contrast to the Self Concept Inventory where higher scores indicate better Self Concept. The subscales of the BYI have been found to have good psychometric properties, including high internal consistency reliability (.89–.94) (Beck et al., 2004), construct validity, and clinical utility (Bose-Deakins & Floyd, 2004).

Parent-Rated Internalizing Symptoms

The Brief Child Family Phone Interview (BCFPI) (completed by parents in Study group I, Paper I) is a structured telephone interview used as a triage assessment method, administered to parents of 3–18-year-old children and adolescents. Raw scores are converted to T scores ($m=50$, $SD=10$), standardized on Canadian community and clinical samples (Cunningham et al., 2009). The BCFPI includes two mental health composite scales of externalizing and internalizing behavior, one composite scale of children’s global functioning, and one composite scale of family functioning.

Parents completed the Five to Fifteen (FTF) scale (Kadesjo et al., 2004) at baseline (Paper II and IV, Study group III). The FTF is administered to parents and teachers to screen for development-related impairments and behavioral problems in children and adolescents. It consists of 181 items involving eight main domains: Motor Skills, Executive Functions, Perception, Memory Function, Language, Learning Ability, Social Skills, and Emotional Difficulties/Behavioral Problems, each containing further subdomains, rated on three-point scales (0 = Does not apply, 1 = Applies sometimes/to some extent, and 2 = Applies). In Paper II, scores on the parent-reported FTF at baseline were used to describe the additional impairments of the ADHD group. In Paper IV, the 90th percentile cut-off of the Internalizing subscale was used as the baseline measure of Parent-Rated Internalizing Symptoms. The items of the Internalizing subscale cover the child’s self-esteem, depressive symptoms, nervousness, anxiety, self-harm behaviors, and psychosomatic manifestations of internalizing symptoms. The Internalizing subscale has been found to have good psychometric properties and to compare well to the internalizing

scale of the Child Behavior Check List (CBCL) (Achenbach, 1991; Bohlin & Janols, 2004).

Parents finished the Strengths and Difficulties Questionnaire (SDQ) at follow-up (Paper III and IV, Study group III) (Goodman, 1999). The SDQ was developed for general mental health screening in 3–17-year-olds and is available in child, parent, and teacher report versions. The first part of the SDQ consists of 25 questions clustered into five subscales: Emotional Symptoms, Conduct Problems, Hyperactivity/Inattention, Peer Relationship Problems, and Total Stress. The second part covers the child's overall impairment of home life, friendships, classroom learning, and leisure activities by a five-item Impact Supplement ranked on a four-point scale (0 = not at all, 1 = only a little, 2 = quite a lot, 3 = a great deal). Goodman (1999) suggested that Impact scores were better than the subscale scores at identifying clinical samples. The Impact score was used as a measure of overall functional impairment in Paper III. The Emotional Symptoms subscale (90th percentile cut-off) was used as an index of Parent-Rated Internalizing Symptoms at follow-up in Paper IV. The SDQ has shown good psychometric properties, including support for concurrent validity between the Total and Emotional Symptoms subscales of the SDQ and CBCL (Stone et al., 2010).

Parent-Rated Executive Functioning

At baseline and follow-up, parents completed the Behavior Rating Inventory of Executive Function (BRIEF) (Paper III and IV, Study group III) (Gioia et al., 2000). At follow-up, some parents of the participants who were more than 18 years old at follow-up, completed the 75-item informant version of the BRIEF-Adult version (BRIEF-A) (see Figure 3) (Roth et al., 2005). The BRIEF evaluates the everyday behavioral manifestations of EF in children aged 5–18 years, by statements rated on a three-point frequency scale (1 = never, 2 = sometimes, 3 = often), generating an overall general executive composite (GEC) and two index scores. The Behavior Regulation Index (BRI) is based on the Inhibit, Shift, Emotional Control, and Monitor subscales. The Metacognitive Index (MI) is based on the Initiate, Working Memory, Plan/Organize, and Organization of Materials subscales. Raw scores are converted to T scores with a mean of 50 (SD = 10), standardized according to age and sex based on a U.S. national standardization sample ($n = 1419$; 815 girls, 604 boys, aged 5–18 years). Higher T scores imply more severe impairment in EF. The BRIEF was used in Papers III and IV. BRIEF has psychometric support for the composite and index scores, including high internal consistency (.89–.98) and adequate test-retest reliability (.76–.91) (Gioia et al., 2000).

Parent-Rated ADHD Symptoms

Parents and teachers completed the Swanson-Nolan-Pelham Scale, fourth version (SNAP-IV) at baseline (Paper I, Study group I, II) and the parents in the Study group III completed the SNAP-IV at baseline and follow-up (Paper II, III, and IV) (Bussing et al., 2008; Hall et al., 2019). The SNAP-IV consists of 26 items rated on a four-point scale (0 = not at all, 1 = just a little, 2 = quite a bit, 3 = very much), based on the DSM-IV diagnostic criteria of ADHD in a parent and teacher report format. The SNAP-IV consists of four subscales; Inattention symptoms (9 items), Hyperactivity/Impulsivity symptoms (9 items), all items together yield ADHD-Combined Score (18 items), and a scale measuring Oppositional Defiant Disorder symptoms (8 items) The summary scores or the mean scores of the SNAP-IV Inattention, Hyperactivity/Impulsivity, and/or ADHD-Combined Score were used in all papers. The internal reliability coefficients for these three subscales are acceptable (Cronbach's alpha = .90, .79, and .89, respectively) (Bussing et al., 2008). The SNAP-IV has shown validity for use in identifying children with varying levels of ADHD, although not as a diagnostic instrument (Bussing et al., 2008; Hall et al., 2019).

Performance-Based Tests

The youth completed Version II of Conners' Continuous Performance Test (CPT-II) at baseline and follow-up (Paper I, III, and IV, Study group I and III) (Conners, 2002; Conners et al., 2003). The Conners' CPT-II is a computerized psychometric test assessing visual attention, vigilance, response inhibition, reaction time (RT), and reaction time variability (RTV) for individuals aged 6 years and above. Usually, CPTs instructs the individual to press a computer key after an X is presented; conversely, the Conners' CPT-II instructs the individual to press a computer key immediately after every letter except the X, which is a more complex task. Targeted and non-targeted stimuli are randomly shown for 250 ms, with one, two, and four inter-stimuli intervals between presentations, for 14 minutes. The Conners' CPT-II generates twelve measures, of which five were used in Papers I, III, and IV: Omissions, Commissions, Hit RT (mean), Hit RT standard error (SE), and the percentage overall fit to an attention deficit profile, the CPT Confidence Index. Raw scores are converted to T scores with a mean of 50 (SD = 10), standardized according to age and sex, based on a normative sample including 1920 healthy individuals from the general population and 378 individuals with ADHD (Conners, 2002). The Omission score measures the number of times the participant fails to press the space bar when a target letter is presented. The Commission score measures the number of space bar presses in response to a non-target letter. The Hit RT (mean) measures the average speed of correct responses for the entire test, a kind of complex RT, with higher values indicating slower response times.

Psychometric support for the individual measures is provided in the manual; for the subscales of the current study: the split-half reliability is .65–.95 and three-month test-retest reliability coefficients are .55–.84 (Conners, 2002).

Study Groups I and II (Paper I) completed a computerized CPT and activity test, the QbTest (Knagenhjelm & Ulberstad, 2010). Like other CPTs, QbTest measures visual attention, vigilance, response inhibition, reaction time (RT), and reaction time variability (RTV). Additionally, the QbTest evaluates hyperactivity by registering head movements via an infrared emitter and camera, sending infrared light to a reflector placed on the forehead of the individual during the test. As in Conners' CPT-II, the individual being tested is asked to press a key on the computer keyboard each time a target stimulus is shown, but not when a non-target figure is shown. The target stimulus for 6–12-year-old children is a grey circle without a cross and the non-target stimulus is a circle with a cross on it. The stimuli for individuals 13–55 years of age are four different figures: a red circle, a blue circle, a red square, and a blue square; the target stimulus is a repetition of the figure previously shown. Each stimulus is shown for 100 ms for children 6–12 years of age and 200 ms for 13–55-year-olds. The inter-stimulus interval is 2 s (Brocki et al., 2010; Knagenhjelm & Ulberstad, 2010). Parameters used in Paper I were Qb Activity, Qb Impulsivity, and Qb Inattention. The results are expressed as standard deviations from normal values. Qb Activity is calculated from time active, distance, area, and micro-events. The QbTest has been approved by the US Food and Drug Administration (FDA; Ref: K133382) to complement other methods for evaluating the effect of central stimulant treatment for ADHD. The test-retest reliability was found to be high, with $r = 0.87$ for Qb Inattention and $r = 0.88$ for Qb Activity (Ramtvedt & Sundet, 2014).

Youth of Study group I and III (Paper I, II, and IV), aged 6–16 years, completed the WISC-IV (Wechsler, 2003) and youth older than 16 years completed the WAIS-IV (Wechsler, 2008) (see Figure 3). The WISC-IV and the WAIS-IV each comprise ten core battery subtests, yielding four composites. The WISC-IV composites (subtests) are: Verbal Comprehension (Similarities, Vocabulary, Comprehension), Perceptual Reasoning (Block Design, Picture Concepts, Matrix Reasoning), Working Memory (Digit Span, Letter–Number Sequencing), Processing Speed (Coding, Symbol Search), and full scale intelligence quotient (FSIQ). The composites for the WAIS-IV are the same as for the WISC-IV, except for: Verbal Comprehension, in which Comprehension is substituted with Information; Perceptual Reasoning, in which Picture Concepts is exchanged with Puzzles; and Working Memory, in which Letter–Number Sequencing is replaced with Arithmetic. The subtests, as well as the composite scores, are standardized according to age, the composite scores with a mean of 100 and SD of 15. The WISC-IV and WAIS-IV were used in Papers I, II, and IV.

Procedure Paper I

Study Group I (diagnostic)

Members of Study Group I (diagnostic) (see flow-chart Figure 1) were screened for general psychiatric symptoms by specially trained nurses using the parent-reported Brief Child and Family Phone Interview (BCFPI). The assessments were performed by a multidisciplinary team and consensus diagnoses were assigned by the team. The assessments consisted of child psychiatric examinations (including neurological status) performed by child psychiatrists, clinical semi-structured interviews with the parents and teachers, children-completed interviews, and neuropsychological examinations. The age of onset was established from the child's developmental history. See Figure 4 for the screening results of the BCFPI and the results of neuropsychological examinations.

Study Group II (medication)

The screening procedure and diagnostic assessments for Study Group II (see flow-chart Figure 2) were conducted similarly as described above for Study Group I. The participants started central stimulant treatment after the diagnostic feedback. Titration of the optimal dose of methylphenidate in the treatment of ADHD was performed following general principles for dose titration (NICE, 2008). Dosage titration started at a low dose of 18 or 20 mg, and the dose was titrated in steps of 10 mg for Ritalin, Equasym, and Medikinet and of 18 mg for Concerta up to a maximal dose of 60 mg (or less in case of marked side effects). At each dose, the parents and teachers completed the SNAP-IV scale, and the child completed the QbTest. A decrease in SNAP-IV symptom scores of about 0.4 SD was defined as a clinically significant improvement, yielding a decrease in SNAP-IV scores of > 0.2 (0.4 SD lies between the scores of 0.2 and 0.3). Similarly, a decrease in QbTest scores of > 0.4 SD was defined as a clinically significant improvement. The titration was regarded as negative if none of the doses yielded a clinically significant improvement. The titration was regarded as positive if one or more of the doses yielded a clinically significant improvement and the dose with the best results (optimal dose) was used. A good outcome was defined as being on the optimal dose one year after titration.

Procedure Papers II, III, and IV

Baseline Assessments

Figure 3 presents the workflow of the baseline and follow-up assessments. The baseline data of the ADHD group were gathered from their clinical records of the diagnostic assessments. A team of licensed clinicians including child and adolescent psychiatrists, psychologists, and sometimes also social workers conducted the diagnostic assessments. The ADHD diagnoses were based on the DSM-IV criteria using information from multiple sources: comprehensive psychiatric interviews with the children and their parents, semi-structured telephone interviews with the children's teachers, and neuropsychological assessments including the rating scales and performance-based tests used in the papers of this thesis. The assessments of the WISC-IV and WAIS-IV were often performed by the referring school psychologists prior to the child's work-up at the CAP clinic. All ADHD participants were medication naïve at the baseline assessment.

Contemporary with the written informed consent procedure, parents of the Control group finished the SNAP-IV and replied to written questions about their educational level. No diagnostic interview was carried out with the participants in the Control group. Psychological assessments took place at a quiet room of the participant's school by an experienced licensed neuropsychologist, or by supervised clinical psychology students trained to use these assessment methods.

Follow-up Assessments

After the child was assessed and diagnosed with ADHD at baseline, their parents attended a psychoeducation program on ADHD management. Most of the ADHD participants were treated with stimulant medication (81%). Participants in the ADHD and Control groups were invited for reassessment approximately three years after the baseline assessment (see flowchart for the workflow and participation of the different assessment methods, Figure 3). The youth of both groups and the parents of the ADHD group answered some dichotomous questions about their status concerning medication use, support from the school, and school grades. All ADHD participants were prompted to stop taking their stimulant medication 24 hours before the follow-up assessment. The participants of the ADHD group were examined at the CAP clinic and the Control group in a quiet room at their school or the CAP clinic. For both groups, the examinations were performed by a licensed neuropsychologist or supervised clinical psychology students trained to administer these scales.

Analytical and Statistical Methods

Between-group comparisons (ADHD vs. Control group; completers vs. dropouts) were analyzed using Chi-square, Mann-Whitney U-test, Student's independent *t*-tests, logistic regression analyses, and area under the receiver operating characteristics (ROC) curve (AUC) were carried out using version 22 or 25 of SPSS (IBM Corp., Armonk, NY, USA). Linear mixed-model regression analyses were carried out using version 9.4 of SAS (SAS Institute Inc., Cary, NC, USA).

Analytical and Statistical Methods Paper I

Study I (diagnostic)

We examined the clinical diagnostic utility of Conners' CPT II and QbTest in Study Group I (diagnostic). First, we analyzed the ROC curve to examine the diagnostic accuracy of the overall assessment measures concerning the outcome variable, the clinical diagnosis of ADHD. The evaluated variables were continuous values of the Confidence Index in Conners' CPT II as well as Qb Activity, Qb Impulsivity, and Qb Inattention in the QbTest. Only assessment methods with AUC $p \leq .05$ were further analyzed.

Second, the clinical utility was defined by the degree of increment or decrease in post-test probability by stepwise adding different assessment methods. The post-test probabilities were calculated according to Bayes' theorem, which can be formulated as follows: Probability (of a true outcome when the test is positive) = Probability (of the test being positive when having a true outcome) \times Probability (of having a true outcome) / Probability (of the test being positive).

The judgment of clinical utility is based on cost-benefit reasoning (Youngstrom, 2014; Youngstrom et al., 2015). A post-test probability of 85% was judged to be acceptable as an operationalizing of the clinical utility since an 85% chance of ADHD is reasonable for most clinicians to start treatment. Eight possible combinations of test results from dichotomized values of Conners' CPT II Confidence Index (cut-off = 50) and parent and teacher SNAP-IV scores for combined ADHD (MTA cut-off, for parent ratings = 1.67 and for teacher ratings = 2) were analyzed.

Study II (medication)

To examine the clinical utility of the QbTest in medical titration (Study Group II (medication)), we first conducted Spearman correlations of the results of the QbTest, *i.e.*, Qb Activity, Qb Impulsivity, and Qb Inattention, between participants receiving the "optimal dose" and participants with a "good outcome." A good outcome was defined as remaining on the optimal dose one year after titration. An optimal dose was defined as yielding a decrease in SNAP-IV symptom scores or

QbTest scores of > 0.4 SD. QbTest variables yielding $p < .20$ in the correlation analyses were further analyzed. Univariate logistic regression analyses, as well as sensitivity and specificity, were calculated for the SNAP-IV parameters, QbTest variables, and their stepwise combinations. In the stepwise analyses, SNAP-IV ratings by parents were first analyzed. If the results were inconclusive (i.e., no optimal dose could be identified), Qb Inattention was analyzed. If results still were inconclusive, an analysis of Qb Activity was conducted.

Statistical Analyses Study Group III, Papers II, III, and IV

Variables

The variables used in Study group III (Papers II, III, and IV), all administered at both baseline and follow-up, are presented below:

- Self-rated internalizing symptoms in sex-standardized T scores ($m = 50$, $SD = 10$) of the BYI subscales Anxiety, Depression, and Anger
- Parent-rated ADHD symptoms in summary raw scores of the SNAP-IV subscales: SNAP-IV ADHD-Combined, Inattention, and Hyperactivity/Impulsivity summary scores
- Parent-rated EF was measured in age- and sex-standardized T scores ($m = 50$, $SD = 10$) of the BRIEF GEC, the BRIEF BRI and corresponding subscales Inhibit, Shift, Emotional Control, and Monitor, and the BRIEF MI and corresponding subscales Initiate, Working Memory, Plan/Organize, and Organization of Materials
- Performance-based cognitive functioning measured in age-standardized IQ scores ($m = 100$, $SD = 15$) of the composites of the Wechsler Intelligence Scales FSIQ Verbal Comprehension, Perceptual Reasoning, Working Memory, and Processing Speed
- Performance-based EF measured in age- and sex-standardized T scores ($m = 50$, $SD = 10$) of the Conners' CPT-II subscales Omissions, Commissions, Hit RT (mean), and HIT RT SE; the percentage fit of clinical inattention profile yielded the CPT Confidence Index
- A dichotomous variable Parent-Rated Internalizing Symptoms was measured with the internalizing symptom subscales of the FTF at baseline and the SDQ at follow-up. For both the FTF and SDQ internalizing symptom scales, a 90th percentile cut-off (based on sex- and age-normative data) was used (0 = below cut-off; 1 = above cut-off).

The Impact score from the parent version of the SDQ was only administered at the follow-up. We used a cut-off (yes/no) based on the recommended clinical cut-off of a score ≥ 2 .

Linear mixed models, Papers II, III, and IV

Linear mixed models with an autoregressive covariance structure were used to analyze change over time (follow-up time in years) for the Wechsler composites (Paper II), the CPT-II variables, the BRIEF composites, the SNAP-IV (Paper III), and the BYI Anxiety, Depression, and Anger subscales (Paper IV). In Papers II and IV, an interaction term between group and time was included to compare change over time between the ADHD group and the Control group. To reduce the impact of the attrition, estimated and adjusted mean scores from the linear mixed models were used when presenting the mean scores, and when comparing scores between the ADHD group and the Control group. To minimize the effect of attrition, linear mixed models with an autoregressive covariance structure were also used to analyze possible relationships between the dependent and independent variables in Papers II, III, and IV. Long-term measures were analyzed (measured at baseline and follow-up).

Paper II

Linear mixed models were used to analyze the effect of the independent variables, *i.e.*, (1) parent-rated ADHD-symptoms and SNAP-IV ADHD-Combined Score, (2) time (follow-up time in years), (3) gender, (4) use of the WAIS-IV versus WISC-IV, (5) receipt of special educational support, and (6) treatment with ADHD medication, on the dependent variables, *i.e.*, the Wechsler composites, in four models. For the Control group, the same independent variables were evaluated except for parent ratings from the SNAP-IV and treatment with ADHD medication at follow-up. Unstandardized beta values, corresponding 95% CIs, and *p*-values < .05 are reported.

Aside from the linear mixed models, logistic regression models were used to analyze the effect of baseline and follow-up measures of ADHD symptom severity (SNAP-IV ADHD-Combined Score) as well as cognitive functioning (Wechsler composites) on school grades (dependent variable) at follow-up in the ADHD group only. The predictor variables were added in two models: (1) baseline scores from the SNAP-IV (ADHD-Combined Score) and Wechsler composite scores, and (2) with the follow-up scores on these same measures. Several controlling variables (assessed at baseline) were entered in each model: sex (being female), receiving special educational supports, assessment via the WAIS-IV (*vs.* WISC-IV), parents' education level, and scores on the Externalizing and Internalizing subdomains from the parent-rated FTF. Odds ratios with corresponding 95% CIs and *p*-values < .05 are reported.

Paper III

Linear mixed models were used to analyze the effect of the independent variables, *i.e.*, 1) parent-rated EF (BRIEF composites) and 2) performance-based EF (CPT-II subscales), on the dependent variables, *i.e.*, parent-rated ADHD symptoms (SNAP-

IV subscales). Unstandardized b -values, corresponding 95% CIs, and p -values $< .01$ are reported (to balance the risk of type I and type II errors).

Standard linear regression analyses were performed to investigate whether the course of EF was related to ADHD symptoms at follow-up. The independent variables were the changes in standardized T scores for the BRIEF subscales and CPT-II subscales, between baseline and follow-up (follow-up scores minus baseline scores). The dependent variable was ADHD symptoms (SNAP-IV ADHD-Combined Score) at follow-up. The independent variables in the linear regression analyses were analyzed independently, with ADHD symptom severity at baseline used as a covariate in all analyses. Unstandardized b -values with corresponding 95% CIs and p -values $< .01$ are reported.

Simple logistic regression analyses were performed to investigate whether the course of EF was related to overall impairment at follow-up. Changes in BRIEF subscales and CPT-II subscales were calculated as described above. The Impact score from the parent version of the SDQ completed at the follow-up assessment was used as the dependent variable, dichotomized (yes/no) based on the proposed clinical cut-off of a score ≥ 2 . The independent variables in the logistic regression analyses were analyzed independently. Odds ratio with corresponding 95% CIs and p -values $< .01$ are reported.

All analyses in Paper III were adjusted for ADHD medication status and parents' education level. The change in SNAP-IV scores was also adjusted for age. Only results that remained significant after the adjustment analyses are reported in the results.

Paper IV

The possible relationships between each dependent variable, *i.e.*, the Anxiety, Depression, and Anger Inventories from the BYI, were analyzed using linear mixed modeling in two steps:

1. Unadjusted analyses of the potential relationships between each dependent variable and each independent variable, a composite score (BRI and MI scores from the BRIEF), performance-based tests of EF (Confidence Index from the CPT-II, Working Memory and Processing Speed), and ADHD-Combined Score from the SNAP-IV. Composite scores with $p < .05$ were further analyzed.
2. The effects of the subscales of the composite score, with $p < .05$, on the dependent variables were analyzed in four potential models. The independent variables in the first model were scores on the Inhibition, Shift, Emotional Control, and Monitor subscales corresponding to the BRI (BRIEF). The independent variables in the second model were scores on the Initiate,

Working Memory, Plan/Organize, and Organization of Materials subscales corresponding to the MI (BRIEF). The independent variables in the third model were scores on the Omissions, Commissions, Hit RT (mean), Hit RT SE (CPT-II), Working Memory, and Processing Speed (Wechsler scales). The independent variables in the fourth model were the Inattention and Hyperactivity/Impulsivity subscales (SNAP-IV). Unstandardized *b*-values with corresponding 95% CIs and *p*-values < .01 are reported. All analyses were adjusted for age, ADHD medication status, and parents' education level.

Logistic mixed models were used to analyze whether the measurements of EF and ADHD symptoms (measured at baseline and follow-up) had any significant effect on Parent-Rated Internalizing Symptoms (measured at baseline and follow-up). The analyses were conducted in the same two steps, with the same independent variables, as described above. Odds ratios, corresponding 95% CIs, and *p*-values are reported. All analyses were adjusted for age, ADHD medication status and parents' education level.

Only results that remained significant after the adjustment analyses are reported in the Results section.

Ethical Considerations

All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The Studies I, II (Paper I), and the Study III (Paper II, III, IV) were included in a larger project approved by the Research Ethics Committee at Lund University, Lund, Sweden (Reg. No. 2012/88). Written informed consent was obtained from all participants in Study III, *i.e.*, parents of the youth and the youth themselves aged 15 years and older. Study III was registered in the ClinicalTrials.gov Protocol Registration and Result System (ID: NCT04201509, protocol ID: 2012/88).

Results

Paper I

Sociodemographic Characteristics, Attrition, and Clinical Data

Out of 118 children in Study Group I (diagnostic), complete data were obtained for 91 children, for an attrition rate of 23%. In the ADHD group, data were incomplete for 21, while in the non-ADHD group, data were incomplete for 6, see Figure 1. The 27 children with incomplete data were compared with the 91 with complete data with regard to existing common variables. We found no significant differences, according to the Mann-Whitney U-test, for any of the analyzed variables (SNAP-IV parent and teacher rating scale, QbTest, and Conners' CPT-II results) as well as age and gender.

There was no significant difference in intellectual ability (Wechsler Intelligence Scale for Children, FSIQ: for the ADHD group, mean = 87.15, 95% CI [74.58, 99.72], and the non-ADHD group, mean = 91.86, 95% CI [78.59, 105.13]). For clinical data, see Figure 4. There were significant differences in: BCFPI Regulating Impulsivity & Activity ($p = .002$), Regulating Attention, Impulsivity & Activity ($p = .003$), and Family Functioning ($p = .017$); SNAP-IV Parent Hyperactivity/Impulsivity ($p = .035$), Teacher Inattention ($p = .005$), and Teacher Hyperactivity/Impulsivity ($p = .002$); all Conners' CPT II scores, all p values $\leq .008$; and QbTest impulsivity scores ($p = .045$), with more impaired results in the ADHD group than the non-ADHD group.

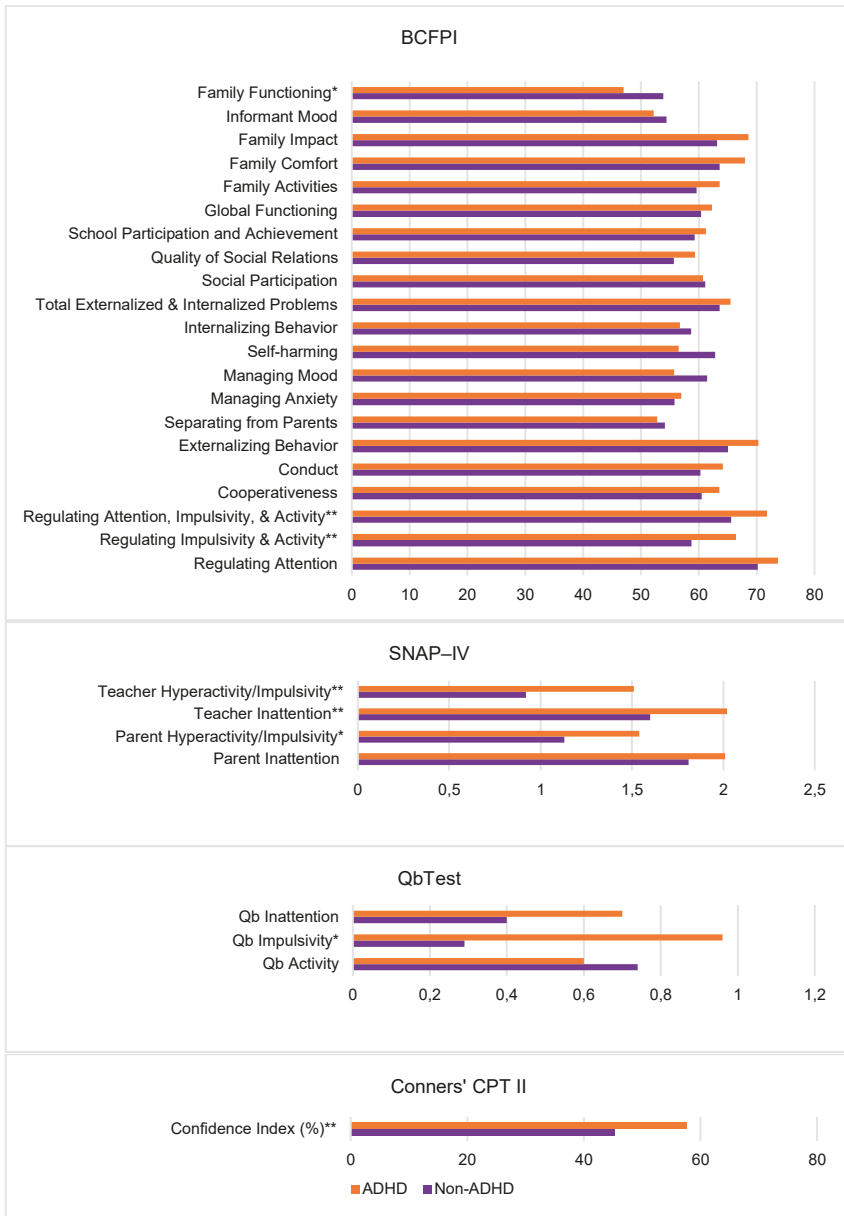


Figure 4. Bar chart of the mean values of Brief Child and Family Phone Interview, SNAP-IV, QbTest, and Conners' CPT II for Study Group 1 (diagnostic).

Note: ADHD = Attention Deficit Hyperactivity Disorder; BCFPI = Brief Child and Family Phone Interview; CPT = Continuous Performance Test; SNAP-IV = Swanson, Nolan and Pelham, version IV, scale. BCFPI are converted into age- and sex-standardized T scores ($m = 50$, $SD = 10$); SNAP-IV is measured in mean raw scores. QbTest results are converted into age- and sex-standardized Q scores, i.e., a statistical model to transform skewed statistical distributions into normally distributed z-scores ($m = 0$, $SD = 1$). Conners' CPT II Confidence Index represents the percentage fit to clinical ADHD profile. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

In Study Group II (medication), QbTest data were incomplete for 130 out of 186 cases. Therefore, only 56 children had QbTest results from assessments of different doses of central stimulants, making titration possible. When comparing the different variables in the group between those with complete versus incomplete data, no significant differences according to the Mann-Whitney U-test were found concerning the number of individuals on the same medication, the indication of the optimal dose one year later, parent and teacher SNAP-IV scores, QbTest results, or sex. There was a significant age difference between the group with complete data (mean age = 12.3, SD = 2.5 years) and the group with incomplete data (mean age = 13.5, SD = 3.0 years) ($p = 0.003$).

Analysis of the Clinical Utility of CPT in Diagnostic Assessments (Study Group I, diagnostic)

The ROC analyses yielded a statistically significant AUC for Conners' CPT II Confidence Index (AUC = .73, $p < .001$). The AUC for the QbTest measures Attention, Activity, and Impulsivity were not statistically significant.

Post-test probabilities were calculated for the eight possible combinations of the outcome measures. Conners' CPT II showed good incremental validity when parent and teacher SNAP-IV ratings were ambiguous. In cases in which both parent and teacher ratings were above the cut-off, the probability of diagnosis was good enough to confirm the ADHD diagnosis, with post-test probability $> .89$. In the case of conflicting results, the probability was not high enough to confirm or low enough to dismiss an ADHD diagnosis, post-test probabilities .70–.74. Adding Conners' CPT II Confidence Index above the cut-off increased the overall probability of an ADHD diagnosis to a sufficiently high level to confirm ADHD, post-test probability .89–.91. Adding Conners' CPT II Confidence Index below the cut-off reduced the probability of an ADHD diagnosis to a sufficiently low level to dismiss ADHD, post-test probability .60–.65.

Analysis of the Clinical Utility of CPT in Treatment Evaluations (Study Group II, medication)

When Spearman correlations were analyzed, only Qb Inattention was significantly correlated with finding the optimal dose one year later ($\rho = .29$, $p = .013$). Qb Impulsivity yielded insignificant results ($p > .20$) in predicting the treatment response one year later and was omitted from further analyses. Logistic univariate analyses of good outcome (being on the optimal dose one year later) were significant with Qb Inattention as the dependent variable (odds ratio 2.64, 95% CI [1.139–6.12]) but not for the SNAP-IV inattention parent-rating scale.

The probability of predicting a good outcome was calculated for the SNAP-IV Parent Inattention rating scale, Qb Inattention, and Qb Activity, as well as for the combinations of SNAP-IV Parent Inattention rating scale and the two QbTest variables (see Table 2 for results). Of the SNAP-IV variables, only SNAP-IV Inattention was analyzed since all other parent- and teacher-reported SNAP-IV scores showed no significance when compared with the treatment effects one year later. Children without an optimal dose, according to SNAP-IV, were identified. For these children, we further analyzed the Qb Inattention results to find an optimal dose. The sensitivity increased when QbTest supplemented SNAP-IV to a high level. For individuals without a clear result for Inattention, using either the SNAP-IV parent-rating scale or Qb Inattention, we also analyzed Qb Activity to find an optimal dose, and then almost all individuals (47 out of 48) with a good outcome were identified (sensitivity 0.98), but the specificity was low.

Table 2. Titration of the optimal dose, Study Group II (medication).

Measures	Sensitivity	Specificity	True positive cases	True negative cases	False positive cases	False negative cases
SNAP-IV Parent Inattention (<i>n</i> = 56)	.56	.75	27	6	2	21
Qb Inattention (<i>n</i> = 60)	.82	.6	41	6	4	9
Qb Activity (<i>n</i> = 60)	.76	.4	38	4	6	12
SNAP-IV Parent Inattention + Qb Inattention (<i>n</i> = 56)	.94	.62	45	5	3	3
SNAP-IV Parent Inattention + Qb Inattention + Qb Activity (<i>n</i> = 56)	.98	.25	47	2	6	1

Note: SNAP-IV Parent Inattention = parent ratings of the Swanson, Nolan, and Pelham, version IV (SNAP-IV), scale for inattention.

QbTest performed with the calculation of the parameters Qb Inattention and Qb Activity. The outcome was defined as being on the optimal dose one year after titration. An optimal dose was defined as a decrease in SNAP-IV symptom scores or QbTest scores of >0.4 SD. Qb Activity, Qb Impulsivity, and Qb Inattention.

Sociodemographic Characteristics, Attrition, and Clinical Data: Study group III (Papers II, III, and IV)

Of the 137 participants in the ADHD group at baseline, 96 (70%) were boys compared with 31 of 59 (52%) in the Control group ($\chi^2(1) = 5.56, p = .018$). The sex ratio at the follow-up assessment was similar. The two groups did not differ in mean age at baseline or follow-up (age at baseline: ADHD 12.4 years [SD = 3.1], Controls 12.0 years [SD = 2.2]; age at follow-up: ADHD 15.2 years [SD = 3.0], Controls 14.8 years [SD = 2.0]). The parents' levels of education at baseline were as follows: Primary school only (to age 16 years) – ADHD 11%, Controls 4%; High school (age 16–19 years) – ADHD 46%, Controls 35%; University or above –

ADHD 43%, Controls 61%. The two groups did not significantly differ for this variable ($\chi^2(2) = 5.38, p = .08$).

There was no significant difference in the attrition rate between the two groups: 111/137 (81%) of the ADHD and 52/59 (88%) of the Controls participating both at the baseline and follow-up assessments. Compared with ADHD participants who completed the follow-up, those lost to follow-up in the ADHD group had more severe parent-rated inattention symptoms (SNAP-IV, mean difference [M_{diff}] = 2.36, $t(126) = 2.09$, 95% CI [0.13, 4.60], $p = .038$) and EF difficulties (BRIEF MI, $M_{\text{diff}} = 4.60$, $t(123) = 2.15$, 95% CI [0.36, 8.35], $p = .034$), as well as poorer cognitive functions (Wechsler scales FSIQ, $M_{\text{diff}} = 8.54$, $t(123) = 3.39$, $p = .001$, 95% CI [3.55, 13.52]; Verbal Comprehension, $M_{\text{diff}} = 7.57$, $t(123) = 2.81$, $p = .006$, 95% CI [2.23, 12.90]; and Perceptual Reasoning, $M_{\text{diff}} = 7.89$, $t(123) = 2.79$, $p = .006$, 95% CI [2.29, 13.50]). No significant differences were observed between completers and non-completers of the follow-up assessment for baseline scores on the BYI, CPT-II, Working Memory, or Processing Speed composites/subscales. There was partial attrition for the BYI at the baseline assessment since 22 participants younger than 9 years old and another 16 children did not complete this measure. The number of children in the ADHD group presenting parent-rated Internalizing Symptoms $\geq 90^{\text{th}}$ normative cut-off at baseline was 58/125 using the FTF, and at follow-up was 12/100 using the SDQ. Figures 5 and 6 presents descriptive clinical data for continuous values of the measures.

Paper II

Group Differences and Stability of Wechsler Scale Composite Scores

There was a significant negative effect of group (ADHD versus Control group) (all $p < .001$) for baseline measures: FSIQ ($M_{\text{diff}} = -7.54$, 95% CI [-11.25, -3.84]), Working Memory ($M_{\text{diff}} = -11.05$, 95% CI [-14.68, -7.42]), Processing Speed ($M_{\text{diff}} = -9.68$, 95% CI [-13.82, -5.55]), and for all the follow-up measures: FSIQ ($M_{\text{diff}} = -12.05$, 95% CI [-15.85, -8.24]), Verbal Comprehension ($M_{\text{diff}} = -10.67$, 95% CI [-14.95, -6.39]), Perceptual Reasoning ($M_{\text{diff}} = -7.30$, 95% CI [-11.63, -2.96]), Working Memory ($M_{\text{diff}} = -8.63$, 95% CI [-12.42, -4.83]), and Processing Speed ($M_{\text{diff}} = -11.76$, 95% CI [-16.06, -7.46]). Figure 5 presents estimated mean values for the baseline and follow-up values of the Wechsler composite score for both groups, after controlling for whether or not the baseline assessment was conducted using the WAIS-IV instead of the WISC-IV. For ADHD participants, there was a significant and negative effect of time (*i.e.*, a slight decline in scores) on the FSIQ ($\beta = -0.51$, 95% CI [-0.097, -0.06], $p = .028$), Verbal Comprehension ($\beta = -0.76$,

95% CI [-1.31, -0.21], $p = .007$), and Processing Speed ($\beta = -0.72$, 95% CI [-1.41, -0.03], $p = .040$). There was a significant and positive effect of time (e.g., a slight increase in scores) on Verbal Comprehension ($\beta = 2.32$, 95% CI [1.35, 3.28], $p < .001$) in the Control group. The slopes for the FSIQ ($p = .001$) and Verbal Comprehension differed significantly between the two groups ($p < .001$).

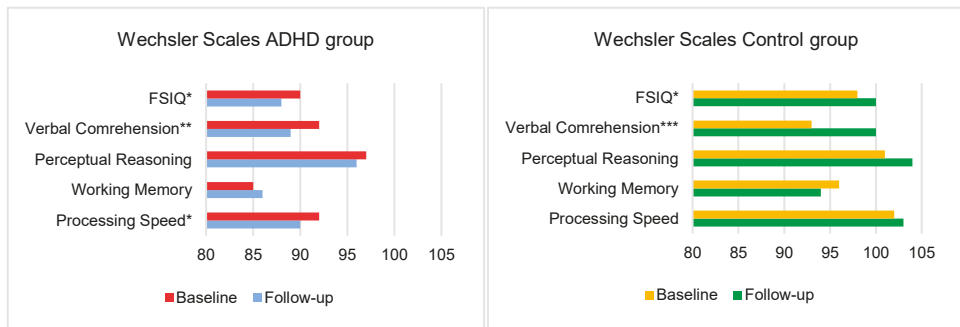


Figure 5. Bar chart presenting estimated mean values for the baseline and follow-up values of the Wechsler composite score for the ADHD and Control groups.

Note: ADHD = Attention Deficit Hyperactivity Disorder; FSIQ = Full-Scale Intelligence Quotient. The mean values are controlled for Wechsler version used in first and second assessments (WISC-IV versus WAIS-IV). WISC-IV and WAIS-IV were measured in age-standardized IQ scores, $m = 100$, $SD = 15$. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Associations Between the Index and Composite Scores and the Severity of ADHD Symptoms and Other Predictors

Significant results ($p < .05$) of linear mixed modeling analyses of the relationships between the Wechsler composite scores (dependent variable) and the independent variables – *i.e.*, time, sex, use of WAIS-IV versus WISC-IV, receipt of special educational support, parent-rating of ADHD (combined) severity (SNAP-IV), and, when applicable, treatment with ADHD medication – are described below.

The severity of ADHD symptoms (SNAP-IV) was negatively associated with Working Memory scores ($b = -0.23$, 95% CI [-0.41, -0.06], $p = .009$) and the use of the WAIS-IV as opposed to the WISC-IV was associated with lower Verbal Comprehension scores ($b = -5.79$, 95% CI [-10.31, -1.27], $p = .014$) in the ADHD group. In the ADHD group, Processing Speed was positively associated with female sex ($b = 6.19$, 95% CI [0.70, 11.68], $p = .028$) and the use of the WAIS-IV as opposed to the WISC-IV ($b = 10.51$, 95% CI [4.98, 16.04], $p = .001$). No other significant association was found for the ADHD group.

Relationship Between Grades, ADHD Symptoms, and Wechsler Composites

Significant results ($p < .05$) of logistic regression analyses evaluating the effect of parent-rated ADHD symptoms (SNAP-IV) and Wechsler composite scores at (1) baseline and (2) follow-up on whether the child received a majority of passing grades (yes/no) at the follow-up for the ADHD group only are described below:

(1) The model with baseline predictors (measures of SNAP-IV [parent version] and Wechsler composites at baseline) was not significant ($\chi^2(5) = 5.86$, $p = .32$, Nagelkerke $R^2 = .09$); however, verbal comprehension at baseline was a significant predictor of having a majority of passing grades at follow-up (odds ratio = 1.05, 95% CI [1.00, 1.10], $p = .031$).

(2) The model with follow-up predictors (measures of SNAP-IV [parent version] and Wechsler composites at follow-up) was significant ($\chi^2(5) = 23.80$, $p < .001$, Nagelkerke $R^2 = .36$). Verbal Comprehension scores at follow-up were associated with a significantly higher likelihood of receiving a simple majority of passing grades at follow-up (odds ratio = 1.11, 95% CI [1.04, 1.19], $p = .001$). Less severe ADHD symptoms (SNAP-IV) were also significantly associated with an increased likelihood of achieving a simple majority of passing grades at follow-up (odds ratio = 0.92, 95% CI [0.87, 0.98], $p = .007$). The results did not differ significantly when we controlled for confounders. No other variables yielded significant odds ratios.

Paper III

Improvements in ADHD Symptoms and EF from Baseline to Follow-Up

Linear mixed models were used to analyze the change in ADHD symptoms and EF between baseline and follow-up (see Figure 6). With respect to ADHD (SNAP-IV), significant improvements between baseline and follow-up were found for Inattention symptoms ($b = -0.60$, 95% CI [-1.01, -0.20], $p = .004$), and the Hit RT SE subscale from the CPT-II ($b = -1.15$, 95% CI [-1.88, -0.41], $p = .003$) in crude analysis and when adjusting for the controlling variables (ADHD medication use and parents' level of education). Crude analysis showed that the changes in Hyperactivity/Impulsivity symptoms, Omissions (CPT-II), and the MI (BRIEF) across time points were significant; however, when adjusting for the controlling variables (ADHD medication use and parents' level of education, and also age for SNAP-IV), these variables were no longer significant. Age at baseline and follow-up significantly affected Hyperactivity/Impulsivity symptoms (older age was associated with decreased symptoms) ($p < .001$). No significant baseline to follow-up change was found for

Commissions, Hit RT (mean) from the CPT-II, or the BRI index from the parent-rated BRIEF in the crude analyses or after adjusting for the controlling variables.

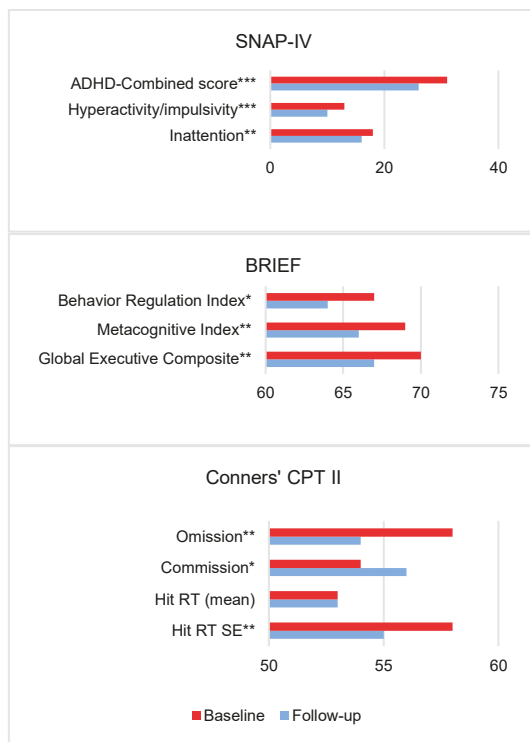


Figure 6. Bar chart presenting estimated mean values for the baseline and follow-up values of the Conners' CPT II, the Swanson-Nolan-Pelham Scale, fourth edition, and the Behavior Rating of Executive function for the ADHD at baseline and the 3-year follow-up.

Note: BRIEF = Behavior Rating of Executive Function; CPT = continuous performance test; RT = reaction time; SE = standard error; SNAP-IV = Swanson-Nolan-Pelham Scale, fourth edition. The CPT II and BRIEF were age and sex standardized in T scores. Parent-rated SNAP-IV was measured as a summary score.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Relationships between EF and ADHD Symptoms

Linear mixed modeling analyses of the effects of EF (BRIEF and CPT-II) on ADHD symptom severity (SNAP-IV) were performed. These analyses used baseline and follow-up data simultaneously. The results yielding $p < .01$ even when adjusting for ADHD medication status (yes/no) and parents' education level are described. Inattention ($b = 0.17$, 95% CI [0.11, 0.22], $p < .001$), Hyperactivity/Impulsivity ($b = 0.38$, 95% CI [0.33, 0.43], $p < .001$), and ADHD-Combined Score ($b = 0.56$, 95% CI [0.48, 0.64], $p < .001$) were significantly associated with T scores on the BRI. Inattention ($b = 0.38$, 95% CI [0.32, 0.44], $p < .001$), Hyperactivity/Impulsivity ($b = 0.29$, 95% CI [0.21, 0.38], $p < .001$), and ADHD-Combined Score ($b = 0.68$, 95%

CI [0.56, 0.79], $p < .001$) were also significantly associated with MI scales from the BRIEF. There were significant effects of Hit RT SE on SNAP-IV inattention ($b = 0.11$, 95% CI [0.04, 0.18], $p = .002$), Hyperactivity/Impulsivity ($b = 0.15$, 95% CI [0.07, 0.23], $p < .001$), and ADHD-Combined Score ($b = 0.25$, 95% CI [0.13, 0.38], $p < .001$).

Relationship between EF Change Scores and ADHD Symptom Severity and Impairment at Follow-Up

Standard linear regressions were performed to assess the effect of change scores, from baseline to follow-up, for the BRIEF and CPT-II subscales on ADHD symptom scores measured at follow-up, when controlling for baseline ADHD symptom scores. The results yielding $p < .01$ even when adjusting for ADHD medication status (yes/no) and parents' education level are reported. Worsened BRIEF subscales were significantly associated with ADHD symptom severity at follow-up. All measures yielded $p < .001$. No other change scores were significantly associated with ADHD symptom scores at follow-up.

Logistic regressions were performed to examine the effect of the change scores, between baseline and follow-up, for the BRIEF and CPT-II subscales on the Impact scores measured at follow-up with the SDQ (baseline to follow-up changes). The results yielding $p < .01$ even when adjusting for ADHD medication status (yes/no) and parents' education level are reported. Worsened T scores for BRIEF Emotional Control (odds ratio = 1.07, 95% CI [1.03, 1.12], $p = .001$), Initiate (odds ratio = 1.09, 95% CI [1.04, 1.14], $p = .001$), and Working Memory (odds ratio = 1.09, 95% CI [1.04, 1.14], $p < .001$) were associated with functional impairment measured with SDQ Impact score at follow-up. Baseline to follow-up changes in the CPT-II subscales were not significantly associated with the Impact scores at follow-up.

Paper IV

The Effect of EF and ADHD Symptoms on Internalizing Symptoms

Significant results ($p < .01$) of linear mixed model analyses of the effect of EF and ADHD symptoms on the self-rated internalizing symptoms of BYI Anxiety, Depression, and Anger, even after adjusting for age, ADHD medication status (yes/no), and parents' education level, are described below.

Concerning Anxiety, in the first step, the effect of parent-rated EF (BRIEF MI) yielded a p -value less than .05 (.031), controlling for age, ADHD medication status

(yes/no), and parents' education level. In the second step, Anxiety was significantly associated with Plan/Organize ($b = 0.30$, 95% CI [0.11, 0.50], $p = .003$) in the model including all MI subscales from the BRIEF (Initiate, Working Memory, Plan/Organize, Organization of Materials).

Concerning Depression, in the first step, there was a significant association with BRIEF MI ($b = 0.23$, 95% CI [0.09, 0.36], $p = .001$). The effect of SNAP-IV ADHD-Combined Score on depression was significant in unadjusted analyses ($b = 0.16$, 95% CI [0.05, 0.28], $p = .007$), but not when controlling for age, ADHD medication status (yes/no), and parents' education level. However, we proceeded to the second step. Depression was significantly associated with SNAP-IV Inattention symptoms ($b = 0.48$, 95% CI [0.23, 0.73], $p < .001$) in the model with the Inattention and Hyperactivity/Impulsivity subscales.

Concerning Anger, in the first step, there were significant associations with the BRI ($b = 0.27$, 95% CI [0.16, 0.38], $p < .001$) and MI ($b = 0.28$, 95% CI [0.13, 0.42], $p < .001$) indexes from the BRIEF.

In the second step, Anger was significantly associated with the Emotional Regulation subscale ($b = 0.23$, 95% CI [0.06, 0.40], $p = .008$) from the BRI (BRIEF) in the model with all the BRI subscales (Inhibition, Emotional Regulation, Flexibility, and Monitor).

Significant results of logistic mixed modeling analyses of the effect of EF and ADHD symptoms on Parent-Rated Internalizing Symptoms, after adjusting for age, ADHD medication status (yes/no), and parents' education level, are described below

Parent-Rated Internalizing Symptoms were significantly associated with BRI (odds ratio = 1.08, 95% CI [1.05, 1.11], $p < .001$) and MI scores (odds ratio = 1.10, 95% CI [1.06, 1.15], $p < .001$) from the BRIEF.

Group Differences and Changes in Internalizing Symptoms between Baseline and Follow-up

Significant results ($p < .01$) of linear mixed model analyses of the change in self-rated internalizing symptoms of BYI Anxiety, Depression, and Anger, even after adjusting for age, ADHD medication status (yes/no), and parents' education level, are reported below.

The ADHD group rated significantly higher levels of Anxiety ($b = 9.92$, 95% CI [6.65, 13.19], $p < .001$), Depression ($b = 9.69$, 95% CL [6.55, 12.83], $p < .001$), and Anger ($b = 10.27$, 95% CI [7.00, 13.53], $p < .001$) T scores at baseline and follow-up, analyzed simultaneously. There was a significant improvement in crude analysis of the change in Anger symptoms for the ADHD group ($b = 0.89$, 95% CI [-1.54,

-0.24], $p = .008$). Sensitivity analyses suggested that after adjusting for the controlling variables, age, ADHD medication status and parents' education level, there was no significant change in Anger T scores ($p = .036$) in the ADHD group and no significant change in Anxiety ($p = .242$) or Depression ($p = .331$) T scores in the Control group. There were significant positive effects of age in Anxiety ($p = .002$), Depression ($p = .008$) (both groups).

Comprehensive discussion

Main findings

Paper I

The aim was to examine the clinical utility of CPT in diagnostic assessments of ADHD as well as in treatment evaluations. As previously shown by Jarrett (2017), we found that the Conners' CPT II was clinically useful as a complement to questionnaires, to confirm or reject the diagnosis in cases in which results of parent and teacher assessment questionnaires were ambiguous. Clinical uncertainty may delay assessments and therefore CPT can be cost-effective, even if an extra test slightly increases the time required for the assessments.

Previous studies have found that CPT may be clinically useful when following up the response to treatment with medications (Park et al., 2012; Ramtvedt & Sundet, 2014). Similarly, we found that QbTest may be useful in treatment evaluations in undermedicated populations. Supplementing rating scales with QbTest increased sensitivity, identifying more patients who possibly would benefit from the medical treatment of ADHD.

Paper II

The aim was to examine the changes in age-standardized measures of cognitive functions between baseline and three-year follow-up and their relationship with ADHD symptoms and school grades. The pattern of our results is essentially in agreement with past findings, that impairment in cognitive function persisted over time in the youth with ADHD, and no association with ADHD outcome was seen (Agnew-Blais et al., 2019; Biederman et al., 2007; Murray et al., 2017; Nyden et al., 2001). Perceptual reasoning, working memory, and processing speed remained largely stable between baseline and three-year follow-up compared with normative development for both groups and no association with ADHD symptoms was found for verbal function, perceptual reasoning, and processing speed in the ADHD group. By contrast, age-standardized scores of verbal function, worsened in the ADHD group compared with the control group, which displayed improvement.

Verbal function is intimately connected to learned knowledge (Schipolowski et al., 2014). In line with this, the level of verbal function at baseline and the levels of verbal function and ADHD symptoms at three-year follow-up were related to passing school grades at three-year follow-up. One study has previously shown that

verbal function is positively associated with scholastic achievement, and negatively related to hyperactivity and impulsivity (Vigil-Colet & Morales-Vives, 2005). Furthermore, low intelligence is a well-known risk factor for impairment in education and working life (Cheung et al., 2015; Ramos-Olazagasti et al., 2018; Roy, Hechtman, et al., 2017). Taken together, concurrent evaluation of cognitive functioning seem to provide important information in terms of intervention planning for school supports to prevent school failure.

Paper III

The aim was to investigate the changes in standardized measures of EF between baseline and three-year follow-up and their relationship with ADHD symptoms and overall impairment at follow-up in youth with ADHD. Standardized measures of parent-rated EF and performance-based EF remained essentially stable over the three years until the follow-up, except for RTV, which improved, as did ADHD symptoms. Several studies have shown cross-sectional associations between parent-rated EF and ADHD symptoms (Biederman, Petty, et al., 2008; Dehili et al., 2017; Tan et al., 2018; Toplak et al., 2009). Correspondingly, we found significant associations between several measures of parent-rated EF and ADHD symptoms when using longitudinal data. Furthermore, worsened parent-rated EF between baseline and follow-up were associated with ADHD symptom severity and overall impairment at three-year follow-up.

The pattern of results concerning the associations between the changes in performance-based EF and the development of symptoms in ADHD is consistent with the previous literature, not being able to ascertain any such associations (Biederman et al., 2009; Gordon & Hinshaw, 2019; Karalunas et al., 2017; Lin & Gau, 2019; Murray et al., 2017; van Lieshout et al., 2019; Vaughn et al., 2011; Wang et al., 2015). However, we found that RTV was associated with ADHD symptoms, when using longitudinal data. This result is consistent with cross-sectional findings that RTV is a sensitive parameter for measuring impairment in ADHD (Kofler et al., 2013).

Diversities in the relationship between parent-rated EF and parent-rated ADHD symptoms versus CPT and ADHD symptoms may be explained by the type of measurement used. For example, meta-analyses have shown higher agreement between informants from the same environments than informants from different environments (parents at home contrasted with teachers in school) (Achenbach et al., 1987; De Los Reyes et al., 2015). Still, our results strengthen the temporal validity of parent-rated EF in the home context in youth with ADHD.

Paper IV

The aim was to examine the changes in self-rated internalizing symptoms between baseline and follow-up in youth with ADHD as well as in a control group and, in the ADHD group only, their relationships with EF and ADHD symptoms. Using longitudinal data, parent-rated EF was associated with self-rated and parent-rated internalizing emotional symptoms among youth with ADHD, consistent with previous cross-sectional studies (Jarrett, 2016; Knouse et al., 2013; Sorensen et al., 2012; Sorensen et al., 2011). Specifically, self-rated internalizing anger and parent-rated internalizing symptoms were associated with parent-rated EF composite scores globally. Self-rated anger was related to planning and organizational skills when controlling for other aspects of metacognitive EF. Self-rated anger was also related to emotional regulation when controlling for other aspects of behavioral regulation. Self-rated depression was associated with metacognitive aspects of EF, while anxiety was associated with planning and organizational skills when controlling for other aspects of metacognitive EF.

Using longitudinal data, we did not find any significant association between internalizing symptoms and performance-based EF in youth with ADHD. Previous studies have obtained inconsistent results concerning the link between internalizing symptoms and performance-based EF in youth with ADHD (Roy, Oldehinkel, et al., 2017; Schwaren et al., 2019; Øie et al., 2018).

When controlling for age, self-rated internalizing symptoms of anxiety, depression, and anger remained largely stable over the three years in both the ADHD group and the Control group. Internalizing symptoms in youth may go unnoticed because parents and teachers are more concerned about the child's obvious behavior disorder (Al Ghriwati et. al., 2017). Impairments in the behavioral aspects of EF and their contributions to impairments in day-to-day functioning may have a negative effect on the child's self-esteem. The correspondence between internalizing symptoms and parent-rated EF is important because it reveals prospects for treatment interventions that can contribute to a better outcome for young people with ADHD. For instance, one meta-analysis, as well as a recent overview, suggest that physical exercise might be effective for mitigating ADHD (Cerrillo-Urbina, et al., 2015; Christiansen et al., 2019) and also internalized symptoms and EF impairments in youth with ADHD (Cerrillo-Urbina, et al., 2015).

Methodological Considerations

This thesis must be considered in light of certain limitations and strengths. First, it is crucial to consider that all the clinical ADHD study groups were clinically referred and received treatment for ADHD, based on DSM-IV, in specialist CAP

services. As such, the present sample attained at the higher end on parent-rated measures of ADHD, with additional impairments in cognitive, executive, and emotional functioning at baseline. The generalizability of the results is consequently limited to clinical ADHD. It cannot be ruled out that population-based study groups would present results that differ from the results of the study groups of this dissertation. Furthermore, the baseline datasets were collected from clinical records from the diagnostic workups. The current CAP clinic did not use validated, structured diagnostic interviews when data was collected. Consequently, the diagnostic methodology to examine co-morbidity in the ADHD group was not consistently applied; thus, no reliable data of comorbid conditions were generated. This is partly because learning-related diagnoses were made in other units and partly because the main focus in the clinical evaluations was ADHD. Instead, results were available from well-validated global screening assessments (*i.e.*, FTF) highlighting developmental and child psychiatric symptoms. However, not being able to control for comorbidity is a weakness, which calls for further investigations in future studies. For the same reason, there was also some attrition, for example, concerning the WISC-IV standard battery that was usually administered at school and the Beck Youth Scales that younger children were unable to complete. The statistical approach, using linear mixed models compensated for the attrition because all participants who contributed at least one observation participated in the analyzes. No diagnostic assessment was made in the Control group, so it cannot be ruled out that some participants in the Control group suffered from psychiatric disorders. Furthermore, there were significantly more boys compared to girls in the ADHD group, contrary to the Control group, with equal amount of boys/girls. The participants' age range in the ADHD group was larger compared with the Control group.

Paper I (Study group I) reports on the evaluation of various methods used in the diagnostic assessments. The diagnoses were primarily based on diagnostic interviews with parents and teachers, as well as on an assessment questionnaire and psychological testing. The study methods were included as part of the overall assessment, but these did not serve as the basis for any diagnosis. However, there remains a risk of “criteria contamination”, which could have biased the results (Youngstrom, 2014).

Paper II, III, and IV report on the change in standardized measures of cognitive, executive, and emotional functioning at a group level. The dissertation's results on stable standardized measures of cognitive, executive, and emotional functioning must not be mistaken to apply to individuals clinically. Analyses at the group level may conceal variability in individuals. Additionally, attention needs to be paid to the use of standardized measures in this regard. Stability in standardized measures implies that the group follows the normative development and that their percentage deviation is maintained.

There were many analyses conducted in paper II,III, and IV. Multiple comparison problems cannot be ruled out. However, we used p-values $< .01$ in paper III and IV as a compromise between type I error (false positives) and type II error (false negatives).

The main finding of paper III is that parent-rated EF is associated with parent-rated symptoms of ADHD. Instruments that use the same respondent are based on information from a single context. Other studies have found that respondents from different contexts have low to moderate correlation (De Los Reyes et al., 2015). Consequently, the results cannot be generalized to other contexts, such as schools. To reduce bias from using one and the same respondent, the study would have benefited from the addition of teacher assessments.

There are also some strengths to note. First, the longitudinal prospective design was accomplished with a relatively low level of attrition. Follow-up studies pose a challenge when it comes to obtaining follow-up data from all individuals. Some children with ADHD may balk at coming to a child psychiatry clinic to work on cognitively demanding tasks without a clinical purpose. Second, the methods used in the papers are widely used in clinical work as well as in research and have been validated for youth with ADHD in independent scientific studies. Third, both performance-based testing and assessment questionnaires were administered at both measurement points. Finally, all core subtests from the WISC-IV or WAIS-IV were administered to the study groups, which few studies have undertaken on two occasions with such a large clinical group.

Despite the limitations described above, this research can be seen as a first step towards integrating clinical validity of both performance-based and behavioral ratings of cognitive and executive functioning in a longitudinal perspective. This is crucial to find the psychological mechanisms to base new treatment methods upon.

Conclusion and Future Perspectives

Impairments in cognitive functions, EF, and internalizing symptoms among youth diagnosed and treated for ADHD were largely stable, at a group level remaining below age-expected norms over the three-year follow-up period. Behavioral executive functioning seems to be important for the development of the child with ADHD, affecting symptoms of ADHD, internalizing problems, and overall impairment. The thesis results suggest that behavioral EFs appear to be psychological mechanisms that should be taken into consideration when developing new treatment approaches, which could have the added benefit of improving the school situation as well as the emotional well-being of children with ADHD.

Research

Future studies need to be expanded to include data on comorbid disorders, and the views of both teachers and children concerning EF and functional impairment.

In line with Faraone et al. (2021) the study results indicate that more research is needed on effective new therapies for supporting children with ADHD and behavioral executive dysfunction, as well as on how to train children to reduce EF impairment. Moreover, studies on how to combine such interventions with pharmaceutical treatment are needed. Many children with ADHD grow up in vulnerable socioeconomic and psychosocial conditions (Choi et al., 2017; Larsson et al., 2014). Because ADHD is primarily caused by genetic factors, many children with ADHD have parents who also have developmental or psychiatric diagnoses that entail EF issues. Thus, there is a need for community-oriented research on how to best provide support for families, so that children with ADHD get the help they need to function in their daily lives concerning routines, guidance, homework, exercise, and recreational activities. So far, there is very limited evidence that computerized cognitive/EF training programs improve outcomes in respect of the core symptoms of ADHD (Cortese et al., 2015; Meyer et al., 2020; Rapport et al., 2013). However, one meta-analysis found that organizational skills training in children with ADHD improve these skills moderately according to ratings by teachers and large improvements as rated by parents. In line with Cortese et al. (2015), Meyer et al. (2020), and Rapport et al. (2013) only modest improvements were observed on the ratings of symptoms of inattention and academic performance. Further work is needed to improve the efficacy of these EF-focused interventions in ADHD youth. For example, more needs to be done to understand how parents

influence the child's EF so that parent-focused interventions can be developed, evaluated, and potentially added to child-focused EF training programs (Fay-Stammach et al., 2014; Mazursky-Horowitz et al., 2018; Valcan et al., 2018). Future treatment methods should be flexible and easy to implement since these children and their families often have stressful everyday lives.

Clinical Aspects

While neuropsychological tests may generate some cost-effective information in diagnostic assessments of ADHD, in cases when parental and teacher reports are ambiguous, as they can facilitate the clinical judgments by reducing clinical uncertainty. The most important contribution seems to be to further our understanding of overall impairment and influences on individuals with ADHD. This is important since the treatments for ADHD should be person-centered and based on holistic information about the children (NICE, 2021). Furthermore, assessment, treatment, and treatment evaluations should be interconnected. In this context, behavioral ratings of EF seem cost-effective providing useful information about the children with ADHD.

The treatment arsenal should be expanded to include interventions to support impaired EF and strengthen the personal resources of these children. In both clinical practice and at school, it is important to monitor children with ADHD for their cognitive functioning. Children who once achieved average scores in verbal ability may not be following normative development because of problems with learning as well as their school and homework situations. Internalizing symptoms in children with ADHD should be monitored, even when they do not manifest in the child's behavior. Instead, internalizing symptoms represent invisible suffering for these children. Reducing stress and failure in daily life for youth with ADHD can strengthen their self-esteem, reduce internalizing symptoms, and perhaps enable them to manage better in school.

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