Pre-attention and executive attention in ADHD: A 20-year follow-up study

Bendik Rund Torgalsbøen

Master Thesis
Department of Psychology

THE UNIVERSITY OF OSLO
Spring 2018
Pre-attention and executive attention in ADHD: A 20-year follow-up study
Pre-attention and executive attention in ADHD: A 20-year follow-up study

Bendik Rund Torgalsbøen

http://www.duo.uio.no
Abstract

Author: Bendik Rund Torgalsbøen
Title: Pre-attention and executive attention in Attention-Deficit/Hyperactivity Disorder: A 20-year follow-up study
Main supervisor: Professor Merete Glenne Øie; Co-supervisor: Associate professor Pål Zeiner

Background: Attention-Deficit/Hyperactivity Disorder (ADHD) is commonly understood as a neurodevelopmental disorder whose trajectory is mediated by changes in brain structure and function in response to an array of interacting genetic and environmental factors throughout development. Deficits in higher-order cognitions, such as executive attention (i.e. attention-regulation skills), have been shown to constitute an important component in the complex neuropsychology of ADHD across the lifespan. Research has been consistent in presenting executive attention deficits in ADHD, but few studies have directly compared this to early, preliminary stages of attentional processing, namely pre-attention. Moreover, longitudinal studies of neuropsychological performance have been limited by relatively short follow-up periods. The aim of the present study was to accommodate these shortcomings by comparing measures of pre-attention and executive attention (working memory) over a 20-year follow-up period. Methods: Individuals with ADHD (n=19) and healthy controls (n=26) were followed up 20 years (T3) after initial assessment (T1). All individuals had also been followed up after 13 years (T2). All were between 12-18 years of age at baseline and between 32-38 at T3. They were reassessed with both diagnostic and neuropsychological measures. Our selected attention domains were measured using the Backward masking task (pre-attention) and the Digit span distractibility test (working memory/executive attention). Results: With respect to the Backward masking task, there was a significant group difference at T1, but no group differences at T2 and T3. Concurrent group differences were detected at all three time points for both conditions of the Digit span distractibility test (with and without distractor), with the ADHD group performing consistently below the healthy controls average. Age had a seemingly limited detrimental effect from T2 to T3 on the result of the Digit span test without distractibility, whereas the Digit span test with distractibility was consistently associated with a decline in performance, irrespective of group. With respect to backward masking performance, the ADHD group displayed significant fluctuations over a 20-year period, with a significant improvement from T1 to T2 and a significant decline from
T2 to T3. Additional correlational analyses at T3 yielded no significant association between: 1) neuropsychological performance and symptom severity, or 2) measures of pre-attention and working memory/executive attention. **Conclusion:** Young adults with ADHD in their mid-20s continue to be afflicted with executive attention deficits in their mid-30s, compared to healthy controls. Measures of working memory/executive attention were superior in discriminating between individuals with ADHD and healthy controls, compared to pre-attention performance. Overall, the results are in relative consonance with Barkley’s (1997) theoretical framework, suggesting executive functions as a core deficit in ADHD. The data highlight that ADHD is a cognitively impairing condition, also in adulthood, thus creating an imperative for cognitive rehabilitation techniques to help address attention difficulties.
Preface

The current thesis is written for the research project, “Clinical, Neurocognitive and Functional Outcome in Early-Onset Schizophrenia and Attention-Deficit/Hyperactivity Disorder: A 20-Year Follow-up Study”, which was initiated in 1992. My sincerest gratitude goes to my main supervisor, Professor Merete Øie, for giving me the opportunity to work on this project. Her extensive knowledge on ADHD and the ability to foster new ideas for my thesis have been of tremendous support. She has offered invaluable guidance and direction throughout the process, and has truly opened my eyes to the significance of neuropsychological research.

I also deeply appreciate the thoughtful input and reflections from my secondary supervisor Pål Zeiner. He has contributed with important insights on the methodological/structural outline of the thesis, as well as facilitating my independent work with the statistical analyses. Lastly, I wish to thank all the participants who have contributed to this project over a 20-year period. Without their dedicated cooperation, this thesis would have never seen the light of day.

Although no one can claim to be an ADHD expert in such a short period of time, it would be no exaggeration to state that my personal learning curve has grown exponentially throughout this process. The process of completing this thesis has been time-consuming and occasionally intense, but ultimately enlightening and extraordinarily rewarding. It has given me a unique opportunity to learn more about neuropsychological functioning in a prevalent neurodevelopmental disorder and its patient group. As a future psychologist, I believe that these insights will be of tremendous value in my clinical work.

Oslo, April 2018

Bendik Rund Torgalsbøen
# Table of contents

1 Introduction ................................................................................................................................. 1
  1.1 General characteristics of ADHD.......................................................................................... 1
  1.2 Development of the attention-executive concept in ADHD..................................................... 2
  1.3 Neuropsychological constructs: Automatic and controlled processing .............................. 4
    1.3.1 Automatic processes ........................................................................................................ 5
    1.3.2 Controlled processes ....................................................................................................... 6
  1.4 Neurodevelopment across the lifespan .................................................................................. 8
    1.4.1 Neurodevelopment in healthy controls ........................................................................... 8
    1.4.2 Structural and functional imaging in ADHD; findings of brain abnormalities .............. 9
    1.4.3 Neurodevelopment in ADHD ....................................................................................... 10
  1.5 Neuropsychological functioning across the lifespan ............................................................. 11
    1.5.1 General neuropsychological deficits in ADHD ............................................................... 11
    1.5.2 Longitudinal neuropsychological functioning in healthy controls ............................... 12
    1.5.3 Longitudinal neuropsychological functioning in ADHD .............................................. 13
  1.6 Pharmacological treatment of neuropsychological deficits in ADHD ................................. 14
  1.7 Association between neuropsychological performance and behavioural characteristics in ADHD ................................................................................................................................. 15
  1.8 Neuropsychological deficits and functional outcome in ADHD ....................................... 16
  1.9 Aims of the study .................................................................................................................. 18

2 Methods .................................................................................................................................... 20
  2.1 Participants ............................................................................................................................ 20
  2.2 Neuropsychological measures ............................................................................................. 22
    2.2.1 The Backward masking task .......................................................................................... 22
    2.2.2 The Digit span distractibility test .................................................................................. 24
  2.3 Symptom, behaviour and functional ratings ......................................................................... 24
  2.4 Ethical perspectives .............................................................................................................. 25
  2.5 Data analyses ....................................................................................................................... 25

3 Results ...................................................................................................................................... 27
  3.1 Concurrent group differences at T3 .................................................................................... 27
3.2 Development in attentional measures from T2 to T3 ........................................27
3.3 Correlation analysis ..................................................................................................................31
3.4 Analysis of limited sample ........................................................................................................31

4 Discussion ........................................................................................................................................32
4.1 Concurrent group differences in neuropsychological attention performance at T3.................................................................32
4.2 Differential development in diverse attentional measures ........................................................................................................34
   4.2.1 Development of pre-attention performance ........................................................................34
   4.2.2 Development of working memory/executive attention performance ................................36
4.3 Association between neuropsychological performance and ADHD symptom severity .................................................................37
4.4 Association between measures of pre-attention and working memory/executive attention ........................................................................38
4.5 Implications for treatment ........................................................................................................39
4.6 Recommendations for future research ....................................................................................39
4.7 Strengths and limitations ..........................................................................................................40
4.8 Conclusion ...............................................................................................................................41
4.9 Acknowledgements ................................................................................................................42

5 References .....................................................................................................................................43

Table 1. Characteristics of the ADHD group compared to the HC group at T3 .................................................................................................................................22
Table 2. Neuropsychological test results at T2 and T3 ......................................................................29
Figure 1. Performance on the Backward masking total for the two groups at T1, T2 and T3 ................................................................................................................................................................................30
Figure 2. Performance on the Digit span test without distractor for the two groups at T1, T2 and T3 ................................................................................................................................................................................30
Figure 3. Performance on the Digit span test with distractor for the two groups at T1, T2 and T3 ................................................................................................................................................................................31
1 Introduction

1.1 General characteristics of ADHD

Attention-Deficit/Hyperactivity Disorder (henceforth abbreviated as ADHD) is a neurodevelopmental disorder characterized by a persistent pattern of hyperactivity/impulsivity and/or inattention. The symptoms are pervasive across settings, and lead to various degrees of functional impairment (Biederman & Faraone, 2005). It is a worldwide and highly prevalent disorder, estimated to affect 5%–10% of children (Faraone, Sergeant, Gillberg, & Biederman, 2003) and 5% of adults (Faraone & Biederman, 2005). The prevalence of ADHD is generally greater in males than females, and gender ratios vary by country, ranging from 1:3 to 1:16 in females: males (Nøvik et al., 2006). The diagnosis of ADHD is currently made on the basis of developmentally inappropriate inattention, impulsivity and/or motor restlessness (American Psychiatric Association, 2013), and three subtypes are recognized based on symptom presentation: “inattentive”, “hyperactive–impulsive” and “combined” subtypes (reflecting a combination of the other two subtypes). The inattention component of ADHD is manifested as daydreaming, distractibility and difficulty focusing on a single task for a prolonged period, whereas the hyperactivity component is often expressed as fidgeting, excessive talking and restlessness (Biederman, 2005). According to DSM-5 (American Psychiatric Association, 2013), the abovementioned behavioral characteristics must: 1) be observed early in life (before age 12), 2) be pervasive across at least two situations, 3) interfere with, or reduce the quality of, social, academic, or occupational functioning, and 4) not be better explained by another mental disorder.

Long-term risk of functional impairment in multiple domains, as well as a lower quality of life is well documented in ADHD (Biederman et al., 2012; Shaw et al., 2012). Several studies show that ADHD is associated with higher health-care costs, cigarette smoking and substance-use disorders, decreases in work performance and work productivity, lower educational attainment and a higher prevalence of comorbid psychiatric disorders (Biederman et al., 2004; Klein et al., 2012; Barbaresi et al., 2013). Approximately two-thirds of individuals with ADHD have one or more co-occurring developmental or psychiatric conditions; hence “simple” ADHD is considered the exception rather than the rule (Larson, Russ, Kahn, & Halfon, 2011). Furthermore, evidence indicates that childhood ADHD is associated with a significantly higher risk of early death, particularly from suicide, accidents
and long-term morbidity in adulthood (Biederman et al., 2004; Dalsgaard, Østergaard, Leckman, Mortensen, & Pedersen, 2015).

A feature of ADHD is its tendency to improve with age, with research suggesting a decline in both hyperactivity and inattention as children move into early adulthood (Döpfner et al., 2015). However, longitudinal studies have concurrently substantiated that the majority of individuals diagnosed with ADHD continue to exhibit symptoms into adulthood (Biederman, Petty, Evans, Small, & Faraone, 2010; Cheung et al., 2015), and many of those who do not continue to meet full diagnostic criteria in adulthood still suffer from significant functional impairment (Kooij et al., 2010). When defining only those meeting the full diagnostic criteria for ADHD as having “persistent ADHD”, the rate of persistence is low, typically 15% at age 25. Nevertheless, when including cases consistent with the DSM-IV definition of ADHD in partial remission, the rate of persistence is much higher, typically 65% (Faraone, Biederman, & Mick, 2006).

Although the precise aetiology of ADHD has not yet been fully elucidated, it is commonly understood as a multifactorial disorder with a complex aetiology and strong genetic underpinnings (Nigg, Lewis, Edinger, & Falk, 2012), with a heritability being both substantial and solidly established (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006). While it is well accepted that ADHD is a highly heritable disorder, not all of the risk is genetic. Studies have discovered numerous prenatal risk factors which appear to be associated with ADHD, including maternal substance use and stress during pregnancy, prematurity, low birth weight and a number of other pregnancy, labour, delivery or infancy complications (Sciberras, Mulraney, Silva, & Coghill, 2017).

1.2 Development of the attention-executive concept in ADHD

ADHD, formerly depicted as “hyperactivity”, “hyperkinesis disorder of childhood” or “minimal brain dysfunction”, was first described 100 years ago as a childhood disorder predominantly found in boys (Lange, Reichl, Lange, Tucha, & Tucha, 2010). Revisions in the diagnostic construct have been made numerous times over the past century. The most important shift perhaps occurred in the 1970s, when the concept of attention dysfunction was introduced as the defining feature, and the disorder was re-named accordingly (Seidman, 2006). However, the key characteristics required for the diagnosis were primarily behavioural descriptions of hyperactivity and attentional problems, rather than direct cognitive measures
of “inattention”. Since introducing this feature, virtually all conceptualizations of ADHD or functionally equivalent disorders have included attentional symptoms (Seidman, 2006). Meta analyses have further suggested that attention is one of the neuropsychological domains in which adults with ADHD appear to differ most from healthy controls, as evidenced by more consistent medium-to-large effect sizes across neuropsychological tests (Hervey, Epstein, & Curry, 2004).

Concurrent with this development, the discovery of similarities between symptoms characterizing ADHD, and those of some patients with neurological disorders, led to the hypothesis that ADHD was a brain disorder affecting the prefrontal cortex (PFC) (Mattes, 1980). Early support for the “prefrontal” (PFC) or “fronto-striatal” model of ADHD came from the experiences with stimulant medications, in addition to animal models implicating dopamine pathways (Shaywitz, Klopper, & Gordon, 1978), which have a strong predilection for the PFC (Seidman, 2006). This framework has given rise to several behavioural theories attempting to explain the origins of core ADHD symptoms in terms of dopamine dysfunctions. For example, the “Dynamic developmental theory” (Sagvolden, Johansen, Aase, & Russell, 2005) is based on the hypothesis that a hypo-functioning mesolimbic dopamine branch produces an altered reinforcement of behaviour and a deficient extinction of previously reinforced behaviour. This further results in symptoms like impulsiveness, the development of hyperactivity in novel situations, deficient sustained attention and a failure to inhibit responses.

ADHD is currently characterized as a neurodevelopmental disorder in DSM-5, more appropriately recognizing its onset and chronic developmental course (Shaw & Polanczyk, 2017). From a developmental psychopathology perspective (Hinshaw, 2017b), ADHD is not the result of a fixed deficit, but instead a clinical manifestation of a neurodevelopmental vulnerability whose trajectory is mediated by changes in brain structure and function in response to an array of interacting genetic and environmental factors throughout development (Rajendran et al., 2013). The effect of these factors may again operate in different ways in different individuals (i.e. aetiological heterogeneity) (Sonuga-Barke & Halperin, 2010). Building on knowledge of ADHD neurodevelopment (usually within a “frontal” framework), neuropsychological theories have tended to emphasize putative dysfunctions of the PFC, especially for executive dysfunctions (Seidman, 2006). Discussion continues as to whether executive deficits may in fact represent a proximal causal deficit in the disorder, an idea that was introduced in a highly influential article by Barkley (1997).

Although the attention-executive concept in ADHD has gradually become a
cornerstone in the conceptualization of the ADHD neuropsychology, this emphasis has been at the expense of research focusing on more “primitive” neuropsychological constructs. As a result, current research on ADHD almost exclusively deals with the attention-executive concept, leaving findings of “basic” neuropsychological performance far less consolidated. An important purpose of the present study was to bridge this gap, reinvestigating the attention-executive concept in light of basic neuropsychological constructs.

1.3 Neuropsychological constructs: Automatic and controlled processing

It is challenging to navigate in the field of neuropsychological research, primarily because theoretical definitions and constructs are not consistently used among researchers. Furthermore, these constructs rarely comprise separate entities, as theoretical overlap between constructs is the rule. Building on the current understanding of ADHD as being a neurodevelopmental disorder (Shaw & Polanczyk, 2017), an explanation of relevant theoretical constructs is warranted.

Some kind of selection or control mechanism seems necessary for the optimal functioning of cognition and behaviour. Consistent with this prediction, deficient selection is involved in virtually all known central nervous system related (CNS) neurological and mental diseases (Schneider & Chein, 2003). A basic, yet important, distinction is made between the selection generated by behaviourally relevant goals of the organism (controlled), and the selection generated by properties of the stimuli themselves (automatic). Automatic processes (bottom-up processing) are executed rapidly, can be accomplished simultaneously with other cognitive processes without interference and can be unconscious and involuntary (Ramnani, 2014). Controlled processing (top-down processing) is effortful, and can deal with only a limited amount of information at once; it is slow and susceptible to errors, but – at the same time, flexible and useful to deal with new tasks (Fabio, 2017). When tasks interfere, this is usually meant to indicate competition for limited attentional processing resources. A controlled process requires a conscious allocation of attentional resources (i.e. executive functions), while an automatic process does not (Fabio, 2017).

Importantly, controlled and automatic processes represent overlapping concepts, rather than dichotomous constructs, and in most situations these mechanisms interact to enhance attentional performance (Egeth & Yantis, 1997). In a similar vein, some research indicates that lower-order processes (i.e. automatic), such as encoding, search, decision and
response organization, may form necessary components for higher-order cognitive operations (i.e. controlled) (Rubinstein, Meyer, & Evans, 2001). The underlying logic is that if the lower-order processes are not well automatized, they will accumulate a high cognitive load, ultimately competing for the limited resources used by controlled processes (Fabio, 2017). Hence, impairments in higher-order processes could result from a deficit in its primary related cognitive domain, but also secondarily from deficits in lower-order cognitive processes (indirect effect) (Ríos, Periáñez, & Muñoz-Céspedes, 2004). Still, the distinction between top-down and bottom-up perspectives continues to be a fundamental heuristic in neuropsychological models, and the question of whether deficiencies in specific underlying mechanisms are linked to controlled or automatic processes is a key point to child psychopathology theory development (Fabio, 2017).

1.3.1 Automatic processes

Under the umbrella term of automatic processes, pre-attentive processing is a significant concept. Yet, when operating in this field of research, several terms are used somewhat interchangeably, such as sensory processing, early visual/visuospatial processing and perception. Nonetheless, pre-attentive processing characterizes a preliminary stage of analysis whereby auditive or visual stimuli is processed before conscious attention sets in (Ellenbroek, 2004). An automatic attention response could in principle be triggered by the simple presence of a stimulus, or by the presence of the stimulus only when it appears in a particular context. Consequently, every stimulus has an intrinsic (and modifiable) probability of attracting attention (Schneider & Chein, 2003; Diamond, 2013). Automatic processing has proven important in several tasks loading on neuropsychological capacity, including semantic processing (Kiefer & Martens, 2010), decision-making (Glöckner & Betsch, 2008), multitasking (Musslick et al., 2016) and memory performance (McCabe, Roediger, & Karpicke, 2010). Building on the aforementioned outline of a hierarchical relationship between lower- and higher-order cognitions (Ríos et al., 2009), findings in ADHD samples suggest that early visual processing deficits could constitute the beginning of a cascade that has an impact on higher-level cognitive processes, including selective and sustained attention (Lenz et al., 2010).

Early visual processing disturbances are typically subtle and not behaviourally apparent, and therefore harder to pinpoint without the appropriate tools (Thormodsen, Juuhl-Langseth, Holmen, & Rund, 2012). Visual masking is a classic technique used to examine the differences between conscious and unconscious visual processing (Breitmeyer & Ögmen,
2006), and has been used for at least 40 years as a suitable test for measuring such basic information processing (Rund et al., 2004). Visual masking refers to a condition in which reduction in the visibility of an object (the target) is caused by the presentation of a second object (the mask) nearby in space or time (Enns & Di Lollo, 2000). Adhering to this common format, the Backward masking task has usually been considered to tap information about the processing taking place at the icon level (Rund, Landrø, & Ørbeck, 1993), with deficits in this paradigm implying a slow processing of information from sensory memory to short-term memory (i.e. pre-attention).

Visual masking provides several key advantages for exploring the earliest stages of visual processing, and has been used in research on both ADHD and schizophrenia (Rund et al., 1996; Øie & Rund, 1999; Sergi, Rassovsky, Nuechterlein, & Green, 2006; Øie, Sundet, & Rund, 2010). It allows for control over timing at the millisecond level, there are several well-supported theories of the underlying neurobiology of visual masking, and it is amenable to examination by electroencephalogram (EEG) and functional magnetic resonance imaging (fMRI) (Green et al., 2011). Lastly, it has the advantage over standard reaction time measures by providing measures of processing that are not confounded with execution or motor selection issues (Li, Polat, Scalzo, & Bavelier, 2010).

1.3.2 Controlled processes
Among the family of mental processes that comprise the controlled processes is a set of higher cortical abilities referred to as executive functions. Historically, this is an ill-defined construct, but over the past two decades has reached a more precise definition (Zelazo, Blair, & Willoughby, 2016). Researchers generally characterize executive functions as the attention-regulation skills that make it possible to sustain attention, keep goals and information in mind, refrain from responding immediately, resist distraction, tolerate frustration, consider the consequences of different behaviours, reflect on past experiences and plan for the future (Diamond, 2013; Zelazo et al., 2016). Despite the role of executive functions in determining the focus of our attention, it is important to recognize that behavioural studies of normal persons, brain-injured and mentally ill patients have all emphasized that executive functions and attention are not unitary processes (Posner & Petersen, 1990). Executive functions are further divided into three primary constructs (Miyake et al., 2000): inhibitory control, cognitive flexibility and working memory, all of which are needed to actively and intentionally control attention. In this respect, attention is defined as a complex set of mental operations that includes focusing on- or engaging a target,
sustaining the focus over time using vigilance, encoding stimulus properties and disengaging and shifting the focus (Seidman, 2006).

Inhibitory control involves being able to control one’s attention, behaviour, thoughts and/or emotions to override a strong internal predisposition or external lure, and instead do what is more appropriate or needed (Diamond, 2013). Cognitive flexibility refers to the readiness with which one can selectively switch between mental processes to generate appropriate behavioural responses. It enables an individual to work efficiently, to disengage from a previous task, reconfigure a new response set and implement this new response set to the task at hand (Dajani & Uddin, 2015). Working memory refers to the system or systems assumed to be necessary in order to keep things in mind while performing complex tasks such as reasoning, comprehension and learning (Landrø et al., 2001; Baddeley, 2010). Working memory is critical for making sense of anything that unfolds over time, for that always requires keeping in mind what happened earlier and relating that to what comes later (Diamond, 2013). It is clear that the concept of working memory is not simply attention, and it is also not simply memorial (Sergeant, Geurts, Huijbregts, Scheres, & Oosterlaan, 2003). There are several different theoretical models of working memory, but a common element is that it comprises a higher-order skill related to the ability to allocate attentional resources despite distraction or interference (e.g. Baddeley, 1996). This view was strongly supported by Kane, Bleckley, Conway and Engle (2001), who reported that individuals with a high working memory span had better attentional control than those with lower spans, as elegantly measured by errors on an antisaccade task. This controlled attention perspective views that information maintenance in the presence of interference is a critical function of working memory, and therefore as the primary mechanism linking working memory capacity with higher-order cognition (Kane & Engle, 2002). As a result, the definition of working memory in this thesis is that working memory equals short-term memory (or activated long-term memory) plus selective attention (Kane et al., 2001), in which they invoke executive attention to stress the attentional control component of selective attention. In this respect, executive attention refers to a capability whereby memory representations are maintained in a highly active state in the presence of interference, and these representations may reflect action plans, goal states or task-relevant stimuli in the environment (Kane & Engle, 2002). This construct is simply based on the idea that we can voluntarily choose to ignore (or inhibit attention to) particular stimuli and attend to others, based on our goal or intention (Diamond, 2013). In this regard, the executive attention concept is practically equivalent to that of inhibitory control.
The aforementioned controlled attention perspective of working memory encapsulates a further division of working memory components, namely “maintenance” and “manipulation”. Maintenance generally refers to tasks that require memory for strings of information (i.e. short-term memory/“simple” working memory), whereas manipulation refers to more complex tasks that involve a higher load on executive function processing in memory (i.e. executive attention) (Best & Miller, 2010). Thus, there are discrete sub-components within working memory, characterized by the degree to which they tax complex attentional control processes.

Span tasks are commonly used measures in neuropsychological testing, and methodologically, they have proven to be both reliable and valid measures of both short-term memory span and working memory span (Bopp & Verhaeghen, 2005; Conway et al., 2005). Typically for span tasks, a series of stimuli (digits, letters, or words) are presented, visually or auditorily, normally at the rate of one stimulus per second. The task of the participant is to repeat the stimuli in the order they were presented. The Digit span distractibility test by Oltmanns and Neal (1975) adheres to this common procedure and is further subdivided, namely a Digit span test with distraction (DSD WD) and without distraction (DSD WOD). Hence, the subjects hear short strings of digits with and without distractors, and must then recall the digits in the correct order.

An important feature of the working memory model is the system’s limited capacity, which forces the resources to be shared between storage and processing (Bopp & Verhaeghen, 2005). Consequently, mere storage tasks/”maintenance” (i.e. without distractor) is distinguished from tasks requiring executive interference control/”manipulation” (i.e. with distractor). These tasks differ in that the item manipulation, in this case the maintenance of information in the presence of distraction, presents a task requirement that goes beyond mere storage. The strength of the Digit span distractibility test is that it captures the interaction between concurrent storage and online processing, thereby providing a measure of both short-term memory/”simple” working memory and executive function processes.

1.4 Neurodevelopment across the lifespan

1.4.1 Neurodevelopment in healthy controls

The human central nervous system development proceeds in a systematic manner that begins before conception and continues at least into early adulthood (Halperin & Schulz, 2006).
Nonetheless, brain development is nonlinear and progresses in a localized and region-specific manner that coincides with functional maturation (Gogtay et al., 2004). There is also evidence that brain development is hierarchical, meaning that cortical areas associated with basic processes (e.g., sensory and motor) develop first, and that cortical areas associated with more complex processes, such as executive functions, develop later (Zelazo et al., 2016). Stable and mature levels of visuospatial processing emerge slowly over a protracted period of development, with some abilities not reaching maturity until adolescence (Stiles, Akshoomoff, & Haist, 2013; Pilz, Kunchulia, Parkosadze, & Herzog, 2016). Hence, one could expect pre-attentive capacities to be mature by mid’ teens. The frontal lobes, however, are among the last cortical areas to become anatomically and functionally mature, and this developmental process of “frontalization” may not become completed until the mid-20s, or even later (Arain et al., 2013). Neuroimaging studies have demonstrated that the development of executive processes generally parallels the maturation of the prefrontal cortex from childhood to adolescence (Halperin & Schulz, 2006). Thus, one could reasonably expect executive functions to be fully mature by the mid-20s.

In advanced aging, the prefrontal areas are vulnerable to white matter change, atrophy and certain forms of neurotransmitter depletion (Buckner, 2004), potentially contributing to age-related neuropsychological decline from the mid-20s. This is further corroborated by studies showing that cognitive change strongly mirrors both brain gray matter volume change (Fletcher et al., 2018) and micro-/macrostructural alterations in brain connectivity (Fjell, Sneve, Grydeland, Storsve, & Walhovd, 2017). The mapping of attentional functions onto different brain regions generally supports the notion that neuropsychological performance will be associated with structural and functional brain abnormalities in specific regions (Seidman, 2006).

1.4.2 Structural and functional imaging in ADHD; findings of brain abnormalities

There is a robust amount of evidence of structural, functional and neurochemical brain abnormalities in ADHD, in several regions that support neuropsychological functions (Castellanos et al., 2006). Since its introduction, the “frontal” model of ADHD has gradually garnered support from neuroimaging studies, and research on functional brain abnormalities has consistently involved the PFC (Bush, Valera, & Seidman, 2005; Vaidya, 2012). The most consistently replicated brain structural alterations in ADHD in childhood include
significantly smaller volumes in the dorsolateral PFC, and regions that project to the PFC, including the caudatum, pallidum, anterior cinguli, and cerebellum (Seidman, Valera, & Makris, 2005). A meta-analysis of several brain regions also indicated lower volumes for the ADHD individuals compared to healthy controls (Valera, Faraone, Murray, & Seidman, 2007). Further, changes in cortical thickening have been associated with clinical outcomes, in that ADHD children with a poorer outcome had a “fixed” (i.e. nonprogressive) thinning of the left medial prefrontal cortex, an area important for attentional control (Shaw et al., 2006).

1.4.3 Neurodevelopment in ADHD

There has been an extensive debate as to whether ADHD is partly a consequence of a delay in brain maturation, or as a complete deviation from the template of typical development (Shaw et al., 2007). A developmental lag would imply that within a certain time window, ADHD developmental trajectories are of a normal shape, but delayed. Thus, normal values will be obtained later. However, this concept does not preclude age limits for development, raising the possibility that ADHD individuals never outgrow the delay (Doehnert, Brandeis, Imhof, Drechsler, & Steinhausen, 2010). For this reason, it has been proposed to distinguish among transient developmental lag (ADHD and HC trajectories eventually converge), persistent developmental lag (ADHD and HC have parallel trajectories, but never reach similar values) and developmental deviation (ADHD and HC have qualitatively dissimilar trajectories) (Doehnert et al., 2010).

Pertaining to the question of a developmental delay, a longitudinal study by Shaw et al. (2007) investigated cortical thickness in 223 ADHD children and 223 normally developing children. They reported that the peak of cortical thickness maturation was delayed in children with ADHD compared to healthy peers by an average of three years, with some regions, including frontal and temporal cortex areas, being delayed in their maturation by up to five years. Likewise, Sripada, Kessler and Angstadt (2014) demonstrated a developmental lag in maturation of the brain’s intrinsic functional architecture in individuals with ADHD (age 7.2–21.8 years). Nevertheless, the study by Shaw et al. (2007) specified that the ordered sequence of regional development, with primary sensory and motor areas attaining their peak cortical thickness before high-order association areas (important for executive functions), was similar in both ADHD individuals and healthy controls, suggesting that ADHD is characterized by a delay rather than a deviance in cortical maturation.

The structural abnormalities found in ADHD are likely to have a genetic basis, given
that the same abnormalities are observed in unaffected siblings of children with ADHD (Durston et al. 2004). However, a recent study by Sonuga-Barke et al. (2017) also provided compelling evidence that time-limited exposure to severe adversity, occurring because of institutional deprivation in early childhood, could have a profound and lasting psychological impact, thereby highlighting the role of environmental experience on neurodevelopment. As pointed out by Steinhausen (2009), there is a high degree of heterogeneity considering the “causes and courses” of ADHD. Accordingly, there is substantial inter-individual variability in the manifestation of ADHD characteristics (Wåhlstedt, Thorell, & Bohlin, 2009). Further extrapolating from this concept of heterogeneity, one could also expect variability in anatomical brain irregularities and neurodevelopmental trajectories between ADHD individuals.

1.5 Neuropsychological functioning across the lifespan

1.5.1 General neuropsychological deficits in ADHD

Given the several forms of attention that exist, each with distinctive neurological underpinnings (see Gazzaniga, Ivry, & Mangun, 2014), the question of whether ADHD involve deficits in attention is deceptively complex (Hinshaw, 2017a). Nevertheless, over the past decade research on neuropsychological dysfunctions in adult ADHD has intensified, and the evidence for such deficits is accumulating (Seidman, 2006). A preliminary neuropsychological feature of ADHD is that simple alertness tasks, which are highly dependent on automatically founded processes, are generally less impaired than more complex attention tasks (Schoechlin & Engel, 2005).

Considering automatic processes, a study using backward masking measures suggested that ADHD individuals displayed only nearly significant deficits, compared to healthy controls (Rund et al., 1996). This finding was reported on the same ADHD sample that is used in our current study. More significant deficits, however, have been found in studies of other diagnostic groups, primarily schizophrenia (Green et al., 2003; Rund et al., 1996; Thormodsen et al., 2012).

Following the development of the attention-executive concept, considerable neuropsychological research in ADHD individuals has focused on the cognitive domain of executive functions (including its core sub-components) (Fuermaier et al., 2015). This
literature is consistent in presenting a pattern of domain-specific, neuropsychological deficits (Martinussen, Hogg-Johnson, & Tannock, 2005; Biederman et al., 2007; Marchetta, Hurks, Krabbendam, & Jolles, 2008) – findings that have also garnered support from neuroimaging studies (De La Fuente, Xia, Branch, & Li, 2013; Hart, Radua, Nakao, Mataix-Cols, & Rubia, 2013; Hwang et al., 2015). Examinations of working memory sub-components performance in ADHD individuals suggest that the largest between-group differences are associated with the central executive (i.e. manipulation) (Alderson et al., 2015). This finding has been further supported by studies suggesting that ADHD individuals display ineffective allocation of attentional resources involved in encoding of information in working memory (Kim, Liu, Glizer, Tannock, & Woltering, 2014). However, despite relatively consistent findings in the executive functions domain, not everyone with ADHD experience deficits. Further expanding the notion of heterogeneity from Steinhausen (2009), an overriding tendency is that ADHD is associated with high levels of intraindividual variability in attentional processing (Kofler et al., 2013).

1.5.2 Longitudinal neuropsychological functioning in healthy controls

From a developmental perspective, it is considered a truism that as people grow older, performance on a large number of cognitive tasks declines (Verhaeghen, 2011). Neuropsychological development typically follows an inverted U-curve throughout the lifespan (Craik & Bialystok, 2006), and there is a nearly linear decline from early adulthood on measures representing the efficiency or effectiveness of processing (Buckner, 2004; Salthouse, 2010).

As detailed earlier, the visuospatial processing capacity becomes refined by maturation, and by interaction with the environment, until it reaches its highest level of sophistication in adolescence (Stiles, et al., 2013). However, soon after the zenith, human visual information processing starts to be affected by aging (Waszak, Schneider, Li, & Hommel, 2009). Using a backward masking paradigm, a recent study by Pilz, Kunchuila, Parkosadze and Herzog (2015) reported specific group differences in spatiotemporal performance between young adults and older adults. This age-related decline in performance could not be explained solely by deteriorated visual acuity, pointing to cortical rather than retinal causes. This overall pattern of performance is in accordance with the basic information-processing development as an inverted-U-shaped pattern of rise and fall.

Considering working memory, this capacity improves through adolescence in parallel.
with the continued maturation of critical brain systems supporting cognitive control (Halperin & Schulz, 2006). Consistent with this assumption, Simmonds, Hallquist and Luna (2017) found that working memory-performance in healthy controls continued to improve into the early 20s. Still, several studies have shown a continuous decline in working memory performance across the adult life span (Park et al., 2002; Bopp & Verhaeghen, 2005). The aforementioned notion that simple alertness tasks are generally spared compared to complex attention tasks is also evident with respect to cognitive aging, in which age effects are small or non-existent on many relatively easy tasks, but are magnified when the task becomes sufficiently difficult (Ruthruff & Lien, 2016). In line with this assumption, a recent study by Fjell et al. (2017) found that age-related decline in executive functions was greater than what could be attributed to change in basic, speeded cognitive processes. Despite the brain maturation delay described in ADHD individuals, it is reasonable to believe that their neuropsychological development generally will adhere to the common inverted U-pattern, simply because there is limited evidence to suggest a complete developmental deviation (El-Sayed, Larsson, Persson, Santosh, & Rydelius, 2003; Doehnert et al., 2010; Vaidya, 2012).

1.5.3 Longitudinal neuropsychological functioning in ADHD

Despite the fact that ADHD individuals consistently perform below HC average on several neuropsychological measures throughout the lifespan, longitudinal studies have suggested a stable or improving course in executive functioning performance (Coghill, Hayward, Rhodes, Grimmer, & Matthews, 2014; Murray, Robinson, & Tripp, 2017). In a prospective study from Øie et al. (2010), on which the current study is based, adolescents with schizophrenia, ADHD and normal controls were compared on a comprehensive neurocognitive test battery in a longitudinal design over 13 years. Although they still performed significantly below the HC group on the attention-demanding Digit span test (with and without distraction) at both at baseline (T1) and follow-up (T2), they evidenced a significant improvement from baseline to the 13-year follow-up, in contrast to the other two groups. This was in line with previous longitudinal studies, showing a developmental improvement in ADHD individuals on measures of inattention and inhibition in the Continous Performance Task (CPT) (Fischer, Barkley, Smallish, & Fletcher, 2005). However, these findings have also been nuanced by a 10-year follow up study, reporting a relative stability in working memory and executive function deficits into young adult years (Biederman et al., 2012). With respect to the pre-attentive Backward masking task, a similar improvement from T1 to T2 was found in all
conditions. As a result, the ADHD group displayed concurrent deficits at T1, but similar results at T2, compared to HC.

Generally speaking, these findings of neuropsychological improvement were taken to substantiate results from previous studies, which reported neuroanatomic evidence supportive of delayed cortical maturation in ADHD (Krain & Castellanos, 2006; Shaw et al., 2007). The “normalization” of performance on some neuropsychological measures might suggest gains in executive functions surpassing age-related improvement. It may also reflect a “catching up” in the executive domain, possibly resulting from a fine-tuning of neural connectivity (Carlson, Zelazo, & Faja, 2013) or a more efficient use of neuropsychological resources (Halperin & Schulz, 2006).

1.6 Pharmacological treatment of neuropsychological deficits in ADHD

Psychostimulant medications, such as methylphenidate and amphetamine, are commonly prescribed for ADHD, in addition to being a first-line medication for this disorder for over 60 years (Gerlach, Banaschewski, Coghill, Rohde, & Romanos, 2017). However, the latest Cochrane Review (Storebø et al. 2015) raised doubts regarding its effectiveness in improving the neuropsychological deficits in childhood ADHD – a finding that is also evident in adult ADHD (Advokat, 2010). Thus, there is seemingly limited evidence to support the notion of stimulants as cognitive “enhancers”. Pharmacological treatment may also be limited in a number of ways: normalization is rare (Banaschewski et al., 2006), the long-term effectiveness of stimulant treatment remains elusive (Molina et al., 2009; Craig, Davies, Schibuk, Weiss, & Hechtman, 2015) and patients may experience adverse side effects (Charach, Ickowicz, & Schachar, 2004; Graham & Coghill, 2008). Hence, recent studies have highlighted the superiority of combination treatment for several domains of functional impairment (e.g. academic achievement, social skills, parenting practices) and for comorbid cases, in particular, it is apparent that several channels of intervention are mandated (Hinshaw & Arnold, 2015). Hinshaw and Arnold (2015) concludes, “Most saliently, the field needs to rethink the ways, beyond altering individual neurochemistry per se, in which families, schools, and peer groups must be included in the effort to foster self-regulation and age-appropriate competencies across the lifespan.” (p. 15). Building on this multimodal view of treatment, knowledge of neuropsychological deficits and their longitudinal development are of paramount importance, if we are to better tailor treatment to the individual needs.
1.7 Association between neuropsychological performance and behavioural characteristics in ADHD

Considering the core behavioral characteristics of ADHD, these are of a cognitive nature. Because of this, several theoretical propositions describe ADHD in terms of neuropsychological performance deficits (e.g. Wåhlstedt et al., 2009; Sonuga-Barke & Coghill, 2014). Furthermore, behavioural characteristics have not always proven to be stable over time, and so neuropsychological functions may potentially be a more reliable endophenotypic trait (Nigg et al., 2018). Currently, our understanding of cognitive functioning in ADHD is based almost entirely on data derived from traditional neuropsychological and experimental cognitive tasks administered in laboratory settings (Lawrence et al., 2004). Although this approach has yielded important insights, the methods used in this approach typically provide information regarding general mean level differences between those with and without a particular disorder, and have little to no individual diagnostic sensitivity or specificity. Hence, the ability to use neuropsychological tests to specifically diagnose ADHD is often quoted as being weak (Bledsoe et al., 2016). However, neuropsychological testing can be a useful supplement to diagnostic evaluation and treatment by: 1) identification of neuropsychological dysfunction leading to inferences regarding the presence, type, and aetiology of brain dysfunction, 2) comprehensive assessment of cognitive, perceptual, and motor strengths and weaknesses (i.e. function) as a guide for treatment and 3) assessment of the level of performance over a broad range, for both the initial evaluation and measurement of change over time (Seidman, 2006).

Research addressing the symptomatic expression in ADHD has indicated that while symptoms of hyperactivity/impulsivity may wane with age, symptoms of inattention are more likely to remain stable across the lifespan (Biederman, Mick, & Faraone, 2000; Biederman et al., 2010), emphasizing the importance and centrality of attentional problems to this disorder (Willcutt, Sonuga-Barke, Nigg, & Sergeant, 2008). This is in accordance with the aforementioned studies suggesting that the majority of ADHD individuals with executive function deficits in adolescence continued to meet the criteria for such neuropsychological deficits in young adult years (Biederman et al., 2007). Despite the centrality of attentional problems in ADHD, some researchers stress the potential discrepancy between the clinical inattention symptoms that constitute the diagnostic criteria of ADHD and the attention-executive concept measured by neuropsychological laboratory conditions (Seidman, 2006).
This leads to uncertainty regarding the extent to which executive function deficits detected upon neuropsychological testing are related to performance in real-world activities. This idea has been further accentuated by research showing that executive function deficits only exist in a minority of those with ADHD - a disparity that is largely due to a low ecological validity of the executive function tests used (Barkley, Knouse, & Murphy, 2011). This methodological shortcoming could be due to the fact that laboratory tests are measuring executive functions in highly structured surroundings, thus facilitating a temporarily enhanced performance not representative of that in daily life.

In contrast to this scepticism, Sonuga-Barke (2003) has presented a contrasting view, detailed in the dual-pathway framework. At its heart is the idea that the brain-behaviour link (i.e. clinical symptoms) in ADHD is fully mediated by a set of neuropsychological deficits associated with a dysregulation of behavioural and cognitive activity across a range of domains. Later studies have garnered this view, suggesting that executive functions make independent contributions to the explained variance in clinical ADHD symptom domains (Epstein et al., 2003; Thorell, 2007), particularly inattention (for a review, see Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005), thereby suggesting a functional relationship between neuropsychological functioning and symptom severity in ADHD individuals (Vaidya, 2012). With this outline in mind, one could reasonably expect clinical ADHD symptoms to vary as a function of neuropsychological performance, and vice versa.

1.8 Neuropsychological deficits and functional outcome in ADHD

Research investigating the association between pre-attention deficits and functional outcome in ADHD individuals are virtually non-existent. However, this association has been examined to some degree in individuals with schizophrenia (Thormodsen et al., 2012) - findings that may generalize to an ADHD population. Some initial evidence suggests that deficits in early visual processing (e.g. pre-attention) are related to functional outcome, probably through key mediating variables (Green et al., 2011). In line with this, structural equation modelling has indicated a relationship between early visual processing and functional outcome deficits in schizophrenia individuals – mediated through social perception (Sergi & Green, 2003; Sergi et al., 2006; Rassovsky, Horan, Lee, Sergi, & Green, 2011).

Likewise, executive functions are critical for many of the skills that most people would agree are important for success in the 21st century - mentally playing with ideas,
quickly and flexibly adapting to changed circumstances, resisting temptations and meeting novel, unanticipated challenges (Diamond, 2013). When dysfunctions arise in this cognitive domain, as is evident in many ADHD individuals, they commonly lead to cognitive, emotional, and behavioural impairments (Øie, Sundet, & Ueland, 2011; Eslinger, Flaherty-Craig, & Chakara, 2013). A comprehensive study of ADHD individuals, conducted by Barkley and Fischer (2011), showed that executive function self-ratings were significantly correlated with several occupational outcomes, including current salary, work quality, trouble getting along with others and quitting jobs for various reasons. In line with this, a clinical sample of 414 adult ADHD patients reported that only 24% were employed, compared to 79% in the comparison group and an overall employment rate of 70% in the general adult Norwegian population (Halmøy, Fasmer, Gillberg, & Haavik, 2009). By adolescence, with the increasing demands of secondary school for organization and independence, ADHD-related challenges with executive functions can be quite costly in terms of academic independence and performance (Hinshaw, 2017a), therefore contributing to a feeling of inadequacy and incompetence.

ADHD also has a higher prevalence of comorbidity (Nierenberg et al., 2005), with both mood and anxiety disorders commonly observed in children with ADHD (Wilens, Biederman, & Spencer, 2002). Moreover, children with ADHD are more likely to develop subsequent disorders of abuse/dependence for nicotine, alcohol, marijuana, cocaine, and other substances (i.e. unspecified) (Lee, Humphreys, Flory, Liu, & Glass, 2011). Consequently, ADHD is robustly related (odds ratio of 9) to the likelihood of having an SUD in adolescence (Szobot et al., 2007). There may be several reasons as to why ADHD and substance problems are related, but a lack of cognitive control (e.g. executive functions) over behaviour is likely to directly underpin the impulsive behaviour that is a cardinal feature of both ADHD and substance abuse/dependence (Groman, James, & Jentsch, 2009). This assumption is garnered by findings that deficits in executive function are more often observed in those at risk for alcohol dependence and those who develop alcohol use disorders (Nixon, 2013). Thus, there could be a functional relationship between executive function deficits and substance abuse in ADHD.

Considering the adverse outcomes associated with neuropsychological deficits in ADHD, knowledge about their stability and association with clinical symptoms would be beneficial to clinicians. Hence, researchers advocate for a continued integration of developmentally sensitive strategies, specifically tracing the developmental progression of neuropsychological deficits associated with ADHD (Lee, Sibley, & Epstein, 2016). However,
such information is scarce. Additionally, a shortsightedness of past studies is that they are out of focus when they fail to include a larger context, such as the inextricable relationship between automatic cognitive processes and executive functions (Fabio, 2017). Consistent with this, neuropsychological research has consistently presented attention-executive deficits in ADHD, though few studies have directly compared this to early stages of the attentional process, namely pre-attention. This is problematic, as early processing deficits (i.e. pre-attention) may be a precursor of higher-order deficits (i.e. executive functions) (Lenz et al., 2010; Fabio, 2017). Since both clinical practice and research on ADHD often include neuropsychological assessments, it is of importance to disentangle automatic and controlled cognitive processes as much as possible (Rommelse et al., 2007). From a scientific point of view, a clarification of the hierarchical origin of executive deficits in ADHD individuals will lead to a better understanding of the pathology of the disorder. From a therapeutic point of view, the target of intervention will ultimately be different when deficits stem from bottom-up processes instead of top-down processes (Rommelse & Buitelaar, 2008).

1.9 Aims of the study

Given the significance of the attention-executive concept in ADHD neuropsychology, the primary aim of the current study was to examine the attentional processing capacity in ADHD individuals over a 20-year period. With respect to the potential hierarchical relationship between automatic and controlled cognitive processes, we chose to further disentangle performance in subdomains of attention, namely pre-attention and working memory/executive attention measures. To our knowledge, this is the first study in which contrasting ends of an “attentional processing continuum” are compared both concurrently and longitudinally in ADHD individuals. This will provide a unique opportunity to gain insights into the long-term changes in attentional capacity, and may further contribute to a clearer conception of attention dysfunction in ADHD. It is therefore of both theoretical and clinical importance.

Three main questions will be examined in the present study:

(1) At the 20-year follow-up (T3), do patients with ADHD display greater deficits in attentional measures (pre-attention and working memory/executive attention), compared to healthy controls?
(2) At the 20-year follow-up (T3), do patients with ADHD display deficits of equal magnitude in measures of pre-attention and working memory/executive attention?

(3) Do the two attentional measures display different developmental trajectories in ADHD individuals compared to healthy controls over a 20-year follow-up period?

We hypothesize:

1. Building on the presented research findings of both neuropsychological deficits and a brain maturation delay in ADHD individuals, we expect no group differences for pre-attentional measures at T3. We further hypothesize that the ADHD group will display significant deficits in working memory/executive attentional measures, compared to healthy controls concurrently at T3.

2. Considering the presented research findings that complex attentional capacities are often more susceptible to deficits and aging effects, we expect no age-related decline in measures of pre-attention or “simple” working memory (i.e. maintenance). Nonetheless, we hypothesize that the executive attention task (i.e. manipulation) will display a consistent age-related decline in both groups from T2 to T3.

3a) Building on the research findings suggesting a functional relationship between neuropsychological performance (particularly executive functions) and clinical symptom severity, we expect a statistically significant correlation between working memory/executive attention performance (Digit span distractibility test) and self-reported symptom ratings at T3.

3b) Building on the research findings suggesting a hierarchical relationship between lower-order (i.e. automatic) and higher-order cognitions (i.e. controlled), we expect a statistically significant correlation between pre-attention performance (Backward masking task) and working memory/executive attention performance (Digit span distractibility test) at T3.
2 Methods

The current study is part of a larger research project initiated in 1992 on cognition and associations to functional outcome in individuals with early onset schizophrenia and ADHD. For the purpose of comparison, a healthy control (HC) group was also included. This study, however, is limited to the ADHD and HC groups. Participants were assessed at three time points: at baseline (T1), first follow-up after 13 years (T2) and a second follow-up after 20 years (T3). All individuals were tested with the same comprehensive neuropsychological test battery at all three time points. A detailed description of the tests and the procedure is given in Øie et al. (2010). Results from the T1 and T2 studies have previously been described in depth in published articles (Øie & Rund, 1999; Øie et al., 2010). This thesis will primarily focus on neuropsychological performance results at T3 and its associated development from T2 to T3.

2.1 Participants

Demographic information from T1 and T2 has been described in depth in previous publications (Øie & Rund, 1999; Øie et al., 2010). The sample included at baseline (T1) consisted of 20 participants with a DSM-III-R diagnosis of ADHD, and 30 HC. The ADHD group consisted of 20 males whose mean age was 14.1 years (SD=1.5), with the HC group consisting of 14 female and 16 male individuals whose mean age was 15.7 years (SD=1.6). The individuals in the HC group were volunteers attending regular schools at T1. They were screened for mental problems at T1 using the Child Behavior Checklist (CBCL), and individuals were excluded if they had a higher raw score than 45 (Øie & Rund, 1999). This cut-off was set according to American norms, corrected for sex and age, whereby the 90th percentile was used as a cutoff for psychiatric problems. This corresponded to a rating of 45 on the total behavior problem score (Øie, Rund, Sundet & Bryhn, 1998).

The ADHD individuals were recruited from the National Centre for Child and Adolescent Psychiatry in Oslo, and were all outpatients at the point of inclusion (Øie & Rund, 1999). An expert panel, using semi-structured clinical interviews and standardized rating scales, conducted the diagnostic evaluations of the ADHD sample at T1. The adolescents fulfilled at least eight criteria for the condition, using the Diagnostic and Statistical Manual of Mental Disorders, Third Edition Revised (American Psychiatric Association, 1987). In addition, all had shown significant hyperactivity, impulsivity, and inattention between the ages of 6 to 10
years when assessed by the Parent’s Rating Scale. Participants in both the ADHD and HC
groups were excluded if they reported a history of hearing impairment, head injury with a
significant loss of consciousness or neurological disorder including seizures.

Of the 20 individuals with ADHD at T1, one was deceased after 13 years. Thus, 19
individuals from the original ADHD baseline sample were available for reassessment at T2.
The ADHD group consisted of 15 individuals with a DSM-IV diagnosis of current ADHD
(inattentive or combined subtypes). The remaining four individuals were symptom free at T2
and received no diagnoses. Of the 30 HC, all still fulfilled the criteria to serve as healthy
controls.

All 19 individuals (100%) from the T2 ADHD sample were available for
reassessment with diagnostic and neuropsychological measures after 20 years (T3). Eleven
individuals received a DSM-IV diagnosis of current ADHD (inattentive or combined
subtypes), while the remaining eight individuals had ADHD symptoms below the cut-off for
an ADHD diagnosis, and received no diagnoses. This improvement in ADHD symptoms was
equivalent to those found in studies of age-dependent persistence (Biederman et al., 2010).
Because of this, our sample was considered a satisfactory representation of the typical
clinical presentation in adult ADHD. Moreover, we decided to include the eight symptom
free participants, despite not meeting the diagnostic criteria for the disorder. This was in
accordance with the 13-year longitudinal follow-up from T1 to T2, in which the four
symptom-free ADHD individuals were included in the analyses. The rationale behind this
decision was that the primary objective of the study was to investigate how individuals with a
childhood diagnosis of ADHD developed over time. Hence, those who outgrew their
diagnosis were also relevant for the analyses. Although with some variations in effect sizes
and significance levels, no significant changes were yielded in neuropsychological
performance over time when we removed the ADHD individuals who had become symptom
free at T3. From T2 to T3, HC were reduced from 30 to 26, wherein one had deceased.
Characteristics of the ADHD group at T3 compared to the HC group are presented in Table 1.
All the participants in the ADHD group were males, whereas in the HC group there were 13
male and 13 female participants at T3. The level of intellectual ability in both the ADHD
(110.1 (± 10.5)) and HC group (114.4 ((± 8.0) at T3 were within the normal range. No
significant group differences in intellectual performance were detected (F_{1,43} = 2.42, p=.127).

With regard to medication in the ADHD group, one patient used stimulants (Ritalin),
three used a small dose of atypical antipsychotics (Seroquel), and one used antidepressants
(Venlaflaxin) at T3. Stimulant medication was discontinued at least 15 hours before testing.
Neuropsychological measures

The participants were assessed using the same neuropsychological test battery at T3 as that used at both previous time points, with the exception of replacing the Wechsler Intelligence Scale for Children – Revised (WISC-R), used at T1 with age-appropriate versions of the subtests from the Wechsler Adult Intelligence Scale – Third Edition (WAIS III) (Wechsler, 2003) and the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 2007) to assess IQ. All individuals were tested individually, and received the tests in the same order. Assessment with the entire test battery took approximately three hours, including breaks.

Given the broad description of neuropsychological functioning results in ADHD individuals at both baseline (T1) (Øie & Rund, 1999) and first follow-up (T2) (Øie et al., 2010), we chose to further specify our neuropsychological domains in this thesis, namely pre-attention and executive attention. Thus, we chose to analyse only two attentional measures, the Backward masking task and the Digit span distractibility test, hence representing opposite ends of the attentional capacity continuum.

2.2.1 The Backward masking task

In visual masking paradigms, briefly described earlier, masking occurs when mutually different structures are presented in close temporal association and compete for the “privilege” of becoming explicitly recognized (Bachmann, Luiga, & Põder, 2005). In backward masking, the masking stimulus is presented at some point after the onset of the
target (Rund, Øie, & Sundet, 1996). Intervals between target and mask can be measured
either by stimulus onset asynchronies (SOAs) (interval from onset of the first stimulus) or
interstimulus intervals (ISIs) (interval from offset of the first stimulus) (Green, Nuechterlein,
Breitmeyer, Tsuang, & Mintz, 2003). SOAs/ISIs typically vary from 0-100 ms in both
forward and backward masking paradigms, but can be extended over longer time ranges,
depending on the specific paradigms and task parameters (Green, Lee, Wynn, & Mathis,
2011). Thus, the masking effects one can obtain depend on the choice of stimulus and task
parameters and, therefore, on the theoretically or empirically motivated choices of these
parameters. Hence, one can obtain evidence for masking effects at a number of levels of
visual processing, from the earliest pre-attentive and preconscious levels to levels that engage
attentional and top-down processes. The early component (i.e. ISIs of less than approximately
60 ms) typically reflects pre-attentive processes; in contrast, the later part of the masking
function (greater than approximately 70 ms) reflects a susceptibility to attentional
disengagement (Green, Nuechterlein, Breitmeyer, & Mintz, 1999). Such a distinction is
important, given that they appear to be differentially tied to cognitive dysfunction
vulnerabilities. Despite taxing a preliminary form of attentional engagement at higher ISIs,
the visual masking paradigm does not encompass the necessary methodological complexity
to measure higher-order executive functions.

To assess pre-attentional performance, we utilized a traditional backward masking
paradigm, originally developed by Sperling (1965). Furthermore, an interstimulus interval
procedure (ISI) was used, with intervals of 16, 33, 49 and 116 ms. However, in the present
study, only the 33 and 49 ms conditions were taken into consideration, given these ISIs were
best suited for assessing pre-attentional processes. In this procedure, the subjects were briefly
shown a target stimulus (a two-digit number) presented visually on a computer screen. The
stimulus was then followed by a patterned mask of X’s occupying the same area on the
screen as that where the target stimulus appeared. The task consisted of 60 stimulus
presentations: 10 trials at each of the five ISIs and 10 with a no-mask control condition.
Moreover, a small arrow presented just above the target location provided a fixation point,
and subjects were instructed to report the digits presented on the screen, even if they were not
able to recognize any of the digits (forced response). The identification of each digit in the
pair was scored separately, yielding a maximum score of 20 for each condition. In
consonance with previous studies using the same backward masking paradigm (Rund et al.,
1996), the 33ms and 49ms interstimulus intervals were combined to a mean number of
correctly identified digits (BMtotal). Consequently, there were two distinct measures of pre-
attention in the current study, namely the no-mask condition, and the combined 33ms + 49ms condition (BMtotal).

2.2.2 The Digit span distractibility test
To assess working memory/executive attention performance, we used the Digit span distractibility test by Oltmanns and Neal (1975), whose test format has previously been described. Considering the current study, the series of digits were of varying string lengths to ensure an overlap of difficulty levels between conditions. Thus, the distractor series were 5 and 6 digits long, whereas neutral items were 6 and 7 digits long. In the neutral conditions (i.e. without distraction), subjects listen to a series of digits presented by a tape-recorded female voice at a rate of approximately 1 digit every 2 seconds. However, in the distractor condition, irrelevant digits are read by a male voice in the interval between the relevant digits. Subjects were instructed to ignore the male voice and remember only those digits presented by the female voice. When the sequence was completed, the subjects were then told to write down as many correctly ordered digits as they could remember, even if they did not retain the entire string. In the distractor condition, irrelevant digits were read by a male voice in the interval between relevant digits. Subjects were instructed to ignore the male voice and remember only those digits presented by the female voice. Each sequence was scored by tallying the number of digits correctly reported and subtracting 1 point from the number of digits presented for each error of omission, addition or order. To make scores on the various tests comparable, these point totals were then converted to a percentage of correct responses for each test. Some minimal changes were done to the procedure; all items were presented monaurally and in the Norwegian language, as opposed to the original test, in which the items were presented binaurally and in the English language (Rund, 1989).

2.3 Symptom, behaviour and functional ratings
At all three time points the ADHD group was assessed with the World Health Organization Adult ADHD self-report scale (ASRS; Kessler et al., 2005). The ASRS is an 18-item measure of the DSM–IV criteria for ADHD, in which each item is scored from 0 to 4. High scores indicate more ADHD-like features. The ASRS measures the degree of inattentive and hyperactivity symptoms in ADHD individuals, and to what degree they contribute to functional impairment. The total symptom score is reported in Table 1. (ASRS total).

Both groups were also rated at the three time points with the Global Assessment Scale
of symptoms (GAS; Endicott, Spitzer, Fleiss, & Cohen, 1976). The GAS rates the
individual’s symptoms during a specified time period with scores from 1 (severe
malfunction) to 100 (excellent function) divided into 10 equal intervals. In addition, they
were assessed by the Global Assessment Scale of Function (GAS-F; Endicott et al., 1976),
which rates the individual’s psychological and social functioning during a specified time
period with scores from 1 (severe malfunction) to 100 (excellent function) divided into 10
equal intervals.

2.4 Ethical perspectives

The T1, T2 and T3 studies were all approved by the Regional Committee for Medical
Research Ethics in Eastern Norway (REK Øst-Norge REK 1 # 98-05-04113; 2015/180/REK
sør-øst C), and the study was conducted in accordance with the Helsinki Declaration of the
World Medical Assembly. The project was also approved by the Privacy Protection
Ombudsman for research at the Innlandet Hospital Trust. Patients were assessed using
established and standardized instruments, and there were no known risks associated with the
examination. Ample breaks were given during testing, feedback and results were given to
support their situation and all participants were compensated with NOK 500 at T2 and T3.

2.5 Data analyses

Analyses were conducted using the statistical package SPSS, version 25.0. Preliminary group
characteristics were investigated by a Fisher exact probability test (nominal variables) and an
analysis of variance (ANOVA, continuous variables) followed up by Bonferroni’s post hoc
tests for multiple group comparisons. Changes in test results from T2 to T3 were first
analysed using a conventional repeated measures ANOVA with group (ADHD and HC) as
between-subject factors, and attentional measures (Digit span distractibility test and
Backward masking task) as within-subject factors. In order to directly compare current
results/sample (T3) against the T1 and T2 study, additional RM-ANOVAs were conducted
with a limited sample. Effect sizes ($\eta^2$) for the main effects (group and time) were also
computed. The strength of the effect sizes was determined according to Cohen’s guidelines
(Cohen, 1988). The significance level was conventionally set to 0.05. The RM-ANOVA was
followed up by paired t-tests between scores at T2 and T3 within each group to assess
pairwise comparisons. Pearson’s correlation analyses were also conducted to assess the relationship between: 1) neuropsychological performance and symptom severity, and 2) the relationship between measures of pre-attention and working memory/executive attention (i.e. hierarchical relationship). Lastly, it should be noted that raw scores were used for all analyses.
3 Results

Summary statistics for pre-attention and working memory/executive attention performance at T2 and T3 are presented for the ADHD and HC groups in Table 2.

3.1 Concurrent group differences at T3

There were no significant effects of group across the two assessment times (T2, T3) in either backward masking no-mask (F_{1,43} = .297, p = .589) or backward masking total (F_{1,43} = .040, p = .840). However, significant effects of group across the two assessment times (T2, T3) were found for both the Digit span test with (F_{1,43} =11.7, p = .001) and without distraction (F_{1,43} = 5.5, p = .023). Both group effects met the criteria for small effect sizes, with a $\eta^2 = .214$ and .114, respectively. In order to examine these group effects concurrently at T2 and T3, independent sample t-tests were separately conducted at the two time points. There was a significant group difference for the Digit span test without distractor, both at T3 (F_{1,43} = 2.3, p = .043) and T2 (F_{1,43} = .085, p = .030), in which ADHD individuals consistently performed below the HC average. This trend was also evident in the Digit span test without distractor, in which ADHD individuals displayed significant deficits (i.e. group effects) at both T2 (F_{1,43} = 8.4, p = .004), and T3 (F_{1,43} = 5.1, p = .011) compared to HC.

3.2 Development in attentional measures from T2 to T3

A significant decline in performance from T2 to T3 was found in the Backward masking no-mask condition (F_{1,43} = 5.7, p = .022). This effect of time was primarily explained by a decline in the HC group (F_{1,43} = 9.4, p = .005), and not in the ADHD group (F_{1,43} = .511, p = .484). A significant effect of time was also found for the Backward masking total condition (F_{1,43} = 10.0, p = .003). However, this effect was mainly explained by a decline in the ADHD group (F_{1,43} = 20.5, p = .000). The results in the HC group for the Backward masking total condition remained stable from T2 to T3, as evidenced by a non-significant time effect (F_{1,43} = .44, p = .512). The decline in performance in the total condition for the ADHD group reached a “medium” effect size of $\eta^2 = .533$, using Cohen’s guidelines (Cohen, 1988). Following a decline in the ADHD group and a relative stability in the HC group, a significant time x group-effect (F_{1,43} = 4.7, p = .035) was discovered. This reached a small effect size of
$\eta^2 = .099$. The development in performance in pre-attentional measures is visualized in Figure 1., in which a mean score is plotted for each time point.

A significant decline in performance from T2 to T3 was also found in the Digit span test with distractor ($F_{1,43} = 8.7, p = .005$). This decline achieved a small effect size of $\eta^2 = .168$. The effect of time was jointly explained by both the ADHD ($p = .049$) and the HC group effect ($p = .058$). While only the ADHD group reached the set significance level, the two results will be treated as being identical in the forthcoming discussion, given the marginal difference between the two. For the digit span measures, there were no interaction effects reaching the set significance level, indicating that the ADHD and HC group trajectories on executive attentional measures generally tended to develop in a similar manner from T2 to T3, although with some variations in effect sizes (i.e. steepness of trajectory). The development in performance of working memory/executive attention measures are visualized in Figure 2. and 3., in which a mean score is plotted for each time point.
Table 2. Neuropsychological test results at T2 and T3

<table>
<thead>
<tr>
<th></th>
<th>ADHD (n=19)</th>
<th>Healthy (n=26)</th>
<th>Group (df=1, 43)</th>
<th>Time (df: 1, 43)</th>
<th>Time x Group (df=1, 43)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T2</td>
<td>T3</td>
<td>T2</td>
<td>T3</td>
<td>F</td>
</tr>
<tr>
<td>Digit repetition task without distraction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>82.9 (8.9)</td>
<td>81.3 (13.9)</td>
<td>88.7 (8.2)</td>
<td>88.8 (10.2)</td>
<td>5.5</td>
</tr>
<tr>
<td>Digit repetition task with distraction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>11.7</td>
</tr>
<tr>
<td></td>
<td>83.9 (13.6)</td>
<td>75.7 (18.6)</td>
<td>93.7 (7.7)</td>
<td>88.0 (12.6)</td>
<td></td>
</tr>
<tr>
<td>Backward masking, no mask</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.297</td>
</tr>
<tr>
<td></td>
<td>17.9 (2.0)</td>
<td>17.4 (2.8)</td>
<td>18.0 (1.5)</td>
<td>16.8 (1.8)</td>
<td></td>
</tr>
<tr>
<td>Backward masking total</td>
<td>10.0 (4.9)</td>
<td>6.6 (4.0)</td>
<td>8.4 (3.9)</td>
<td>7.7 (3.9)</td>
<td>.040</td>
</tr>
</tbody>
</table>
Figure 1. Performance on the Backward masking total for the two groups at T1, T2 and T3.

Figure 2. Performance on the Digit span test without distractor for the two groups at T1, T2 and T3.
### 3.3 Correlation analysis

We conducted a correlation analysis (Pearson) to assess whether the degree of symptoms, as measured by the ASRS (hyperactivity, inattentiveness and total), were associated with working memory/executive attention measures (Digit span test with/without distractor) (i.e. if those with greater neuropsychological deficits also had higher symptom severity). No significant results were found. With respect to our hypothesis of a hierarchical relationship between lower- and higher-order cognitions, there was no statistically significant correlation between Backward masking total performance and Digit span with distractor ($r= -.042, p= .784$) or Digit span without distractor ($r= .051, p= .738$) at T3. No significant changes in results were detected when using a Spearman’s rho, thereby controlling for a non-parametric distribution.

### 3.4 Analysis of limited sample

In order to compare the current results (T3) and developmental trajectory (T2 to T3) against the T1 (Øie & Rund, 1999) and T2 (Øie et al. 2010) studies, we had to conduct additional longitudinal RM-ANOVAs, given that our HC sample had been reduced from 30 to 26 over the 20-year follow-up period. These analyses did not yield statistically significant changes in results from T1 to T2, which allowed us to use results from the T1 and T2 studies as a valid reference when discussing our current results.
4 Discussion

4.1 Concurrent group differences in neuropsychological attention performance at T3

There were no concurrent differences between the ADHD and HC groups at T2 and T3 on the Backward masking task, regardless of condition (BMtotal and no-mask). This lack of between-group differences was in line with previous research - from which our current hypotheses are derived - describing “nearly” significant (Rund et al., 1996) or non-significant (Øie et al., 2010) group differences between ADHD and HC groups in backward masking performance. Also in accordance with our first hypothesis (1), as well as reports from the T1 and T2 studies (Øie & Rund, 1999; Øie et al., 2010), we confirmed concurrent group differences at all three time points for both conditions of the Digit span distractibility test (with and without distractor), with the ADHD group performing consistently below the HC average. Our finding that adults with ADHD have impairments in working memory/executive attention (corresponding to the T2 and T3 studies) is in consonance with previously reported studies on neuropsychological performance in adult ADHD (Hervey et al., 2004; Schoechlin & Engel, 2005; Alderson, Kasper, Hudec, & Patros, 2013).

Investigators have increasingly embraced the notion that ADHD is best understood within the context of a developmental trajectory, rather than that of a static medical condition (Hinshaw, 2017b). However, it is still unclear whether adults with ADHD should be expected to have similar neuropsychological deficits - relative to their age-matched healthy peers - as children and adolescents with ADHD. In normal brain development, maturation and myelination of the brain regions involved in attention and executive control, particularly the prefrontal cortex and frontal–subcortical networks, continue into late adolescence and young adulthood (Arain et al., 2013). Despite the common notion of a brain maturation lag in ADHD, some authors (El-Sayed et al., 2003) argue that from the extrapolation of the developmental trajectory curves from fMRI studies of children with ADHD, their trajectories should converge with those of healthy controls by the age of 20 years. Regardless, it remains an open question as to whether adult ADHD is accompanied by a similar cognitive profile once these networks mature (Carr, Nigg, & Henderson, 2006).

Nonetheless, while the abovementioned fMRI study would implicate a “transient
developmental lag” in neuropsychological performance over the ADHD lifespan, a plethora of neuroimaging studies in ADHD individuals suggest that key anatomic regions remain underdeveloped throughout development (Krain & Castellanos, 2006), or experience a selective thinning of the cerebral cortex in networks that subserve attention and executive functions (Makris et al., 2007; Almeida et al., 2010), thus preserving neuropsychological deficits. This persistence of structural and functional changes stands in contrast to the concept of a transient developmental lag (Bollmann et al., 2017), in that they would constitute a continual anomaly in ADHD neurodevelopment (i.e. a persistent developmental lag), whereby ADHD individuals never acquire the same neuropsychological performance values as HC. This would be in consonance with the finding that adults with ADHD continue to demonstrate cognitive problems when the disorder persists (Schoechlin & Engel, 2005; Salomone, Fleming, Bramham, O’Connell, & Robertson, 2016), a finding that is further garnered by our current results, indicating a persistence in working memory/executive attention deficits in ADHD individuals across the 20-year follow-up period.

Although further work is needed to understand the sources for the stability and instability of working memory/executive attention, results from all three assessment points in the current study are worthy of comment. The baseline and 13-year follow up-study reported that ADHD individuals performed significantly below the HC group on the Digit span test (taxing both maintenance and manipulation) concurrently at both T1 and T2. However, they evidenced a significant improvement from baseline to the 13-year follow-up, in contrast to their healthy peers - a finding that has been further replicated (Murray et al., 2017). Thus, noteworthy neuropsychological deficits continue into young adulthood (T2), but at a smaller magnitude than what was evidenced at baseline. This improvement was expected, given that the 13-year period from T1 (mid-teens) to T2 (young adulthood) constituted a crucial developmental period of the PFC, predicting a complete maturation to be present at T2. The essential contribution of the current study was that it examined whether neuropsychological deficits persisted after the expected neurodevelopmental “peak”. Compared to the HC, the ADHD individuals still displayed significant deficits in working memory/executive attention measures at T3, thereby suggesting a continuation of the neuropsychological deficits found in the ADHD group at T1 and T2. This preservation of neuropsychological dysfunctions over time stands somewhat in contrast to the findings of Moffitt et al. (2015), who raised the question that adult ADHD may not represent a continuation of a childhood-onset neurodevelopmental disorder – implicating separate diagnostic entities. Our results demonstrate that ADHD individuals experience a profound “catching up” to a certain level
(mid 20s/T2), and then roughly follow the same developmental pattern (T2 to T3) as the HC group.

With respect to the notion of a developmental delay in ADHD individuals, our current results are somewhat ambiguous. On the one hand, the qualitative similarities in neurodevelopment (i.e. parallel development) between the two groups can be interpreted as confirming the evidence of ADHD not constituting a developmental deviation from the HC. Moreover, the decline seen in the ADHD group from the 13 to 20-year follow-up on Digit span with distractor only marginally exceeds that of the HC group, further supporting the notion of approximate normal development. On the other hand, the fact that ADHD individuals never catch up entirely to their undiagnosed peers – which is expected by the mid-20s - might suggest a permanent, perhaps static, anomaly in ADHD neurodevelopment, which cannot be solely accounted for by a transient developmental lag framework. Consequently, the current results are most in line with a “persistent developmental lag” framework of neuropsychological development in ADHD individuals. However, it should be taken into account that the current results only generalize to a male population, assessed on specific neuropsychological paradigms (working memory/executive attention).

4.2 Differential development in diverse attentional measures

4.2.1 Development of pre-attention performance
The longitudinal stability of neuropsychological deficits in ADHD has not previously been examined in relation to backward masking paradigms. Even though a backward masking deficit has been extensively documented, primarily in schizophrenia (Green et al., 1999; Rund et al., 2004; Thormodsen et al., 2012), the relative stability of this deficit has only been examined to a limited degree in ADHD individuals. To the best of our knowledge, the 13-year follow-up (T2) (Øie et al., 2010) is the only study examining backward masking performance over a substantial period of time (from adolescence to young adulthood). Over the course of 13 years, the ADHD group evidenced a significant improvement in backward masking performance from T1 to T2. Thus, there is little neuropsychological basis of comparison with regard to the present results (T2-T3). Consequently, one must interpret these
findings as a fundamental research contribution, providing some first insights into the development of pre-attentional performance over time.

With respect to our original hypotheses we predicted a more stable development from T2 to T3, parallel with the HC. The current results from the Backward masking task suggest a differential effect of age on development. Thus, age exerts an influence on pre-attentional performance, but only for the ADHD individuals. This is reflected by a significant increase in performance from T1 to T2, and a decline in performance from T2 to T3. In contrast, the HC group experienced stability in performance (i.e. a consistency in neuropsychological values) over the 20-year follow-up. Because of this, the ADHD group seemingly exhibits a vulnerability for larger fluctuations in pre-attentional performance (exclusively in masking conditions) over a 20-year follow up, compared to the overall stability of the HC group. As a result, a significant time x group effect was detected, both from T1 to T2 (Øie et al., 2010), but also from T2 to T3. With respect to our assumption of relative stability in performance over time, this was only partly confirmed, given that the HC group displayed stability over a 20-year period, whereas the ADHD group evidenced significant fluctuations.

The reason for this fluctuation may be twofold. On the one hand, pre-attentional processing capacities, being highly conditioned by basic visuospatial processes (i.e. sensory), should be fully mature by the mid-teens (T1) (Stiles et al., 2013). Therefore, any interaction effects between the ADHD and HC groups beyond this time point could indicate a temporary, non-cortical deviation in ADHD. Given that ADHD performance on pre-attention (BMtotal) is relatively similar at T1 and T3, there might be environmental influences at the T2 follow-up that could cause a temporary improvement in performance. On the other hand - and perhaps more plausible given heritability estimates as high as 88% (Larsson, Chang, D’Onofrio, & Lichtenstein, 2014) - the fluctuation could be explained by genetic, pre-determined developmental tendencies intrinsic to the ADHD aetiology. If this were the case, the fluctuation would categorize as a deviation in ADHD neurodevelopment.

Despite not contributing to any concurrent group differences at T2 and T3, the fluctuations in performance in the ADHD group may be of clinical importance, given that they represent a significant instability over time. To the extent that deficits in pre-attention limit the acquisition of general life skills (e.g. perception of social context; Sergi & Green, 2003), any acceleration of deficits beyond “normal” age-related decline would make it more difficult for patients to acquire the skills needed for daily functioning – some of which were mentioned in the introduction.
4.2.2 Development of working memory/executive attention performance

For the more complex attentional tasks (Digit span distractibility test with/without distractor), the effects of age on development were more coherent, irrespective of group, which was reflected as a parallel development between the ADHD and HC groups in both conditions from T2 to T3. This lack of interaction effect between groups indicates that the ADHD and HC group did not differ in their longitudinal trajectories from T2-T3. Instead, individuals in both groups adhere to a common developmental trend, namely stability in “simple” working memory (Digit span test without distractor), and a decline in executive attention (Digit span test with distractor). Thus, age exerts a seemingly limited effect on the “maintenance” component of working memory capacity, irrespective of group, indicating that this capacity is relatively spared, compared to the “manipulation” capacity, in which increasing age was consistently associated with a decline in performance, irrespective of group.

The first observation to make is that it is hardly surprising that age differences are observed in tasks that require cognitive control (i.e. the Digit span test with distractibility) – after all, just about any study in cognitive aging research shows that age-related change is the rule, and not the exception (Verhaeghen, 2011). Several reviewers have argued that the pattern of spared and impaired cognitive functions observed in the cognitive aging literature can be understood within the context of a neuropsychologically constrained model, which proposes that the prefrontal cortex is more vulnerable to the effects of normal aging than other cortical regions (Buckner, 2004). In general, the more a cognitive task taxes on executive functions, the more likely it is affected by aging (Buckner, 2004). Hence, normal aging has a greater impact on working memory/executive attention (i.e. “manipulation”) than on short-term memory (i.e. “maintenance”) (Bopp & Verhaeghen, 2005). Beginning in the 20s, a continuous, regular decline occurs for processing intensive tasks (e.g. speed of processing and working memory) (Park et al., 2002).

Our results adhere to this general observation, as is reflected by a decline in both the ADHD and HC group on the Digit span test with distractor (“manipulation”) and a relative stability in the Digit span test without distractor (“maintenance”). This may be because the Digit span test with distractor places greater demands on cognitive resources, as it requires information manipulation in addition to basic storage. In line with this differential effect of task complexity on age-related development, researchers have argued that the attention regulation ability, and specifically the ability to inhibit the processing of distracting
information, is a primary determinant of age-related differences in complex neuropsychology (Darowski, Helder, Zacks, Hasher, & Hambrick, 2008).

### 4.3 Association between neuropsychological performance and ADHD symptom severity

In an attempt to explain the commonly observed diminution in ADHD clinical symptoms across the lifespan, Halperin, Trampush, Miller, Marks, & Newcorn (2008) posited a distinct cognitive mechanism for the aetiology of - and relative recovery from ADHD. More specifically, they postulated the idea that ADHD is caused by non-cortical neural dysfunction, which is present early in ontogeny and remains relatively static throughout life. In this regard, ADHD is never really “cured” or “out-grown”. Nonetheless, they posited that the reduction of symptoms oftentimes seen over development are at least partially accounted for by the degree to which prefrontally-mediated executive functions and other higher cortical functions can compensate for these more primary and enduring subcortical deficits (Halperin & Healey, 2011) – a premise that resonates satisfactorily with the dual-pathway framework (Sonuga-Barke, 2003) described earlier. At face value, this framework fits well with the results from both hypothesis 1 and 2, given that it provides an account of the consistent group differences in working memory/executive attention, as well as the relative improvement displayed in the ADHD group. As the ADHD group progresses in their neurodevelopment throughout the lifespan, one could argue that they acquire certain executive/compensating cortical functions, manifesting themselves as the steep “catching up” from T1 to T2. At T2, one would expect them to peak, which our results confirm. From T2 to T3, one might argue that it is the acquired executive functions - although performing at a level below the HC average – that keeps the continued neurodevelopment of ADHD individuals in parallel with the HC.

However, a key notion in the Halperin et al. (2008) framework is that it predicts neuropsychological performance to be closely correlated with a reduction in symptom severity, an assumption that was also reflected in our 3a) hypothesis. With respect to the current correlation analysis, this did not confirm a statistically significant association between the Digit span distractibility test and self-reported symptom ratings at T3— a finding that stands in contrast to extended research confirming associations between neuropsychological performance and clinical ADHD symptoms (Willcutt et al., 2005; Willcutt et al., 2008). This result can be further discussed in light of research findings pertaining to the effect of...
cognitive training in ADHD. There are two ways of understanding the effects exerted by cognitive training on neuropsychological performance. From the first perspective, cognitive training is considered a front-line ADHD treatment; this is based on the hypothesis that because causal pathways to the disorder are mediated by neuropsychological deficits, strengthening deficient neuropsychological functions should reduce ADHD symptoms and associated impairment (Cortese et al., 2015). From the second perspective, it is perceived as an adjunctive treatment that reduces impairment associated with neuropsychological deficits commonly seen in ADHD, independent of any effects on core ADHD symptoms themselves (Cortese et al., 2015). This understanding accentuates an imperative that clinicians should not only focus on clinical symptom relief, but also interventions aimed at improving neuropsychological performance – a clinical mindset that so far is underrepresented.

Taking our own results into consideration, including our non-significant correlation between neuropsychological performance (working memory/executive attention) and symptom severity (ASRS inattention, hyperactivity and total), the latter perspective is most in consonance with our own results. This conforms to a meta-analysis examining the clinical and neuropsychological outcomes from cognitive training (Cortese et al., 2015), whereby they provided little convincing support for cognitive training as a front-line ADHD treatment. The evidence was somewhat stronger for the benefits of cognitive training as an adjunctive treatment, aimed at reducing neuropsychological impairment. Nonetheless, the effects on neuropsychological performance were restricted to the domain of working memory, which were substantial. Based on our results, we argue that strengthening these neuropsychological functions is neither a necessary nor sufficient condition for clinical symptom reduction.

4.4 Association between measures of pre-attention and working memory/executive attention

Results from our second correlation analysis, examining the relationship between the lower-(pre-attention) and higher-order cognitions (working memory/executive attention), did not confirm our hypothesis. Nor did it confirm findings from previous studies, which have suggested an inter-relatedness between executive functions and cognitive functions of the lower order (Piek et al., 2004; Rommelse et al., 2007; Stein, Auerswald, & Ebersbach, 2017). This finding further suggests that lower-order cognitions do not necessarily precede or determine executive dysfunctions in ADHD. The current absence of a statistically significant association, combined with our findings of persistent working memory/executive attention
deficits at T2 and T3, implies that ADHD is primarily characterized by an impaired top-down control (in which case executive function deficits are the primary problem). In sum, this finding corresponds to the theoretical models formulated by Barkley (1997) and Pennington and Ozonoff (1996), wherein ADHD stems from a primary deficit in executive functions.

4.5 Implications for treatment

As detailed earlier, impaired long-term social and occupational functioning are among the impediments found in individuals with ADHD (Halmøy et al., 2009; Eslinger et al., 2013), as executive deficits have consistently been linked to functional deficits (Barkley & Murphy, 2010; van Lieshout et al., 2017). To prevent a serious impairment of daily life function, it may be essential to identify and help individuals with ADHD and executive function deficits (Miller, Nevado-Montenegro, & Hinshaw, 2012). Societal accommodations for ADHD behaviours tend to diminish in adulthood; allowances provided to younger students with ADHD (e.g. extended time on tests, additional breaks) are typically not present in the workplace (Gotlieb & Gotlieb, 2009). Hence, adults with ADHD may not experience the same “alleviation” of working memory/executive attention difficulties on a day-to-day basis.

Considering our results of persistent working memory/executive function deficits well into the mid-20s and mid-30s, it is important for individuals with ADHD to experience continuity in treatment and the facilitation of neuropsychological deficits throughout the full progression of their disorder.

4.6 Recommendations for future research

Considering the high level of neuropsychological deficit continuity into adult years, as evidenced by our own results, serious consideration should be given to include the persistence of neuropsychological deficits in the conceptualization of the persistence of ADHD, which is currently based solely on symptoms of the disorder (Biederman et al., 2012). Along these lines, Hinshaw (2017b) noted that the need for integrative perspectives on ADHD in particular, and developmental psychopathology in general, has never been greater. Identifying the underlying disease mechanisms, such as neuropsychological dysfunctions, is imperative and can lead to major health benefits through the development of new treatment and prevention regimens. Any advance in the understanding of the mechanisms of ADHD has potential benefit to individuals, professional practices and society.
Despite the need for longitudinal methodology in ADHD research, there is still a profound scarcity of longitudinal neuropsychological research from childhood into adulthood. This is unfortunate, knowing that this type of design is necessary to determine the full extent of neuropsychological continuity. As noted by Seidman (2006) over a decade ago, there was relatively little systematic neuropsychological information on ADHD throughout life – an observation that still holds true. In accommodating this need, larger samples using several repeated neuropsychological measures at different time intervals would be advantageous in order to investigate the more exact timing of neuropsychological changes. Adhering to the recommendation of extended sample sizes in particular, The Norwegian Mother and Child Cohort Study (MoBa) initiated a new subproject aimed at understanding the development and causes of ADHD (Magnus, 2009), hence constituting one of the largest samples in ADHD research to date. Moreover, a combination of neuropsychological, structural and functional MRI measures, allowing for an evaluation of structure–function relationships in ADHD, is also considered an imperative for future research.

In summary, a clinical understanding of the neuropsychology of ADHD needs to be taken into account to provide a greater opportunity for improved and more integrated treatment approaches, as knowledge on the course of disorders across the lifespan is essential for planning accurate clinical approaches (Karam et al., 2015). Furthermore, including markers of key domains of dysfunction or impairment in diagnostic systems, such as executive function deficits, could help parse the heterogeneity of the disorder and therefore be crucial in the future refinement of ADHD nosology (Sonuga-Barke, Sergeant, Nigg, & Willcutt, 2008).

4.7 Strengths and limitations

The current results contribute to the limited knowledge about longitudinal outcome in ADHD individuals, more specifically how they compare to their non-ADHD peers with respect to neuropsychological functioning. It therefore meets a longstanding demand for prospective, longitudinal studies of ADHD individuals, following them over a substantial period of time. Another strength of our study is that it investigates a previously unstudied development for both pre-attention and working memory/executive attention performance in an ADHD sample, compared to HC. As such, it constitutes an antithesis to previous studies, primarily utilizing cross-sectional methodologies. Further strengths include a long follow-up time (20 years), a high retention rate (19/20 ADHD individuals), thorough clinical examinations (e.g.
rigorous inclusion criteria and an expert panel review to determine ADHD status), as well as the inclusion of a HC group for the purpose of comparison.

However, the results should be interpreted with some limitations in mind. The relatively small sample size presents methodological constraints, and may reduce the power of statistical tests to detect differences in correlations in particular. Yet, a small sample size is a general problem inherent in longitudinal studies, reflecting the challenges associated with repeated assessments of this neuropsychiatric group over time. As previously noted, the current longitudinal findings are only provisional and in need of replication.

A second limitation concerns comorbidity, which is a substantial problem in ADHD individuals with respect to diagnosis. Not taking comorbidity into consideration when conducting analyses leads to a potential confounding of results in terms of attributing any deficits solely to a primary attentional disorder, given that depression and anxiety may also impair executive functions (American Psychiatric Association, 2013). Consequently, these symptoms may have influenced the behavioural executive function outcomes in the present study. Lastly, our ADHD group consisted of only males - a distribution that stands in contrast to the HC group, where males and females were equally represented. A generation ago – and up until recent decades - clinical knowledge strongly suggested that ADHD rarely existed in girls (Hinshaw, 2017a). Hence, the reason for our gender discrepancy was simply due to the prominence of this clinical bias when the study was initiated in 1992. However, it is true that, as with all other neurodevelopmental disorders—including autism spectrum disorders, aggressive conduct problems and Tourette’s disorder—boys exhibit a higher prevalence than do girls (Willcutt, 2012). Thus, our selective sampling can to a certain degree be rationalized.

4.8 Conclusion

The current longitudinal results confirm and extend on previous findings by adolescence (mid-teens) and young adulthood (mid-20s) by documenting that ADHD individuals growing up continue to be afflicted with neuropsychological attention deficits, compared to HC. The current study demonstrated, similarly to the T1 and T2 study, specific deficits in the “maintenance” (Digit span test without distractibility) and “manipulation” (Digit span test with distractibility) sub-categories of working memory. It demonstrates that working memory/executive attention dysfunctions tend to persist in ADHD, suggesting that deficits in executive functions might be at the core of ADHD pathology, as postulated by Barkley (1997) two decades ago. Pre-attentional measures, however, did not display any deficits at T2
and T3. This may imply that as the complexity in task requirements to processing ability rise, the differences between the ADHD and HC group increase accordingly. The current results have both applied and heuristic implications for the field, assuming the findings can be generalized to the larger population of affected individuals.

Generally speaking, the results support the notion that the development of executive processes parallels the maturation and aging of the prefrontal cortex (Halperin & Schulz, 2006) in both the ADHD and HC groups throughout the lifespan. Furthermore, our results seem to fit well into a framework of the consistent brain abnormalities presented in ADHD individuals throughout their development (Krain & Castellanos, 2006; Makris et al., 2007), which may contribute to the neuropsychological deficits displayed by ADHD individuals, particularly in working memory/executive attention measures across the 20-year follow-up. Nevertheless, these results emphasize the importance of studying neuropsychological performance in ADHD within the context of brain development to help identify possible interactions between developmental and disease-related mechanisms on cognition.

The data highlight that ADHD is a cognitively impairing condition, also in adulthood, which should be taken seriously. In particular, executive dysfunctions, while less obviously disruptive, should not be dismissed by clinicians, given that they may contribute to long-term impairment in real-world functioning (Stavro, Ettenhofer, & Nigg, 2007). This provides an imperative for the continued development of cognitive rehabilitative techniques to assist in addressing attention difficulties early on, and possibly counteract these negative effects (Wasserstein & Lynn, 2001).

### 4.9 Acknowledgements

Data on cause of death was obtained from the Norwegian Cause of Death Registry. The present study was funded by the Regional psychosis network (Project 39685; 2014-2016) and ExtraStiftelsen (nr. 2015/FO4270).
References


hyperactive/impulsive and combined subtypes. *Behavioral and Brain Sciences*, 28(3), 397-419. doi: 10.1017/S0140525X05000075


Addiction, 102(7), 1122-1130. doi: http://dx.doi.org/10.1111/j.1360-0443.2007.01850.x


Wilens, T. E., Biederman, J., & Spencer, T. J. (2002). Attention deficit/hyperactivity disorder
across the lifespan. *Annual Review of Medicine, 53*, 113-131. doi: http://dx.doi.org/10.1146/annurev.med.53.082901.103945


