Article

Pre-attention and Working Memory in ADHD: A 25-Year Follow-Up Study

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Abstract

Objective: The aim of the study was to compare the development of working memory and preliminary stages of attentional processing in individuals with ADHD over a 23- to 25-year period. **Method:** Individuals with ADHD ($n = 19$) and healthy controls ($n = 26$) were followed up after 13 years (T2) and 23 to 25 years (T3) after initial assessment (T1). They were reassessed with diagnostic measures and the Backward masking task (pre-attention) and the Digit span distractibility test with and without distraction conditions (working memory). **Results:** The ADHD group performed below the healthy controls on all time points on the Digit span distractibility test. On the distractibility condition, we found a selective decline in performance from T2 to T3 for the ADHD group. **Conclusion:** The results highlight that ADHD individuals continue to display working memory deficits, also in adulthood, thus creating an imperative for cognitive rehabilitation techniques to help address attention difficulties. *(J. of Att. Dis. XXXX; XX(X) XX-XX)*

Keywords

ADHD, neurodevelopment, longitudinal, pre-attention, working memory

Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is 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). Neuropsychological theories of ADHD have tended to emphasize 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). Current research on ADHD almost exclusively deals with the executive concept, leaving findings of "basic" neuropsychological performance far less consolidated. This is questionable as early processing deficits (i.e., pre-attention) may be a precursor of higher order deficits (i.e., executive functions; Fabio, 2017; Lenz et al., 2010). Moreover, longitudinal studies of neuropsychological performance to date have been limited by relatively short follow-up periods. An important purpose of the present study was to accommodate these shortcomings by comparing measures of pre-attention and executive attention (working memory) over a 23- to 25-year follow-up period. 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.

Some kind of selection or control mechanism seems necessary for the optimal functioning of cognition and behavior. A basic distinction is made between the selection generated by behaviorally 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).

Pre-attentive automatic processing refers to a preliminary stage of analysis whereby auditive or visual stimuli is processed before conscious attention sets in (Ellenbroek, 2004). Visual masking is a classic technique used to examine the differences between conscious and unconscious visual

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processing (Breitmeyer & Öğmen, 2006) and has been used for at least 40 years as a suitable test for measuring such basic information processing (Rund et al., 2004). 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 (Øie & Rund, 1999; Øie, Sundet, & Rund, 2010; Rund, Øie, & Sundet, 1996; Sergi, Rassovsky, Nuechterlein, & Green, 2006).

Executive functions represent controlled processes that integrate information from working memory with information about context to select optimal action (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Executive functions may be 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. 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 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).

The 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 subcomponents within working memory, characterized by the degree to which they tax complex attentional control processes. Examinations of working memory subcomponents performance in ADHD individuals suggest that the largest between-group differences are associated with the central executive (i.e., manipulation; Alderson et al., 2015).

Despite the fact that ADHD individuals consistently perform below healthy controls (HC), on average, on several neuropsychological measures throughout the life span, longitudinal studies have suggested a stable or improving course in executive functioning performance (Biederman et al., 2012; Coghill, Hayward, Rhodes, Grimmer, & Matthews, 2014; Fischer, Barkley, Smallish, & Fletcher, 2005; 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 HC 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 (Øie et al., 2010). 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 with HC. This "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). A less consolidated finding in research literature, and an interesting research question, is whether this normalization continues after the mid-20s—generally considered the "peak" of executive functions development (Anderson, Jacobs, & Anderson, 2008)

Aims of the Study

The primary aim of the current study was to examine the attentional processing capacity in ADHD individuals over a 23- to 25-year period. With respect to the potential hierarchical relationship between automatic and controlled cognitive processes mentioned earlier, we chose to further disentangle performance in pre-attention and working memory/executive attention measures in a longitudinal design.

Three main questions will be examined in the present study:

Research Question 1: At the 25-year follow-up (T3), do patients with ADHD display greater deficits in attentional measures (pre-attention and working memory/executive attention), compared with HC?

Research Question 2: At the 25-year follow-up (T3), do patients with ADHD display deficits of equal magnitude in measures of pre-attention and working memory/executive attention?

Research Question 3: Do the two attentional measures display different developmental trajectories in ADHD individuals compared with HC over a 25-year follow-up period?

Method

Participants were assessed at three time points: at baseline (T1), first follow-up after 13 years (T2), and a second follow-up after 25 years (T3).

Table I. Characteristics of the ADHD Group Compared with the HC Group at T3.

Variable	ADHD (N = 19)	HC (N = 26)	ANOVA (df = 1, 43)		Comparisons
			F	p	
Sex (male/female)	19/0	13/13		.000	Fisher
Age (years)	36.6 (1.6)	38.0 (1.6)	7.9	.007	
Education (years)	11.5 (2.1)	15.1 (1.6)	43.0	.000	
Mother's education (years)	12.6 (2.5)	14.7 (2.5)	7.8	.008	
FSIQ (WASI)	110.1 (10.5)	115.1 (8.3)	3.2	.081	
GAS-S	69.3 (11.3)	81.0 (8.0)	16.1	.000	
GAS-F	70.6 (13.4)	83.8 (6.2)	19.2	.000	
ASRS total	27.8 (13.7)	—	—	—	—
Medication					
Stimulants	n = 1	—			
Atypical antipsychotics	n = 3	—			
Antidepressants	n = 1	—			

Note. HC = healthy controls; FSIQ = full-scale intelligence quotient; ANOVA = analysis of variance; WASI = Wechsler Abbreviated Scale of Intelligence; GAS-S = Global Assessment Scale of symptoms; GAS-F = Global Assessment Scale of function; ASRS = Adult ADHD Self-Report Scale.

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 *Diagnostic and Statistical Manual of Mental Disorders* (3rd Ed., Revised; *DSM-III-R*; American Psychiatric Association, 1987) diagnosis of ADHD and 30 HC. The HC were screened for emotional and behavioral 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 cutoff was set according to American norms, corrected for sex and age, whereby the 90th percentile was used as a cutoff for psychiatric problems. The ADHD individuals were recruited from the National Center for Child and Adolescent Psychiatry in Oslo, and were all outpatients at the point of inclusion (Øie & Rund, 1999). Both semi-structured clinical interviews and standardized rating scales were used to confirm a diagnosis of ADHD and to assess the presence of comorbid disorders at T1. Parents were interviewed by a child psychiatrist. The adolescents fulfilled at least eight of the *DSM-III-R* criteria for the condition. Attention problems were marked both at home and at school. In addition, all had significant hyperactivity, impulsivity, and inattention between age 6 and 10, as assessed by the Parent's Rating Scale (Wender, Wood, & Reimherr, 1985), a standardized measure of hyperactivity, inattention, and impulsivity. At T1, 14 of the participants in the ADHD group were given additional diagnoses: oppositional defiant disorder (ODD; *N* = 9), developmental reading disorder (DRD; *N* = 2), and both ODD and DRD (*N* = 3).

Of the 20 individuals with ADHD at T1, one was deceased after 13 years (T2; Norwegian Cause of Death Registry). Thus, 19 individuals from the original ADHD baseline sample were available for reassessment at T2. The ADHD group consisted of 15 individuals with a *Diagnostic and Statistical Manual of Mental Disorders* (4th Ed.; *DSM-IV*) diagnosis of current ADHD (inattentive or combined subtypes). Four participants in the ADHD group were diagnosed with comorbid antisocial personality disorder and two with bipolar disorder at T2. 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 HC.

All 19 individuals (100%) from the T2 ADHD sample were available for reassessment with diagnostic and neuropsychological measures after 25 years (T3). Eleven individuals received a *DSM-IV* diagnosis of current ADHD (five inattentive and six combined subtypes). Among these 11, four participants fulfilled the criteria for ADHD only, whereas seven participants also fulfilled criteria for other disorders: five for depression or anxiety, one participant for a bipolar disorder, and one for Tourette's syndrome. Eight individuals had ADHD symptoms below the cutoff for an ADHD diagnosis, and received no diagnoses.

The HC group was reduced from 30 to 26, wherein one had deceased (Norwegian Cause of Death Registry). They were screened and assessed using identical criteria as the ADHD group. 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 (Venlafaxin) at T3. Stimulant medication was discontinued at least 15 hr before testing at all three follow-ups (T1, T2, and T3). Characteristics of the ADHD group at T3 compared with the HC group are presented in Table 1.

Neuropsychological Measures

A detailed description of the tests and the procedure is given in Øie et al. (2010). 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, 2007) and the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 2007) to assess IQ. All participants were evaluated with an extensive clinical and neuropsychological assessment. Only the instruments relevant to this part of the study are presented here.

The Backward Masking Task

To assess pre-attentional performance, we utilized a traditional backward masking paradigm, originally developed by Sperling (1965). 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). In backward masking, the masking stimulus is presented at some point after the onset of the target (Rund et al., 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). 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). In the present study, we used a 33 and 49 ms condition, given these ISIs were best suited for assessing pre-attentional processes. The task consisted of 60 stimulus presentations: 10 trials at each of the five ISIs and 10 with a no-mask control condition. 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 33 ms and 49 ms ISIs 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 33 ms + 49 ms condition (BMtotal).

The Digit Span Distractibility Test

To assess working memory/executive attention performance, we used the Digit span distractibility test by Oltmanns and Neale (1975). The distractor and neutral items were matched for difficulty level and reliability to avoid problems associated with differential discriminating power (Chapman & Chapman, 1989). Thus, the distractor series were five and six digits long, whereas neutral items were six and seven digits long. In the neutral conditions (i.e., without distraction), participants listen to a series of digits presented by a tape-recorded female voice at a rate of approximately one digit every 2 s. However, in the distractor condition, irrelevant digits are read by a male voice in the interval between the relevant digits. Participants 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.

Symptom, Behavior, and Functional Ratings

At T2 and T3, 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 rated at the three time points with the Global Assessment Scale of symptoms (GAS-S; 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.

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 # 98-05-04,113; 2015/180/ REK sør-øst C) and the study was conducted in accordance with the Helsinki Declaration of the World Medical Assembly. Written informed consent was obtained from all participants. Data on cause of death were obtained from the Norwegian Cause of Death Registry.

Data Analyses

Analyses were conducted using the statistical package SPSS, Version 25.0. Preliminary group characteristics were

Table 2. Neuropsychological Test Results at T2 and T3.

	ADHD (N = 19)		Healthy (N = 26)		Group (df = 1, 43)		Time (df = 1, 43)		Time × Group (df = 1, 43)		
	T2	T3	T2	T3	F	p	F	p	F	p	η^2
Digit repetition task without distraction	82.9 (8.9)	81.3 (13.9)	88.7 (8.2)	89.7 (8.2)	7.3	**.010**	0.066	.799	0.857	.360	.020
Digit repetition task with distraction	83.9 (13.6)	75.7 (18.6)	93.7 (7.7)	89.6 (10.0)	14.6	**.001**	8.0	**.007**	0.887	.351	.020
Backward masking, no mask	17.9 (2.0)	17.4 (2.8)	18.0 (1.5)	16.8 (1.8)	0.297	.589	5.7	**.022**	1.3	.261	.029
Backward masking total	10.0 (4.9)	6.6 (4.0)	8.4 (3.9)	7.7 (3.9)	0.040	.84	10.0	**.003**	4.7	**.035**	.099

Note. Boldface represents p < 0.05.

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 analyzed using a conventional repeated measures (RM) 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. To directly compare current results/sample (T3) against the T1 and T2 study, additional RM-ANOVAs were conducted with a limited sample, to account for the fact that several ADHD individuals outgrew their diagnosis over the 25-year follow-up period. Effect sizes (η^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 .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 measures of pre-attention and working memory/executive attention (i.e., hierarchical relationship). Raw scores were used for all analyses.

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.

Concurrent Group Differences at T2 and T3

There were no significant effects of group across the two assessment times (T2 and T3) in either the Backward masking no-mask condition, $F(1, 43) = .297, p = .589$, or in the Backward masking total, $F(1, 43) = .040, p = .840$. However, significant effects of group across the two assessment times (T2 and T3) were found for both the Digit span test with, $F(1, 43) = 14.6, p = .001$, and without distraction, $F(1, 43) = 7.3, p = .010$. Both group effects met the

criteria for small effect sizes, with a $\eta^2 = .253$ and .144, respectively. 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, $F(1, 43) = 5.5, p = .015$, and at 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 with distractor, in which ADHD individuals displayed significant deficits (i.e., group effects) at both T2, $F(1, 43) = 8.4, p = .004$, and T3, $F(1, 43) = 10.5, p = .002$, compared with HC.

Longitudinal Group Differences 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, $F(1, 43) = 20.5, p < 001$. The results in the HC group for the Backward masking total condition remained stable from T2 to T3, as evidenced by a nonsignificant 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 × 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, $F(1, 43) = 8.0, p = .007$. This decline achieved a small effect size of $\eta^2 = .156$. The effect of time was explained primarily by the ADHD group ($p = .049$), indicating a selective, yet
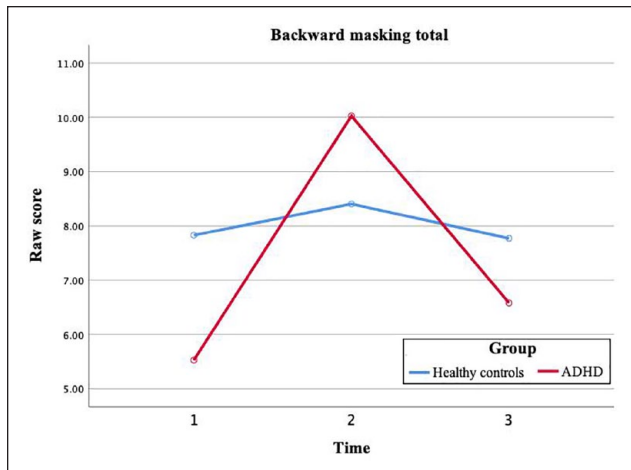
Figure 1. Performance on the backward masking total for the two groups at T1, T2, and T3.
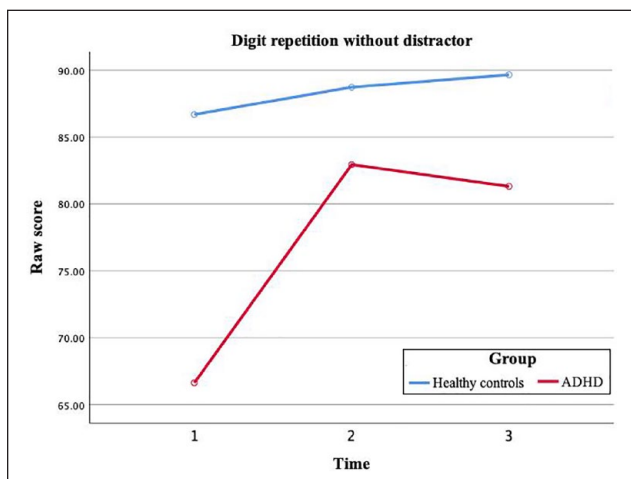

Figure 2. Performance on the Digit span test without distractor for the two groups at T1, T2, and T3.

small, aging effect. 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 relatively 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 is visualized in Figures 2 and 3 in which a mean score is plotted for each time point.

Correlation Analysis

With respect to previous research findings describing a hierarchical relationship between lower and higher order cognitions (Fabio, 2017; Lenz et al., 2010), our correlation
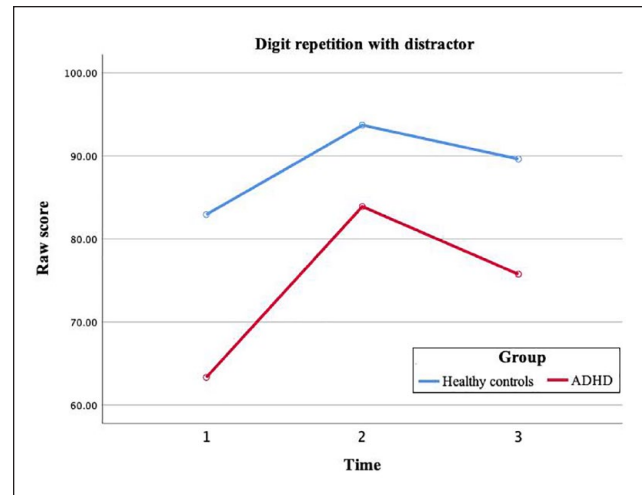

Figure 3. Performance on the Digit span test with distractor for the two groups at T1, T2, and T3.

analysis did not support this notion as there was no statistically significant correlation between the Backward masking total performance and the Digit span with distractor, $r(43) = .026$, $p = .863$, or the Digit span without distractor, $r(43) = .087$, $p = .572$, at T3. No significant changes in results were detected when using Spearman's rho, thereby controlling for a nonparametric distribution.

Discussion

The main findings in this 23- to 25-year follow-up study (T3) demonstrated, similarly to the baseline (T1) and the 13 years follow-up study (T2), specific deficits compared with HC in the "maintenance" (Digit span test without distractibility) and the "manipulation" (Digit span test with distractibility) subcategories of working memory in the ADHD group. Pre-attentional measures, however, did not display any deficits in the ADHD group compared with HC at T2 or T3. Furthermore, we found no significant association between measures of pre-attention and working memory/executive attention at T3.

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 pre-attention automatic measures measured by the Backward masking task, regardless of condition (BMtotal and no mask). This lack of between-group differences was in line with previous research (Øie et al., 2010), showing nonsignificant group differences between the ADHD and HC groups in backward masking performance.

In accordance with results 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 (i.e., at T2 and T3) is in consonance with previously reported studies on neuropsychological performance in adult ADHD (Alderson, Kasper, Hudec, & Patros, 2013; Hervey, Epstein, & Curry, 2004; Schoechlin & Engel, 2005).

In both the baseline (T1) and the 13-year follow-up study (T2), the ADHD individuals performed significantly below the HC group on the Digit span test (taxing both maintenance and manipulation). However, the individuals in the ADHD group 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 working memory 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 prefrontal cortex, predicting a complete maturation to be present at T2 (Arain et al., 2013). The essential contribution of the current study was that it examined whether neuropsychological deficits persisted after the expected neurodevelopmental "peak." Compared with the HC, the ADHD individuals still displayed significant deficits in working memory/executive attention measures at T3, thereby suggesting a continuation of this neuropsychological deficit found in the ADHD group at T1 and T2.

With respect to the notion of a developmental delay in ADHD individuals, our current results are somewhat ambiguous. On one hand, it could be argued that our results show qualitative similarities in neurodevelopment, reflected by the approximate parallel development between the two groups (although with marginal differences in effect sizes and significance level). This can be interpreted as confirming the evidence of ADHD not constituting a marked developmental deviation from the HC. On the other hand, the fact that ADHD individuals never catch up entirely with 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 mostly in line with a "persistent developmental lag" framework of neuropsychological development in ADHD individuals.

Differential Development in Diverse Attentional Measures

Development of pre-attention performance. As mentioned earlier, 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.

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 BMtotal values) over the 23- to 25-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 23- to 25-year follow-up, compared with the overall stability of the HC group. As a result, a significant Time × Group effect was detected, both from T1 to T2 (Øie et al., 2010) and also from T2 to T3.

The reason for this fluctuation may be severalfold. On 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, Akshoomoff, & Haist, 2013). Therefore, any interaction effects between the ADHD and HC groups beyond this time point could indicate a temporary, noncortical 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 ADHD heritability estimates as high as 88% (Larsson, Chang, D'Onofrio, & Lichtenstein, 2014)—the fluctuation could be explained by genetic, predetermined developmental tendencies intrinsic to the ADHD etiology. If this were the case, the fluctuation would categorize as a deviation in ADHD neurodevelopment. Finally, daily variations in patient motivation and cognitive performance level during test administrations may also have been decisive.

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. There was a lack of interaction effect between the groups, indicating that the ADHD and HC groups did not differ substantially in their longitudinal trajectories from T2 to T3. However, only the ADHD group displayed a significant decline in manipulation performance.

Research indicates 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). This may explain why age exerts a seemingly limited effect on the "maintenance" component of working memory capacity, irrespective of group, indicating that this capacity is relatively spared, whereas the "manipulation" capacity was associated with a selective decline in performance for the ADHD group. 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).

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 findings from previous studies, which have suggested an interrelatedness 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 in adulthood is primarily characterized by an impaired top-down control (in which case working memory 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.

Strengths and limitations. A 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 with an HC group. As such, it constitutes an antithesis to previous studies, primarily utilizing cross-sectional methodologies. Further strengths include a long follow-up time (25 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 an 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. Similarly, our limited sample size, combined with the amount of analyses made, increase the probability of making Type I errors, given our set significance level of .05. 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. Furthermore, the ADHD group consisted of only males—a distribution that stands in contrast to the HC group, where males and females were equally represented. Similarly, there was a significant difference in age distribution between the ADHD and the HC groups. Finally, some individuals in the ADHD group were using medication at T1, but not at T2 or T3, which could have confounded the course of cognition with potential medication effects. Also, the discontinuation of medications (set to 15 hr) before neuropsychological assessments could ideally have been longer, but this was difficult to implement in practice.

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). Furthermore, participants with ADHD frequently have comorbid substance abuse. Many of the participants in the ADHD group (~70%) had a history of substance use after T1, which may independently be associated with cognitive deficits. Consequently, these symptoms may have influenced the behavioral executive function outcomes in the present study.

Conclusion

Young adults with ADHD in their mid-20s continue to be afflicted with working memory/executive attention deficits in their mid-30s, compared with HC. Measures of working memory/executive attention were superior in discriminating between individuals with ADHD and HC, compared with 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, 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).

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Declaration of Conflicting Interests

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References

Alderson, R. M., Kasper, L. J., Hudec, K. L., & Patros, C. H. G. (2013). Attention-deficit/hyperactivity disorder (ADHD) and working memory in adults: A meta-analytic review. *Neuropsychology*, *27*, 287-302. doi:10.1037/a0032371

Alderson, R. M., Kasper, L. J., Patros, C. H., Hudec, K. L., Tarle, S. J., & Lea, S. E. (2015). Working memory deficits in boys with attention deficit/hyperactivity disorder (ADHD): An examination of orthographic coding and episodic buffer processes. *Child Neuropsychology*, *21*, 509-530. doi:10.1080/09 297049.2014.917618

American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed., Rev.). Washington, DC: Author.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author.

Anderson, V., Jacobs, R., & Anderson, P. (2008). Developmental trajectories of executive functions across the lifespan. In V. Anderson, R. Jacobs, & P. J. Anderson (Eds.), *Executive functions and the frontal lobes: A lifespan perspective* (pp. 23-56). Philadelphia, PA: Taylor & Francis.

Arain, M., Haque, M., Johal, L., Mathur, P., Nel, W., Rais, A., . . . Sharma, S. (2013). Maturation of the adolescent brain. *Neuropsychiatric Disease and Treatment*, *9*, 449-461. doi:10.2147/NDT.S39776

Baddeley, A. (1996). The fractionation of working memory. *Proceedings of the National Academy of Sciences of the United States of America*, *93*, 13468-13472.

Barkley, R. A. (1997). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. *Psychological Bulletin*, *121*, 65-94.

Best, J. R., & Miller, P. H. (2010). A developmental perspective on executive function. *Child Development*, *81*, 1641-1660. doi:10.1111/j.1467-8624.2010.01499.x

Biederman, J., Petty, C. R., Woodworth, K. Y., Lomedico, A., Hyder, L. L., & Faraone, S. V. (2012). Adult outcome of attention-deficit/hyperactivity disorder: A controlled 16-year follow-up study. *Journal of Clinical Psychiatry*, *73*, 941-950. doi:10.4088/JCP.11m07529

Bopp, K. L., & Verhaeghen, P. (2005). Aging and verbal memory span: A meta-analysis. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, *60*, 2223-2233. doi:10.1093/geronb/60.5.P223

Breitmeyer, B., & Öğmen, H. (2006). *Visual masking: Time slices through conscious and unconscious vision*. Oxford, UK: Oxford University Press.

Buckner, R. L. (2004). Memory and executive function in aging and AD: Multiple factors that cause decline and reserve factors that compensate. *Neuron*, *44*, 195-208. doi:10.1016/j.neuron.2004.09.006

Carlson, S. M., Zelazo, P. D., & Faja, S. (2013). Executive function. In P. D. Zelazo (Ed.), *The Oxford handbook of developmental psychology: Vol. 1. Body and mind* (pp. 706-742). New York, NY: Oxford University Press.

Chapman, L. J., & Chapman, J. P. (1989). Strategies for resolving the heterogeneity of schizophrenics and their relatives using cognitive measures. *Journal of Abnormal Psychology*, *98*, 357-366.

Coghill, D. R., Hayward, D., Rhodes, S. M., Grimmer, C., & Matthews, K. (2014). A longitudinal examination of neuropsychological and clinical functioning in boys with attention deficit hyperactivity disorder (ADHD): Improvements in executive functioning do not explain clinical improvement. *Psychological Medicine*, *44*, 1087-1099. doi:10.1017/S0033291713001761

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale, NJ: Lawrence Erlbaum.

Darowski, E. S., Helder, E., Zacks, R. T., Hasher, L., & Hambrick, D. Z. (2008). Age-related differences in cognition: The role of distraction control. *Neuropsychology*, *22*, 638-644. doi:10.1037/0894-4105.22.5.638

Ellenbroek, B. A. (2004). Pre-attentive processing and schizophrenia: Animal studies. *Psychopharmacology*, *174*, 65-74. doi:10.1007/s00213-003-1684-7

Endicott, J., Spitzer, R. L., Fleiss, J. L., & Cohen, J. (1976). The Global Assessment Scale: A procedure for measuring overall severity of psychiatric disturbance. *Archives of General Psychiatry*, *33*, 766-771.

Enns, J. T., & Di Lollo, V. (2000). What's new in visual masking? *Trends in Cognitive Sciences*, *4*, 345-352.

Fabio, R. A. (2017). The study of automatic and controlled processes in ADHD: A reread and a new proposal. *Mediterranean Journal of Clinical Psychology*, *5*, 1-33. doi:10.6092/2282-1619/2017.5.1507

Fischer, M., Barkley, R. A., Smallish, L., & Fletcher, K. (2005). Executive functioning in hyperactive children as young adults: Attention, inhibition, response perseveration, and the

impact of comorbidity. *Developmental Neuropsychology*, *27*, 107-133. doi:10.1207/s15326942dn2701_5

Green, M. F., Nuechterlein, K. H., Breitmeyer, B., & Mintz, J. (1999). Backward masking in unmedicated schizophrenic patients in psychotic remission: Possible reflection of aberrant cortical oscillation. *The American Journal of Psychiatry*, *156*, 1367-1373.

Green, M. F., Nuechterlein, K. H., Breitmeyer, B., Tsuang, J., & Mintz, J. (2003). Forward and backward visual masking in schizophrenia: Influence of age. *Psychological Medicine*, *33*, 887-895. doi:10.1017/S003329170200716X

Halperin, J. M., & Schulz, K. P. (2006). Revisiting the role of the prefrontal cortex in the pathophysiology of attention-deficit/hyperactivity disorder. *Psychological Bulletin*, *132*, 560-581. doi:10.1037/0033-2909.132.4.560

Hervey, A. S., Epstein, J. N., & Curry, J. F. (2004). Neuropsychology of adults with attention-deficit/hyperactivity disorder: A meta-analytic review. *Neuropsychology*, *18*, 485-503. doi:10.1037/0894-4105.18.3.485

Kane, M. J., & Engle, R. W. (2002). The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: An individual-differences perspective. *Psychonomic Bulletin & Review*, *9*, 637-671. doi:10.3758/BF03196323

Kessler, R. C., Adler, L., Ames, M., Demler, O., Faraone, S., Hiripi, E., . . . Walters, E. E. (2005). The World Health Organization Adult ADHD Self-Report Scale (ASRS): A short screening scale for use in the general population. *Psychological Medicine*, *35*, 245-256. doi:10.1017/S0033291704002892

Larsson, H., Chang, Z., D'Onofrio, B. M., & Lichtenstein, P. (2014). The heritability of clinically diagnosed attention deficit hyperactivity disorder across the lifespan. *Psychological Medicine*, *44*, 2223-2239. doi:10.1017/S0033291713002493

Lenz, D., Krauel, K., Flechtner, H. H., Schadow, J., Hinrichs, H., & Herrmann, C. S. (2010). Altered evoked gamma-band responses reveal impaired early visual processing in ADHD children. *Neuropsychologia*, *48*, 1985-1993.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology*, *41*, 49-100. doi:10.1006/cogp.1999.0734rix

Murray, A. L., Robinson, T., & Tripp, G. (2017). Neurocognitive and symptom trajectories of ADHD from childhood to early adolescence. *Journal of Developmental & Behavioral Pediatrics*, *38*, 465-475. doi:10.1097/DBP.0000000000000476

Øie, M., & Rund, B. R. (1999). Neuropsychological deficits in adolescent-onset schizophrenia compared with attention deficit. *The American Journal of Psychiatry*, *156*, 1216-1222. doi:10.1176/ajp.156.8.1216

Øie, M., Sundet, K., & Rund, B. R. (2010). Neurocognitive decline in early-onset schizophrenia compared with ADHD and normal controls: Evidence from a 13-year follow-up study. *Schizophrenia Bulletin*, *36*, 557-565. doi:10.1093/schbul/sbn127

Oltmanns, T. F., & Neale, J. M. (1975). Schizophrenic performance when distractors are present: Attentional deficit or differential task difficulty? *Journal of Abnormal Psychology*, *84*, 205-209. doi:10.1037/h0076721

Park, D. C., Lautenschlager, G., Hedden, T., Davidson, N. S., Smith, A. D., & Smith, P. K. (2002). Models of visuospatial and verbal memory across the adult life span. *Psychology and Aging*, *17*, 299-320. doi:10.1037/0882-7974.17.2.299

Pennington, B. F., & Ozonoff, S. (1996). Executive functions and developmental psychopathology. *Journal of Child Psychology and Psychiatry*, *37*, 51-87. doi:10.1111/j.1469-7610.1996.tb01380.x

Piek, J. P., Dyck, M. J., Nieman, A., Anderson, M., Hay, D., Smith, L. M., . . . Hallmayer, J. (2004). The relationship between motor coordination, executive functioning and attention in school aged children. *Archives of Clinical Neuropsychology*, *19*, 1063-1076. doi:10.1016/j.acn.2003.12.007

Rajendran, K., Trampush, J. W., Rindskopf, D., Marks, D. J., O'Neill, S., & Halperin, J. M. (2013). Association between variation in neuropsychological development and trajectory of ADHD severity in early childhood. *The American Journal of Psychiatry*, *170*, 1205-1211. doi:10.1176/appi.ajp.2012.12101360

Ramnani, N. (2014). Automatic and controlled processing in the corticocerebellar system. In A. Björklund & A. Cenci-Nilsson (Eds.), *Progress in brain research* (Vol. 210, pp. 255-285). Amsterdam, The Netherlands: Elsevier. doi:10.1016/B978-0-444-63356-9.00010-8

Rommelse, N. N. J., Altink, M. E., de Sonneville, L. M., Buschgens, C. J., Buitelaar, J., Oosterlaan, J., & Sergeant, J. A. (2007). Are motor inhibition and cognitive flexibility dead ends in ADHD? *Journal of Abnormal Child Psychology*, *35*, 957-967. doi:10.1007/s10802-007-9146-z

Rund, B. R., Øie, M., & Sundet, K. (1996). Backward-masking deficit in adolescents with schizophrenic disorders or attention deficit hyperactivity disorder. *The American Journal of Psychiatry*, *153*, 1154-1157. doi:10.1176/ajp.153.9.1154

Rund, B. R., Egeland, J., Sundet, K., Asbjørnsen, A., Hugdahl, K., Landrø, N. I., . . . Stordal, K. I. (2004). Early visual information processing in schizophrenia compared to recurrent depression. *Schizophrenia Research*, *68*, 111-118. doi:10.1016/S0920-9964(03)00193-2

Rund, B. R., Landrø, N. I., & Ørbeck, A. L. (1993). Stability in backward masking performance in schizophrenics, affectively disturbed patients, and normal subjects. *The Journal of Nervous and Mental Disease*, *181*, 233-237. doi:10.1097/00005053-199304000-00004

Schoechlin, C., & Engel, R. R. (2005). Neuropsychological performance in adult attention-deficit hyperactivity disorder: Meta-analysis of empirical data. *Archives of Clinical Neuropsychology*, *20*, 727-744. doi:10.1016/j.acn.2005.04.005

Seidman, L. J. (2006). Neuropsychological functioning in people with ADHD across the lifespan. *Clinical Psychology Review*, *26*, 466-485. doi:10.1016/j.cpr.2006.01.004

Sergi, M. J., Rassovsky, Y., Nuechterlein, K. H., & Green, M. F. (2006). Social perception as a mediator of the influence of early visual processing on functional status in schizophrenia. *The American Journal of Psychiatry*, *163*, 448-454. doi:10.1176/appi.ajp.163.3.448

Sperling, G. (1965). Temporal and spatial visual masking: I. Masking by impulse flashes. *Journal of the Optical Society of America*, *55*, 541-559.

Stavro, G. M., Ettenhofer, M. L., & Nigg, J. T. (2007). Executive functions and adaptive functioning in young adult attention-deficit/hyperactivity disorder. *Journal of the International Neuropsychological Society*, *13*(2), 324-334. doi: 10.1017/S1355617707070348

Stein, M., Auerswald, M., & Ebersbach, M. (2017). Relationships between motor and executive functions and the effect of an acute coordinative intervention on executive functions in kindergartners. *Frontiers in Psychology*, *8*, Article 859. doi:10.3389/fpsyg.2017.00859

Stiles, J., Akshoomoff, N., & Haist, F. (2013). The development of visuospatial processing. In J. L. R., Rubenstein & P. Rakic (Ed.), *Comprehensive developmental neuroscience: Neural circuit development and function in the brain* (pp. 271-296). Amsterdam, The Netherlands: Elsevier.

Wechsler, D. (2007). *Wechsler Abbreviated Scale of Intelligence (WASI)* (Norwegian manual supplement). Stockholm, Sweden: Pearson Assessment.

Wender, P. H., Wood, D. R., & Reimherr, F. W. (1985). Pharmacological treatment of attention deficit disorder, residual type (ADD, RT, "minimal brain dysfunction," "hyperactivity") in adults. *Psychopharmacology Bulletin*, *21*, 222-223.

Willcutt, E. G., Doyle, A. E., Nigg, J. T., Faraone, S. V., & Pennington, B. F. (2005). Validity of the executive function theory of attention-deficit/hyperactivity disorder: A meta-analytic review. *Biological Psychiatry*, *57*, 1336-1346. doi:10.1016/j.biopsych.2005.02.006

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