**Journal of
Attention Disorders**

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 23-25 year period. **Methods**: Individuals with ADHD (n=19) and healthy controls (n= 26) were followed up after 13 years (T2) and 23-25 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 distractions 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.

1. 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.

1

executive functions) (Lenz et al., 2010; Fabio, 2017). 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-

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 behaviour. A basic 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).

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 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

2

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, Øie, & Sundet, 1996; Sergi, Rassovsky, Nuechterlein, & Green, 2006; Øie, Sundet, & Rund, 2010; Øie & Rund, 1999).

Executive functions represent controlled processes that integrate information from working memory with information about context in order 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 sub-components within working memory, characterized by the degree to which they tax complex attentional control processes. Examinations of working memory sub-components performance in ADHD individuals suggest that the largest between-group differences are associated with the central

3

executive (i.e. manipulation) (Alderson et al., 2015).

Despite the fact that ADHD individuals consistently perform below healthy controls (HC) average on several neuropsychological measures throughout the lifespan, 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 to 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)

4

Aims of the study

The primary aim of the current study was to examine the attentional processing capacity in ADHD individuals over a 23-25 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:

(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 to healthy controls?

(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?

(3) Do the two attentional measures display different developmental trajectories in ADHD individuals compared to healthy controls over a 25-year follow-up period?

2. METHODS

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).

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 HC were screened for emotional and behavioral problems at T1 using the Child Behavior Checklist

5

(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 cut-off for psychiatric problems. 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). Both semi-structured clinical interviews and standardised 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 fourteen 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 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 healthy controls.

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 (5 inattentive and 6 combined subtypes).

6

Among these eleven, four participants fulfilled the criteria for ADHD only, while 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 cut-off 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 (Venlaflaxin) at T3. Stimulant medication was discontinued at least 15 hours before testing at all three follow-ups (T1, T2 and T3). Characteristics of the ADHD group at T3 compared to the HC group are presented in Table 1.

Insert Table 1 about here

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, 2003) 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

7

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 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).

The Digit span distractibility test

To assess working memory/executive attention performance, we used the Digit span

distractibility test by Oltmanns and Neal (1975). The distractor and neutral items were

matched for difficulty level and reliability to avoid problems associated with differential

8

discriminating power (Chapman & Chapman, 1989). 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. 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, behaviour 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; 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.

9

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. Written informed consent was obtained from all participants. Data on cause of death was 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 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, to account for the fact that several ADHD-individuals outgrew their diagnosis over the 25-year follow-up period. Effect sizes ($\eta2$) 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 measures of pre-attention and working memory/executive attention (i.e. hierarchical relationship). Raw scores were used for all analyses.

3. RESULTS

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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.

Insert Table 2 about here

Concurrent group differences at T2 and T3

There were no significant effects of group across the two assessment times (T2, 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, 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 $\eta2 = .253$ and $.144$, 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 $(F(1, 43) = 5.5, p = .015)$ 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 to 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

11

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 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 $\eta2 = .533$, 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 $\eta2 = .099$. 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 $\eta2 =$

.156. The effect of time was explained primarily by the ADHD group $(p = .049)$, indicating a

selective, yet 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 Figure 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 (Lenz et al., 2010; Fabio, 2017), our correlation 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

12

changes in results were detected when using a Spearman's rho, thereby controlling for a non-parametric distribution.

<u>Insert figures 1, 2 and 3 about here.</u>

4. DISCUSSION

The main findings in this 23-25 year follow up study (T3) demonstrated, similarly to the baseline (T1) and the 13 years follow up study (T2), specific deficits compared to HC in the "maintenance" (Digit span test without distractibility) and the "manipulation" (Digit span test with distractibility) sub-categories of working memory in the ADHD group. Pre-attentional measures, however, did not display any deficits in the ADHD group compared to HC at T2 or T3. Further, 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 non-significant 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,

13

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 to 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 the 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 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

14

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 23-25-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 23-25-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.

The reason for this fluctuation may be severalfold. 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, Akshoomoff, & Haist, 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

15

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, pre- determined developmental tendencies intrinsic to the ADHD aetiology. If this

were the case, the fluctuation would categorize as a deviation in ADHD neurodevelopment.

Lastly, 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 group did not differ substantially in

their longitudinal trajectories from T2-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

16

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 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 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,

17

compared to a 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 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. 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 0.05. 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 HC group. Lastly, some individuals in the ADHD group

were using medication at T1, but not on T2 or T3, which could have confounded the course of

cognition with potential medication effects. Also, the discontinuation of medications (set to

15 hours) 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). Further, subjects with

ADHD frequently have comorbid substance abuse. Many of the subjects in the ADHD group

18

Consequently, these symptoms may have influenced the behavioural 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 to HC. Measures of working memory/executive attention were superior in discriminating between individuals with ADHD and HC, 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, 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).

19

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Tables

Table 1. Characteristics of the ADHD group compared to the HC group at T3

Variable	ADHD (*n*=19)	HC (*n*=26)	ANOVA (*df*=1,43) F	p	Comparisons
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) [a]	110.1 (10.5)	115.1 (8.3)	3.2	.081	
GAS-S [b]	69.3 (11.3)	81.0 (8.0)	16.1	.000	
GAS-F [c]	70.6 (13.4)	83.8 (6.2)	19.2	.000	
ASRS total [d]	27.8 (13.7)	---	---	---	---
Medication					
Stimulants	*n*= 1	---			
Atypical antipsychotics	*n*= 3	---			
Antidepressants	*n*= 1	---			

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Table 2. Neuropsychological test results at T2 and T3

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	ADHD (*n*=19)		Healthy (*n*=26)		Group (*df*=1, 43)		Time (*df*=1, 43)		Time x 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**	.066	.799	.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**	.887	.351	.020
Backward masking, no mask	17.9 (2.0)	17.4 (2.8)	18.0 (1.5)	16.8 (1.8)	.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)	.040	.84	10.0	**.003**	4.7	**.035**	.099

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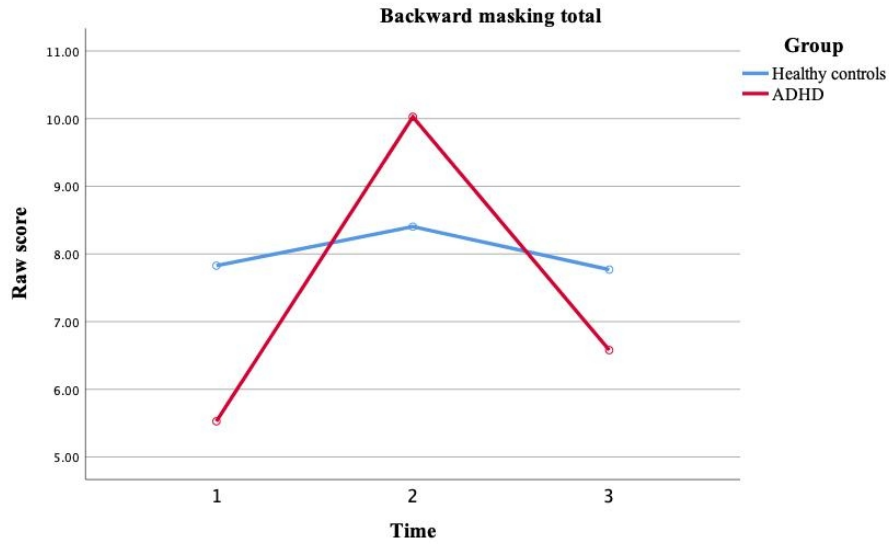44
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Figure 1. Performance on the Backward masking total for the two groups at T1, T2 and T3

Figure 1. Performance on the Backward masking total for the two groups at T1, T2 and T3

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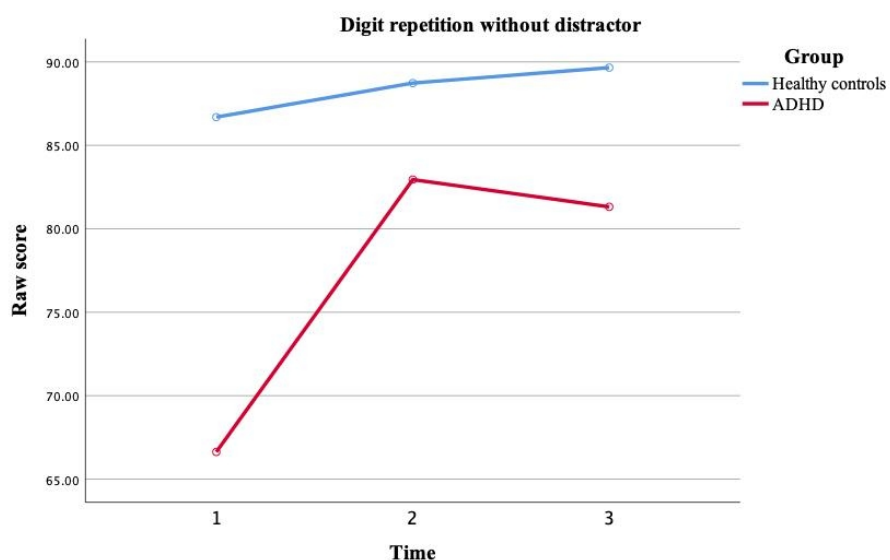45
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Figure 2. Performance on the Digit span test without distractor for the two groups at T1, T2 and T3

Figure 2. Performance on the Digit span test without distractor for the two groups at T1, T2 and T3
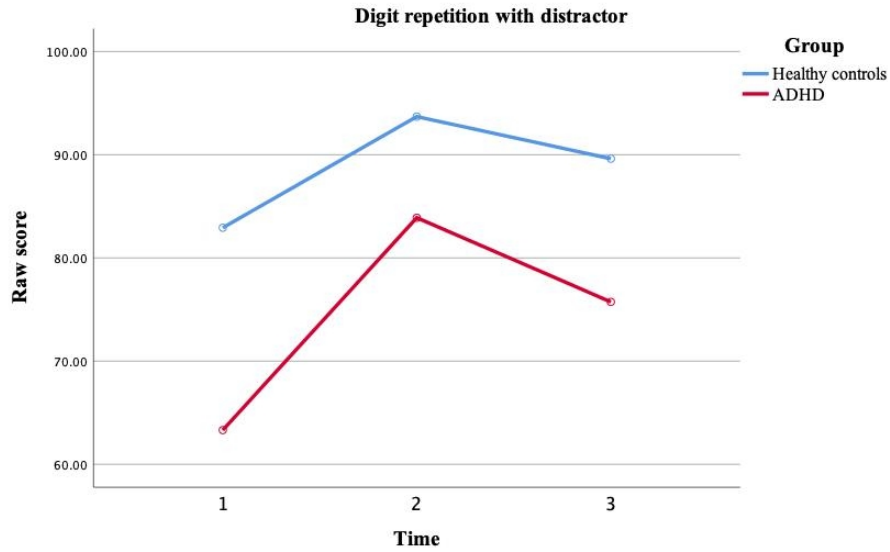
322x197mm (72 x 72 DPI)

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

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

321x193mm (72 x 72 DPI)