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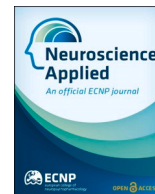
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Research Articles

Verbal memory performance in adolescents and adults with ADHD



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ABSTRACT

Beyond well-established difficulties with working memory in individuals with attention deficit hyperactivity disorder (ADHD), evidence is emerging that other memory processes may also be affected. We investigated, first, which memory processes show differences in adults and adolescents with ADHD in comparison to control participants, focusing on working and short-term memory, initial learning, interference, delayed and recognition memory. Second, we investigated whether ADHD severity, co-occurring depressive symptoms, IQ and physical fitness are associated with the memory performance in the individuals with ADHD.

We assessed 205 participants with ADHD (mean age 25.8 years, SD 7.99) and 50 control participants (mean age 21.1 years, SD 5.07) on cognitive tasks including the digit span forward (DSF) and backward (DSB), the Rey Auditory Verbal Learning Test (RAVLT), and the vocabulary and matrix reasoning subtests of the Wechsler Abbreviated Scale of Intelligence. Participants with ADHD were additionally assessed on ADHD severity, depression symptoms and cardiorespiratory fitness. A series of regressions were run, with sensitivity analyses performed when variables were skewed.

ADHD-control comparisons were significant for DSF, DSB, delayed and recognition memory, with people with ADHD performing less well than the control participants. The result for recognition memory was no longer significant in sensitivity analysis. Memory performance was not associated with greater ADHD or depression symptoms severity. IQ was positively associated with all memory variables except DSF. Cardiorespiratory fitness was negatively associated with the majority of RAVLT variables.

Individuals with ADHD showed difficulties with working memory, short-term memory and delayed memory, as well as a potential difficulty with recognition memory, despite preserved initial learning.

1. Introduction

A range of cognitive differences or impairments have been associated with attention deficit hyperactivity disorder (ADHD), with broadly similar patterns emerging in children and adults (Frankle et al., 2018).

While difficulties with working memory (WM) are among the most consistently reported cognitive differences in people with and without ADHD (Pievsky and McGrath, 2018), detailed investigations of other memory processes are not as well researched. Yet, forgetfulness and the misplacing of items are among the core clinical symptoms of inattention

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in the diagnostic criteria for ADHD (DSM-5, APA), highlighting the need for a thorough investigation of memory in individuals with ADHD.

Through meta-analysis of 49 studies including children and adolescents with ADHD, WM performance was investigated using the digit span backward (DSB) subtest of the Wechsler Intelligence Scale for Children or Wechsler Adult Intelligence Scale, which indicated poorer performance in those with ADHD compared to controls, with an effect size of 0.56 (Ramos et al., 2019). Poorer performance in participants with ADHD in comparison to controls was also reported in 38 studies in adults with ADHD using a variety of different verbal and visuospatial WM tasks, with an effect size of 0.55 for verbal and 0.49 for visuospatial WM (Alderson et al., 2013).

Other meta-analyses assessing cognition in people with ADHD have focused on memory as part of a wider cognitive profile. A meta-analysis covering data from a wide variety of tasks found difficulties with verbal but not visual short-term memory in adults with ADHD (Hervey et al., 2004). A partially overlapping meta-analysis reported similar findings for verbal memory (Schoechlin and Engel, 2005). More recently, a review of meta-analyses of cognition in individuals with ADHD reached the overall conclusion that memory was affected in both adults and children with ADHD, but results were not reported separately for specific processes (Pievsky and McGrath, 2018).

A further meta-analysis specifically assessed long-term visual and verbal memory in adults with ADHD (Skodzik et al., 2017), rather than assessing memory as part of a wider cognitive profile. The memory tasks included the Rey Auditory Verbal Test (RAVLT), the Californian verbal learning test (CVLT), the Paragraph subtest of the Learning and Memory Battery and the Logical Memory subtest of the Wechsler Memory Scale-Revised. Significant ADHD-control group differences emerged for verbal but not visual long-term memory, with an effect size of 0.49 in verbal memory, although the authors postulated that they may not have had the power to detect differences in visual memory due to a smaller number of studies available for their analysis. These difficulties with long-term verbal memory were significantly related to difficulties with memory acquisition. Similarly, the studies in their meta-analysis showed worse long-term verbal recognition performance in individuals with ADHD, which was statistically related to the difficulties with memory acquisition.

A small number of individual studies have investigated recognition memory in children and adolescents with ADHD, with conflicting results. In some studies, initial learning in children with ADHD was equal to control participants despite impairments in recall and recognition (Cutting et al., 2003). In other studies, children and adolescents with ADHD scored significantly below control participants in initial learning and recognition (Andersen et al., 2013). The reasons for this disparity in results are unclear.

The available evidence therefore indicates that memory is an aspect of cognition that deserves further detailed investigation in individuals with ADHD. The previous research also highlights the need for a new exploration of factors highlighted above that may contribute to memory performance in individuals with ADHD. Given that the core symptoms of ADHD can range from mild to severe, one question when investigating memory-related impairments in individuals with ADHD is whether memory performance relates to the severity of ADHD. Another question that emerges, given the association of ADHD with on average lower general cognitive ability scores (Kuntsi et al., 2004), is whether memory performance in individuals with ADHD may relate to general cognitive ability. While this possibility has not been explored in many of the studies, one meta-analysis found that IQ did not explain the long-term memory differences between adults with ADHD and controls, as the group differences remained significant when controlling for IQ (Skodzik et al., 2017). Additionally, many people with ADHD also have one or more co-occurring conditions. Depression is one of the most common comorbidities, observed in approximately 60 % of adults with ADHD (Jacob et al., 2007; Mayer et al., 2018; Mostert et al., 2015) found there was no moderating impact of comorbid depression in a study of

cognition in ADHD which included working memory and long-term memory. In contrast, (Hervey et al., 2004) reported that ADHD participants with a comorbidity showed stronger memory deficits. The impact of co-morbidities in memory performance is therefore not clear and further work is required.

Further emerging evidence from population samples suggests that both acute and chronic physical activity may improve positive affect (Koch et al., 2022) and executive functions (Gawrilow et al., 2016) in people with ADHD, and that it may improve memory performance (Loprinzi et al., 2021). Of particular relevance to our current study, research suggests a link between verbal learning capacity and cardiorespiratory fitness (Hotting et al., 2012). Overall, the question arises whether cardiorespiratory fitness can be another factor contributing to memory performance in people with ADHD.

Here, our first aim is to investigate which memory processes differ in adults and adolescents with ADHD, in comparison to control participants. We focus on working and short-term memory, as well as delayed and recognition memory, all in the verbal domain. Our second aim is to investigate whether ADHD severity, major depressive disorder symptoms, general cognitive ability and cardiorespiratory fitness are associated with memory performance in participants with ADHD.

2. Methods

2.1. Participants

Participants were 205 adolescents and adults with ADHD, and 50 controls. The ADHD group was recruited through advertisements, internet/social media campaigns, University circulars and inpatient/outpatient clinics at the four participating sites: a) Goethe University Hospital Frankfurt, b) Radboud University Medical Centre, Nijmegen, c) Vall d'Hebron Research Institute Barcelona, and d) The Institute of Psychiatry, Psychology and Neuroscience, King's College London. Control participants were recruited through advertisements in London and Frankfurt. The data reported here were collected within a larger randomised clinical trial, (Mayer et al., 2018).

The study protocol was initially reviewed and approved by the institutional review board (IRB) of the Medical Faculty, Goethe University, Frankfurt am Main, Germany (No. 353/16, 13 January 2017). Subsequent approval of this protocol was obtained from the ethical committees of Vall d'Hebron Research Institute, Barcelona, Spain (No. PR(AG)105/2017, 19 April 2017), King's College London, UK (No. 17/LO/0958, 11 July 2017), and Radboud University Medical Centre, Nijmegen, The Netherlands (No. 2017-3238, 5 October 2017). The research was conducted according to GCP guidelines and the declaration of Helsinki.

The inclusion/exclusion criteria are described in Table 1. The control group was screened for current psychopathology using the Child Behavior Checklist (parent reports) and the Youth Self-Report in adolescents (YSR) and the Adult Self-Report (ASR) in adults. Adult control participants were also screened for ADHD using the Adult ADHD Self-Report Scale (ASRS). Control participants with a first-degree family history of ADHD were excluded. All controls were medication free.

2.2. Procedures

The data are from the participants taking part in the 'Pilot randomized controlled phase-IIa trial on the prevention of comorbid depression and obesity in attention-deficit/hyperactivity disorder' (PROUD) clinical trial (Mayer et al., 2018). The PROUD trial investigated the use of bright light therapy and an exercise intervention in treating ADHD and its comorbidities; only data from baseline assessments are used here.

For participants with ADHD, cognitive tasks were administered in a fixed order as part of a more extensive testing session in a quiet, comfortable room with minimal distractions. The testing session was part of the PROUD baseline assessment, which lasted approximately 4 h.

Table 1
Inclusion and exclusion criteria.

Inclusion criteria	<p>All participants must meet DSM-5 criteria for a lifetime history of childhood onset ADHD (DSM-5314.00, 314.01) as well as current ADHD criteria established by a specialist in the field</p> <p>Aged 14 – 45 years</p> <p>Written informed consent of the legal caretakers of the participant (age <18 years) and, if possible, written assent of the participant (age <18 years) themselves</p> <p>Written informed consent of the participant (age ≥18 years)</p> <p>Stable treatment as usual (TAU) comprising pharmacotherapy, group-based or individual cognitive behavioural therapy (not including elements of bright light therapy or exercise)</p> <p>Normal or corrected to normal vision</p> <p>Ability to understand, read, write, and speak fluently in the language of the study site</p> <p>Ability to regularly and reliably attend appointments</p>
Exclusion criteria	<p>IQ < 75 (measured by WAIS-IV or WISC-IV vocabulary and matrix reasoning subtests)</p> <p>Any severe co-morbid psychiatric disorder other than the co-morbid conditions explicitly studied with necessary additional psychopharmacotherapy or psychiatric intervention involving day-care/inpatient treatment at start of study, especially a diagnosis of bipolar disorder, schizophrenia, autism spectrum disorder, schizoaffective disorder or organic psychiatric disorder (current or lifetime)</p> <p>Any severe medical or neurological condition interfering with interventions</p> <p>Any severe medical or neurological condition not allowing BLT or EI</p> <p>Use of antipsychotic or anti-epileptic medication, photo-sensitizing medication (e.g., lithium, St. John's Wort)</p> <p>Substance use disorder (DSM-5) or dependency (DSM-5)</p> <p>History of epilepsy</p> <p>Acute suicidal ideation</p> <p>Pregnancy</p> <p>Participant is related to the investigator or study staff</p> <p>Participation in other clinical trials and observation period of competing trials (participation in other studies is permitted if the respective study is a no-medication or psychotherapy trial and if its aims do not interfere with the aims of the present study)</p> <p>No participant was allowed to enroll in this trial more than once</p>

For the purposes of the present analyses, only data on neurocognitive abilities, IQ, ADHD severity, depressive symptoms, and cardiorespiratory fitness are included.

Control participants attended the research centre for one visit. Their assessment included a measure of neurocognitive abilities and IQ, as well as a screening for ADHD and other psychopathologies using the YSR or ASR.

2.3. Measures

2.3.1. Cognitive assessments

2.3.1.1. Digit span. The digit span forward and backward from the Wechsler Intelligence Scale for Children (Wechsler, 2003) or Wechsler Adult Intelligence Scale were administered to participants aged <16 years and participants aged 16 years or older. Digit span forward (DSF) requires participants to verbally repeat a sequence of digits in straight-forward order and measures short-term verbal memory. Digit span backward (DSB) requires participants to repeat digits in backward order, and measures verbal working memory. The total scores for digit span forward and backward were calculated.

2.3.1.2. Rey Auditory Verbal Learning Test – (RAVLT). The RAVLT consists of 15 concrete nouns (list A) that are read five times, at a rate of approximately one word per second. An assessment of free recall follows after each iteration. The total number of words remembered correctly across all 5 trials was summed and taps short-term verbal memory (RAVLT trial 5). Following this, a new list is read (interference list) (List B). Next, recall of list A is assessed again, measuring short-term memory

following interference (RAVLT trial 6). After a delay of approximately 30 min, recall of list A is again assessed (delayed memory) (RAVLT trial 7). One week later a recognition memory test, which consists of a list of 50 words (including previously unseen words and words from List A), is emailed to participants. Validated versions were available in English, German, Spanish and Dutch. All other RAVLT trials were simply calculated by summing the total score for that individual trial.

2.3.1.3. IQ. The vocabulary and matrix reasoning subtests of the Wechsler Abbreviated Scale of Intelligence (WASI) were administered to all ADHD and control participants to derive an estimate of IQ (Wechsler, 1999).

2.3.2. Clinical interviews

2.3.2.1. Diagnostic Interview for ADHD in adults (DIVA). The Diagnostic Interview for ADHD in adults (DIVA) is a semi-structured interview evaluating DSM-IV criteria for adult ADHD symptoms and impairment (Kooij, 2012). The DIVA was administered to adults with ADHD by trained researchers or clinicians. Diagnosis of ADHD was adjusted to DSM-5 criteria. The severity of ADHD symptoms was rated based on information from the DIVA 2.0 using the ADHD Rating Scale for adults (Barkley, 2011), an 18-item scale assessing ADHD symptoms by a 4-point Likert-type severity scale. Validated versions were available in English, German, Spanish and Dutch. The ADHD Rating Scale total score was analysed. The total score on the ADHD Rating Scale total score was utilised for analysis.

2.3.2.2. Kiddie-SADS-present and lifetime version (K-SADS-PL). The K-SADS-PL is a semi-structured interview assessing current and past psychopathology in children and adolescents according to DSM-IV criteria (Kaufman et al., 1997). In participants with ADHD under the age of 18 years, the ADHD supplement of the K-SADS-PL was administered as an alternative to the DIVA. For the most comprehensive picture of a participant's symptoms and impairment, the K-SADS-PL was conducted separately with the adolescent and one primary caregiver. For the final rating, the trained researchers took both sources of information into account to arrive at a summary score. In cases where there was a discrepancy in the rating of parent and adolescent, the parent's rating was prioritised. The severity of ADHD symptoms was rated by a trained researcher or clinicians based on information from the K-SADS-PL using the ADHD Rating Scale for children, which is an 18-item scale assessing ADHD symptoms by a 4-point Likert-type severity scale (DuPaul et al., 1998). The total score was analysed. Validated versions were available in English, German, Spanish and Dutch.

2.3.2.3. Inventory of Depressive Symptomatology (IDS-C30). The severity of depressive symptoms was rated by a trained researcher or clinician using the Inventory of Depressive Symptomatology (IDS-C30). The IDS-C30 rating (Rush et al., 1996) includes all DSM-5 diagnostic criterion items for major depressive disorder (e.g. mood, vegetative, psychomotor, and cognitive symptoms) as well as commonly associated symptoms such as anxiety, irritability, melancholic, and atypical symptom features to assess the severity of depressive symptoms over the last seven days. Items are rated by the researchers on a 4-point Likert scale based on the information obtained during a semi-structured interview. The IDS-C30 was administered to all participants in the ADHD group. Validated versions were available in English, German, Spanish and Dutch.

2.3.3. Fitness test

2.3.3.1. Chester step test. The Chester step test is a submaximal, multi-stage aerobic capacity test and can predict maximal oxygen uptake (VO_2max) (Sykes and Roberts, 2004). The participant wears a heart rate monitor and steps onto a 30 cm high box at a set rate, which increases in

tempo every 2 min. After each 2-min interval, the participant's heart rate and rate of perceived exertion (RPE) are checked. The test continues in this progressive manner until the participant reaches 80 % of their maximum level, the RPE reaches 14, or the participant requests to stop. Maximum heart rate is calculated by 220 minus the participant's age. VO₂max (ml O₂/kg/min) is then calculated taking gender and age into account using the Chester Step Test software (Cartwright Fitness).

2.4. Statistical analyses

Chi square was used to assess the proportion of males and females in control and ADHD groups, and t-tests to compare the groups on age. We used linear regression to compare individuals with ADHD to control individuals on their working memory (DSB), short-term memory (DSF), total number of words remembered, the interference list, short term memory following interference, delayed memory and a recognition test. A regression was also run to compare groups on IQ. Comparisons between ADHD and control participants were adjusted for age, given an older mean age in the ADHD group. As gender did not differ between ADHD and control groups, we did not adjust for gender (see Results below). Analyses comparing ADHD and control groups did not adjust for study centre, as only two of the four study centres included control participants and, thus, would be conflated with whether the participant is a case or a control.

To investigate whether general cognitive ability, ADHD severity, depressive symptoms and physical fitness were associated with memory performance in participants with ADHD, we conducted a series of linear regressions estimating the association of IQ, ADHD Rating Scale score, IDS-C30 score, and VO₂max with digit span and RAVLT tasks. These analyses were adjusted for age, and for study centre as a fixed effect as participants in the ADHD group were present at all four centres.

Several RAVLT measures, including the interference list, delayed memory and recognition memory were non-normally distributed and we observed ceiling effects such that a large portion of participants received a maximum score (e.g., >35 % of all participants (ADHD and controls) achieved the highest score on trial 6). Therefore, in sensitivity analyses we analysed performance comparing ADHD and control groups on these skewed outcomes using hurdle models, which are two part-models that separately estimate: (1) the chance of achieving the highest possible score on the task, using logistic regression and (2) using linear regression, performance on the task conditional on not having achieved the highest score.

3. Results

The ADHD group was significantly older than the control group, with a mean age of 25.8 years (SD 7.99) vs a mean age of 21.1 years (SD = 5.07) in the control group ($df = 253$, $t = -4.0$, $p < 0.001$). All analyses controlled for age. The proportion of males and females did not differ between the ADHD and control groups ($\chi^2 = 2.57$, $df = 1$, $p = 0.11$). In the ADHD group, 75 % ($n = 153$) were receiving ADHD medication at the time the tasks were performed and 25 % ($n = 51$) were not receiving ADHD medication. There was one subject for whom medication status was not available.

3.1. Which memory processes are impaired in adults and adolescents with ADHD in comparison to control participants?

Medicated and unmedicated participants with ADHD were combined into a single ADHD participant group, as there were no differences between these groups on digit span or core RAVLT measures (Supplemental Table S1). The only exception was on the interference list, in which medicated participants with ADHD performed significantly better than unmedicated participants with ADHD ($p = 0.04$).

Statistically significant ADHD versus control group differences were observed for DSF, DSB and the RAVLT delayed and recognition memory

variables, with control participants performing better than people with ADHD. Table 2 shows means and standard deviations for performance on these tasks. Effect sizes (standardized betas) for these comparisons (Table 3) ranged from -0.52 (digit span backward) to -0.18 (RAVLT trial B list). Effect sizes comparing performance on immediate memory tasks (RAVLT short term memory, interference list and short-term memory following interference) were smaller, ranging from -0.18 (RAVLT list B) to -0.26 (RAVLT trial 6). There was no difference in estimated IQ between the ADHD and control groups (effect size -0.07).

In sensitivity analyses using hurdle models for the skewed RAVLT variables, significant differences remained between the ADHD and control groups for the delayed memory task, but not for recognition memory (Supplemental Table S2).

3.2. Is ADHD severity, depressive symptom severity, IQ and physical fitness associated with memory performance in individuals with ADHD?

Among participants with ADHD, IQ was significantly associated with DSB and all RAVLT tasks (Table 3). Effect sizes (standardized betas) demonstrated the association of IQ with task performance, ranging from 0.26 for DSB to 0.35 for the interference list (Table 4). In sensitivity analyses using hurdle models for the skewed RAVLT tasks, IQ remained significantly associated with all skewed RAVLT memory variables (Supplemental Table S3).

There was no association between any memory measure (digit span or RAVLT) and ADHD severity (score on ADHD Rating Scale) or depression rating (score on the IDS-C30). Effect sizes were small, ranging from 0.02 to -0.16 for the ADHD Rating Scale total score and -0.02 to 0.14 for the IDS, (Table 4). A significant negative association emerged between VO₂max and several RAVLT memory variables, including RAVLT trial 5, trial 6, trial 7 and recognition memory in the participants with ADHD. Effect sizes ranged -0.05 (digit span) to -0.30 (RAVLT recognition memory), (Table 4). Those with higher cardiorespiratory fitness performed more poorly on the memory tasks (Table 4). These findings remained significant when using hurdle models, with the exception of RAVLT recognition memory (supplement S4).

4. Discussion

Our study reveals difficulties with delayed memory and potential difficulties with recognition memory, as well as confirming the presence of working memory (WM) and short-term memory difficulties, in adults

Table 2
Demographic information and cognitive assessments among the ADHD group and control group; clinical assessments and fitness (VO₂max) in the ADHD group.

	ADHD group N = 205	Control group N = 50
Male, N (%)	93 (45.4)	29 (58.0)
Age, Mean (SD)	25.8 (8.0)	21.1 (5.1)
IQ, Mean (SD)	107.5 (12.54)	106.8 (11.1)
Digit span forward, Mean (SD)	9.4 (2.2)	10.0 (2.2)
Digit span backward, Mean (SD)	8.8 (2.2)	9.8 (2.2)
RAVLT trial 5, Mean (SD)	56.1 (10.5)	57.7 (10.2)
RAVLT list B, Mean (SD)	6.9 (2.5)	7.1 (2.2)
RAVLT trial 6, Mean (SD)	12.8 (2.6)	13.4 (2.0)
RAVLT trial 7, Mean (SD)	11.8 (3.2)	12.8 (2.1)
RAVLT recognition memory, Mean (SD)	12.4 (3.0)	13.3 (1.7)
IDS-C30 score, Mean (SD)	14.1 (9.4)	NA
ADHD Rating Scale total score, Mean (SD)	26.6 (8.9)	NA
VO ₂ max, Mean (SD)	40.5 (8.4)	NA

NA: not applicable; these tests were administered only to the ADHD group. RAVLT: Rey Auditory Verbal Learning Test; IQ: intelligence quotient, estimated by the vocabulary and matrix reasoning subtests of the Wechsler Abbreviated Scale of Intelligence; IDS: Inventory of Depressive Symptomatology; DIVA: Diagnostic Interview for ADHD in adults.

Table 3

Performance on memory tasks and IQ comparing the ADHD group and the control group.

	ADHD group vs control group	
	β (95 % CI)	<i>p</i>
Digit span forward	-0.38 (-0.70, -0.06)	0.018
Digit span backward	-0.52 (-0.83, -0.20)	0.001
RAVLT trial 5	-0.22 (-0.55, 0.10)	0.175
RAVLT list B	-0.18 (-0.51, 0.14)	0.266
RAVLT trial 6	-0.26 (-0.63, 0.10)	0.158
RAVLT trial 7	-0.38 (-0.70, -0.06)	0.021
RAVLT recognition memory	-0.38 (-0.75, -0.01)	0.046
IQ	-0.07 (-0.39, 0.25)	0.673

Analyses adjusted for participant age.

RAVLT: Rey Auditory Verbal Learning Test; IQ: intelligence quotient, estimated by the vocabulary and matrix reasoning subtests of the Wechsler Abbreviated Scale of Intelligence; CI: confidence interval.

and adolescents with ADHD. This pattern of results suggests that ADHD may be characterised by wide-ranging difficulties with memory beyond those reported for working memory.

In line with previous research (Ramos et al., 2019; Alderson et al., 2013; Hervey et al., 2004), we observed difficulties with WM and short-term memory, using the digit span backward and forward scores, in adults and adolescents with ADHD. Our study is consistent with previous meta-analyses reporting worse delayed memory performance in ADHD participants (Hervey et al., 2004; Schoechlin and Engel, 2005; Skodzik et al., 2017). However, in contrast to these meta-analyses, we did not find that people with ADHD are impaired in initial learning, as performance on the RAVLT trial 5 task in our study did not differ between participants with ADHD and control participants. Our finding of potential difficulties with the retention and recognition of verbally presented information, separate from initial learning, is therefore largely novel (though see Pollak et al that was included in the Skodzik et al., 2017 meta-analysis). Further research on verbal memory over varying lengths of delays is required to better understand the relationship between encoding and retrieval in individuals with ADHD, as the reasons for the disparity of our findings with previous research are not clear. One possible explanation is that the somewhat higher than expected IQs of our participants with ADHD may have contributed to good performance on initial learning, while no such protective effect of IQ was observed for retrieval.

IQ was associated with most memory performance domains in participants with ADHD, with the exception of short-term memory (DSF). One potential explanation for our findings is the role of IQ as a moderator of outcome (Cheung et al., 2015). Participants with ADHD who have higher general cognitive ability may be better able to employ compensatory mechanisms which are less available those with ADHD and lower general cognitive ability. Further work is needed to assess general cognitive ability more directly as a possible protective factor for

Table 4

Association of IQ, ADHD severity, depression rating and cardiorespiratory fitness in the ADHD group.

	IQ		ADHD rating scale score ^a		IDS-C30		VO ₂ max	
	β (95 %CI)	<i>p</i>	β (95 % CI)	<i>p</i>	β (95 % CI)	<i>p</i>	β (95 % CI)	<i>p</i>
Digit span forward	0.11 (-0.04, 0.27)	0.15	0.03 (-0.11, 0.17)	0.65	-0.06 (-0.20, 0.08)	0.38	-0.05 (-0.19, 0.09)	0.52
Digit span backward	0.26 (0.11, 0.41)	0.001	0.02 (-0.13, 0.16)	0.84	0.06 (-0.08, 0.21)	0.37	-0.05 (-0.19, 0.10)	0.53
RAVLT trial 5	0.32 (0.18, 0.46)	<0.001	0.05 (-0.08, 0.19)	0.44	0.02 (-0.12, 0.16)	0.78	-0.17 (-0.30, -0.03)	0.02
RAVLT List B	0.28 (0.13, 0.43)	<0.001	-0.02 (-0.16, 0.11)	0.73	-0.02 (-0.16, 0.12)	0.74	-0.09 (-0.22, 0.05)	0.21
RAVLT trial 6	0.35 (0.18, 0.52)	<0.001	0.05 (-0.12, 0.22)	0.58	0.14 (-0.06, 0.35)	0.16	-0.20 (-0.37, -0.04)	0.02
RAVLT Trial 7	0.32 (0.17, 0.46)	<0.001	0.06 (-0.08, 0.20)	0.39	0.08 (-0.07, 0.22)	0.29	-0.25 (-0.39, -0.12)	<0.001
RAVLT recognition memory	0.34 (0.15, 0.52)	0.001	-0.16 (-0.33, 0.01)	0.06	-0.05 (-0.22, 0.12)	0.59	-0.30 (-0.49, -0.12)	0.001

Analyses adjusted for participant age and study centre.

RAVLT: Rey Auditory Verbal Learning Test; IQ: intelligence quotient, estimated by the vocabulary and matrix reasoning subtests of the Wechsler Abbreviated Scale of Intelligence; IDS: DIVA: Diagnostic Interview for ADHD in adults; Inventory of Depressive Symptomatology; CI: confidence interval.

^a If 6/9 behaviours with a score of 2 or 3 for inattention or hyperactivity this meets DSM-5's criteria for ADHD.

memory among individuals with ADHD.

Memory performance was not associated with ADHD severity or severity of depressive symptoms in the participants with ADHD. The mean IDS score, which served as an index of depression symptoms, was 14. Given that the optimal cut-off-point of 13 or above is typically taken to indicate the presence of mild clinical relevant depressive symptomatology (Rush et al., 1996), floor effects may explain the lack of association and further research in participants with depression is warranted. Our result is, however, in line with previous research that showed that difficulties with short-term and working memory may reflect processes in ADHD associated with persistence of impairments regardless of severity of ADHD symptoms and impairment (Michellini et al., 2021). Similarly, Mostert et al. (2015), found no difference in WM performance in people with ADHD with or without a history of depression.

An unexpected negative association emerged between several RAVLT memory variables and cardiorespiratory fitness, as expressed by VO₂max, in the participants with ADHD. The direction of the observed association is unexpected, given previous research studies showing that physical activity may have beneficial effects on cognition (Hotting and Roder, 2013; Mora-Gonzalez et al., 2019), and a positive link between verbal learning capacity and cardiorespiratory fitness (Hotting et al., 2012). The reasons for this negative association are not clear, although overall physical fitness was high in our samples and so a ceiling effect may be present. Moreover, it should be acknowledged that due to practical reasons the fitness assessment was done in a clinical setting and therefore a step-test was selected. We chose the most valid and reliable step-test according to previous literature (Bennett et al., 2016; Buckley et al., 2004), but still it is a sub-maximal test, which adds a source or error in the estimation of vo2max, compared to gold-standard protocols using incremental maximal tests. This could also have influenced the results. Cardiorespiratory fitness was not associated with WM or short-term memory performance.

There are some technical limitations to our study. Hurdle models were adopted, as the delayed and recognition variables were skewed due to ceiling effects. Whilst differences remained for delayed memory, recognition memory was not significantly different between participants with and without ADHD with the hurdle model applied, although there was still a trend for participants with ADHD to perform worse on the recognition memory task. When applying the hurdle model there is a loss of power, as the study population is in effect divided for a logistic regression examining risk of obtaining the top score versus not obtaining the top score and a linear regression predicting participant score on the rest of the scale. Further research should use different tasks that are not subject to such ceiling effects and may thus be better suited for probing any differences in recognition memory between controls and those with ADHD. Relatively little is known about recognition memory in individuals with ADHD and research has reported both impaired (Hervey et al., 2004) and intact (Pollak et al., 2008) recognition memory in adult ADHD.

Another limitation of our study is that 75 % of participants with ADHD were receiving ADHD medication at the time the tasks were performed. Although we observed no differences between medicated and unmedicated participants with ADHD on any measures except the RAVLT interference list (i.e. no differences on digit span or core RAVLT measures), future studies should replicate the findings with unmedicated participants. A further limitation relating to our group of participants with ADHD is that they had a higher than expected mean IQ.

Our study represents a comprehensive assessment of verbal memory in adolescents and adults with ADHD, whilst considering variables which may potentially associate with memory performance such as IQ, ADHD severity, cardiorespiratory fitness and mood. Our data suggest that while initial learning is preserved, people with ADHD show difficulties with delayed memory and a potential difficulties with recognition memory. Confirmation and replication of these findings is required, but if confirmed, could open the door for training and compensatory strategies targeting longer-term and recognition memory in people with ADHD. Although evidence for cognitive training improving outcomes in individuals with ADHD is overall limited, a recent comprehensive meta-analysis reported that computerised cognitive training led to shorter-term improvements in short-term and working memory that were not observed for other neuropsychological domains (Westwood et al., 2023). Yet it remains the case that evidence for clinical effects is largely lacking (Westwood et al., 2023). In participants with ADHD, memory performance was not associated with greater ADHD or depression severity. IQ was positively associated with all memory variables except DSF, but given the high IQ of our sample, further work should probe this in more detail, employing people with a wider range of IQs. Lastly, to our surprise, cardiovascular fitness was negatively associated with the majority of RAVLT variables.

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Declaration of competing interest

Christine Freitag receives royalties for books on ADHD, ASD, and MDD (publishers Beltz, Hogrefe, Kohlhammer, Springer, Reinhardt).

Andreas Reif serves on advisory boards and has received speaker's fees from Medice, Shire/Takeda, Janssen, SAGE/Biogen and Boehringer Ingelheim.

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All other authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

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References

- Alderson, R.M., Kasper, L.J., Hudec, K.L., Patros, C.H., 2013. Attention-deficit/hyperactivity disorder (ADHD) and working memory in adults: a meta-analytic review. *Neuropsychology* 27 (3), 287–302. <https://doi.org/10.1037/a0032371>.
- Andersen, P.N., Hovik, K.T., Skogli, E.W., Egeland, J., Oie, M., 2013. Symptoms of ADHD in children with high-functioning autism are related to impaired verbal working memory and verbal delayed recall. *PLoS One* 8 (5), e64842. <https://doi.org/10.1371/journal.pone.0064842>.
- Barkley, R.A., 2011. *Barkley Adult ADHD Rating Scale-IV (BAARS-IV)*. Guilford Press.
- Bennett, H., Parfitt, G., Davison, K., Eston, R., 2016. Validity of submaximal step tests to estimate maximal oxygen uptake in healthy adults. *Sports Med.* 46, 737–750.
- Buckley, J., Sim, J., Eston, R., Hession, R., Fox, R., 2004. Reliability and validity of measures taken during the Chester step test to predict aerobic power and to prescribe aerobic exercise. *Br. J. Sports Med.* 38 (2), 197–205.
- Cheung, C.H., Rijdsdijk, F., McLoughlin, G., Faraone, S.V., Asherson, P., Kuntsi, J., 2015 Mar 1. Childhood predictors of adolescent and young adult outcome in ADHD. *J. Psychiatr. Res.* 62, 92–100.
- Cutting, L.E., Koth, C.W., Mahone, E.M., Denckla, M.B., 2003. Evidence for unexpected weaknesses in learning in children with attention-deficit/hyperactivity disorder without reading disabilities. *J. Learn. Disabil.* 36 (3), 259–269. <https://doi.org/10.1177/002221940303600305>.
- DuPaul, G.J., Power, T.J., Anastopoulos, A.D., Reid, R., 1998. *ADHD Rating Scale—IV: Checklists, Norms, and Clinical Interpretation*. Guilford press.
- Franke, B., Michelini, G., Asherson, P., Banaschewski, T., Buitelaar, J.K., Cormand, B., Faraone, S.V., Ginsberg, Y., Haavik, J., Kuntsi, J., Larsson, H., Lesch, K.P., Ramos-Quiroga, J.A., Rethelyi, J.M., Ribases, M., Reif, A., 2018. Live fast, die young? A review on the developmental trajectories of ADHD across the lifespan. *Eur. Neuropsychopharmacol* 28 (10), 1059–1088. <https://doi.org/10.1016/j.euroneuro.2018.08.001>.
- Gawrilow, C., Stadler, G., Langguth, N., Naumann, A., Boeck, A., 2016. Physical activity, affect, and cognition in children with symptoms of ADHD. *J. Atten. Disord.* 20 (2), 151–162. <https://doi.org/10.1177/1087054713493318>.
- Hervey, A.S., Epstein, J.N., Curry, J.F., 2004. Neuropsychology of adults with attention-deficit/hyperactivity disorder: a meta-analytic review. *Neuropsychology* 18 (3), 485–503. <https://doi.org/10.1037/0894-4105.18.3.485>.
- Hotting, K., Roder, B., 2013. Beneficial effects of physical exercise on neuroplasticity and cognition. *Neurosci. Biobehav. Rev.* 37 (9 Pt B), 2243–2257. <https://doi.org/10.1016/j.neubiorev.2013.04.005>.
- Hotting, K., Schauenburg, G., Roder, B., 2012. Long-term effects of physical exercise on verbal learning and memory in middle-aged adults: results of a one-year follow-up study. *Brain Sci.* 2 (3), 332–346. <https://doi.org/10.3390/brainsci2030332>.
- Jacob, C.P., Romanos, J., Dempfle, A., Heine, M., Windemuth-Kieselbach, C., Kruse, A., Reif, A., Walitza, S., Romanos, M., Strobel, A., Brocke, B., Schafer, H., Schmidtke, A., Boning, J., Lesch, K.P., 2007. Co-morbidity of adult attention-deficit/hyperactivity disorder with focus on personality traits and related disorders in a tertiary referral center. *Eur. Arch. Psychiatr. Clin. Neurosci.* 257 (6), 309–317. <https://doi.org/10.1007/s00406-007-0722-6>.
- Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., Williamson, D., Ryan, N., 1997. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. *J. Am. Acad. Child Adolesc. Psychiatry* 36 (7), 980–988. <https://doi.org/10.1097/00004583-199707000-00021>.
- Koch, E.D., Freitag, C.M., Mayer, J.S., Medda, J., Reif, A., Grimm, O., Ramos-Quiroga, J.A., Sanchez, J.P., Asherson, P., Kuntsi, J., Pawley, A.D., Buitelaar, J.K., Bergsma, D., Ortega, F.B., Muntaner-Mas, A., Reinhard, I., Reichert, M., Giurgiu, M., Ebner-Priemer, U.W., 2022. The dynamical association between physical activity and affect in the daily life of individuals with ADHD. *Eur. Neuropsychopharmacol* 57, 69–74. <https://doi.org/10.1016/j.euroneuro.2022.01.110>.
- Kooij, J.S., 2012. *Adult ADHD: Diagnostic Assessment and Treatment*. Springer Science & Business Media.
- Kuntsi, J., Eley, T.C., Taylor, A., Hughes, C., Asherson, P., Caspi, A., Moffitt, T.E., 2004. Co-occurrence of ADHD and low IQ has genetic origins. *Am J Med Genet B Neuropsychiatr Genet* 124B (1), 41–47. <https://doi.org/10.1002/ajmg.b.20076>.
- Loprinzi, P.D., Roig, M., Etnier, J.L., Tomporowski, P.D., Voss, M., 2021 Oct 20. Acute and chronic exercise effects on human memory: What we know and where to go from here. *J. Clin. Med.* 10 (21), 4812.
- Mayer, J.S., Hees, K., Medda, J., Grimm, O., Asherson, P., Bellina, M., Colla, M., Ibanez, P., Koch, E., Martinez-Nicolas, A., Muntaner-Mas, A., Rommel, A., Rommelse, N., de Ruiter, S., Ebner-Priemer, U.W., Kieser, M., Ortega, F.B., Thome, J., Buitelaar, J.K., Kuntsi, J., Ramos-Quiroga, J.A., Reif, A., Freitag, C.M., 2018. Bright light therapy versus physical exercise to prevent co-morbid depression and obesity in adolescents and young adults with attention-deficit/hyperactivity disorder: study protocol for a randomized controlled trial. *Trials* 19 (1), 140. <https://doi.org/10.1186/s13063-017-2426-1>.
- Michelini, G., Cheung, C.H., Kitsune, V., Brandeis, D., Banaschewski, T., McLoughlin, G., Asherson, P., Rijdsdijk, F., Kuntsi, J., 2021 Jan. The etiological structure of cognitive-neurophysiological impairments in ADHD in adolescence and young adulthood. *J. Atten. Dis.* 25 (1), 91–104.
- Mora-Gonzalez, J., Esteban-Correo, I., Cadenas-Sanchez, C., Migueles, J.H., Rodriguez-Ayllon, M., Molina-García, P., Hillman, C.H., Catena, A., Pontifex, M.B., Ortega, F.B., 2019. Fitness, physical activity, working memory, and neuroelectric activity in children with overweight/obesity. *Scand. J. Med. Sci. Sports* 29 (9), 1352–1363.

- Mostert, J.C., Onnink, A.M., Klein, M., Dammers, J., Harneit, A., Schulten, T., van Hulzen, K.J., Kan, C.C., Slaats-Willemse, D., Buitelaar, J.K., Franke, B., 2015 Nov 1. Cognitive heterogeneity in adult attention deficit/hyperactivity disorder: A systematic analysis of neuropsychological measurements. *European Neuropsychopharmacology* 25 (11), 2062–74.
- Pievsky, M.A., McGrath, R.E., 2018. The neurocognitive profile of attention-deficit/hyperactivity disorder: a review of meta-analyses. *Arch. Clin. Neuropsychol.* 33 (2), 143–157.
- Pollak, Y., Kahana-Vax, G., Hoofien, D., 2008. Retrieval processes in adults with ADHD: a RAVLT study. *Dev. Neuropsychol.* 33 (1), 62–73. <https://doi.org/10.1080/87565640701729789>.
- Ramos, A.A., Hamdan, A.C., Machado, L., 2019. A meta-analysis on verbal working memory in children and adolescents with ADHD. *Clin. Neuropsychol.* 1–26 <https://doi.org/10.1080/13854046.2019.1604998>.
- Rush, A.J., Gullion, C.M., Basco, M.R., Jarrett, R.B., Trivedi, M.H., 1996. The inventory of depressive symptomatology (IDS): psychometric properties. *Psychol. Med.* 26 (3), 477–486. <https://doi.org/10.1017/s0033291700035558>.
- Schoechlin, C., Engel, R.R., 2005. Neuropsychological performance in adult attention-deficit hyperactivity disorder: meta-analysis of empirical data. *Arch. Clin. Neuropsychol.* 20 (6), 727–744. <https://doi.org/10.1016/j.acn.2005.04.005>.
- Skodzik, T., Holling, H., Pedersen, A., 2017. Long-term memory performance in adult ADHD. *J. Atten. Disord.* 21 (4), 267–283. <https://doi.org/10.1177/1087054713510561>.
- Sykes, K., Roberts, A., 2004. The Chester step test—a simple yet effective tool for the prediction of aerobic capacity. *Physiotherapy* 90 (4), 183–188.
- Wechsler, D., 2003. *Wechsler Intelligence Scale for Children—Fourth Edition (WISC-IV)*, 3. The Psychological Corporation, San Antonio, TX.
- Wechsler, D., 1999. *Wechsler abbreviated scale of intelligence (WASI)*.
- Westwood, S.J., Parlatini, V., Rubia, K., Cortese, S., Sonuga-Barke, E.J.S., European, A.G. G., 2023. Computerized cognitive training in attention-deficit/hyperactivity disorder (ADHD): a meta-analysis of randomized controlled trials with blinded and objective outcomes. *Mol. Psychiatr.* 28 (4), 1402–1414. <https://doi.org/10.1038/s41380-023-02000-7>.