Thesis

Non-pharmacological interventions for the treatment of adult ADHD

A narrative literature review with a special focus on physical activity and exercise interventions

submitted by

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Graz, 24 February 2026

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Graz, 24 February 2026 Georg Resch m.p.

Zusammenfassung

Einleitung Die Aufmerksamkeitsdefizit-/Hyperaktivitätsstörung (ADHS) wird zunehmend auch bei Erwachsenen anerkannt und behandelt. First-line-Therapie sind Stimulantien. Für diese sind kurz-bis mittelfristig eine gute Wirksamkeit und Verträglichkeit nachgewiesen, jedoch sind Langzeitdaten rar. Es besteht ein großer Bedarf an nichtmedikamentösen Therapien für ADHS bei Erwachsenen als Ergänzung sowie als Alternative zur medikamentösen Therapie. Körperliches Training (physical exercise, PE) wurde noch kaum für Erwachsene mit ADHS untersucht. Es gibt jedoch zunehmend Belege für seine Wirksamkeit bei anderen psychiatrischen Störungen, wie Depressionen, Angststörungen und ADHS bei Kindern und Jugendlichen. Die vorliegende narrative Literaturübersicht untersucht drei nicht-pharmakologische Interventionen: kognitive Verhaltenstherapie (KVT), achtsamkeitsbasierte Interventionen (ABI) und PE.

Methoden PubMed und Google Scholar wurden nach Studien aus dem Zeitraum zwischen 2010 und Dezember 2025 durchsucht. Zu KVT und ABIs wurden ausschließlich RCTs mit Erwachsenen mit einer ADHS-Diagnose eingeschlossen. Zu PE wurden Studien nach den selben Kriterien bevorzugt. Aufgrund der geringen Zahl verfügbarer RCTs wurden jedoch auch andere Studiendesigns und breitere Populationen eingeschlossen, und als ergänzende Evidenz berücksichtigt. Primärer Endpunkt waren ADHS-Kernsymptome. Sekundäre Endpunkte waren unter anderem exekutive Funktionen, Komorbiditäten und Lebensqualität. Eine narrative Synthese der Ergebnisse wurde durchgeführt.

Ergebnisse Insgesamt wurden 24 Studien eingeschlossen: zehn RCTs zu KVT, sechs RCTs zu ABIs und acht Studien unterschiedlicher Designs zu PE. Sowohl für KVT als auch für MBIs gab es Hinweise auf eine Wirksamkeit zur Verbesserung der ADHS-Kernsymptome. Bei PE erschwerte die hohe Heterogenität der Studien die Identifizierung möglicher Effekte. Die Evidenz für alle drei Interventionen war begrenzt durch hohe Heterogenität der Kontrollgruppen und der Ergebnismaße, methodische Limitationen und kleine Stichproben.

Diskussion Es liegen Hinweise für die Wirksamkeit von KVT und ABIs als Therapien für ADHS bei Erwachsenen vor, jedoch bestehen noch Unsicherheiten hinsichtlich der Evidenz. Trotz einiger vielversprechender Daten zu PE können aufgrund der Limitationen keine eindeutigen Schlussfolgerungen gezogen werden. Es besteht Bedarf an weiteren Studien hoher Qualität und strikter wissenschaftlicher Methodik, insbesondere zu PE.

Abstract

Introduction Attention-deficit/hyperactivity disorder is increasingly recognised and treated in adults. While stimulants are an effective and well-tolerated treatment in the short-to medium term, evidence regarding their long term efficacy is scarce. There is a great need for effective non-pharmacological treatments for adults with ADHD, both as an adjunct, and as an alternative to medication. While physical exercise has been rarely investigated for adult ADHD, there is mounting evidence on its efficacy for numerous other psychiatric disorders, including depression, anxiety disorders, and ADHD in children and adolescents. The present narrative review investigated three non-pharmacological interventions: cognitive-behavioural therapy (CBT), mindfulness-based interventions (MBIs), and physical activity (PA) and exercise (PE).

Methods PubMed and Google Scholar were searched for studies published between 2010 and December of 2025. For CBT and MBIs, only RCTs on adults with an ADHD diagnosis were included. For PE, studies that met similar criteria were preferred. Due to the limited number of available RCTs on PE, other study designs and broader populations were also included as supplementary evidence. The primary outcome was ADHD core symptoms. Several secondary outcomes were included, such as executive functioning, comorbidities and quality of life. A narrative synthesis of results was conducted.

Results A total of 24 studies was included: ten RCTs on CBT, six RCTs on MBIs, and eight studies of mixed designs on PA/PE. For both CBT and MBIs, there was suggestive evidence on their efficacy in improving ADHD core symptoms. On PA/PE, the high heterogeneity of studies limited the identification of potential effects. Results on secondary outcomes were mixed. For all three interventions, the evidence was constrained by high heterogeneity of control groups, methodological limitations and small sample sizes.

Conclusions CBT and MBIs may be effective treatments for adult ADHD, but some uncertainties regarding the evidence remain. While there were some promising data on PA/PE, because of multiple limitations currently no strong conclusions can be drawn. More rigorous research on all three interventions, particularly on PE, is needed.

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List of abbreviations

AMN action-mode network

ClinRO clinician-reported outcome

DA dopamine

DMN default mode network

DSM Diagnostic and Statistical Manual of Mental Disorders

EF executive function

fMRI functional magnetic resonance imaging

GWAS genome-wide association study

ICD International Classification of Diseases

ITT intention-to-treat

MDD major depressive disorder

NE norepinephrine

ObsRO observer-reported outcome

PerfO performance outcome

PFC prefrontal cortex

PRO patient-reported outcome

PRS polygenic risk score

QoL quality of life

RCT randomised controlled trial

SMD standardised mean difference

SUD substance use disorder

TAU treatment as usual

UCC unspecific control condition

VTA ventral tegmental area

WL waiting list

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Chapter 1

Introduction

1.1 ADHD: definition and concept

In the most recent editions of the two most widely used diagnostic manuals, the International Classification of Diseases (ICD-11)[1] and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR),[2] Attention Deficit Hyperactivity Disorder (ADHD) is classified as a neurodevelopmental disorder.

In both manuals, ADHD refers to a syndrome, which is defined by similar basic characteristics. Its defining features are developmentally inappropriate levels of inattention or hyperactivity/impulsivity, or both. The symptoms must have an onset in childhood, and lead to impairments of functioning in more than one context of daily life (for example home, school, work or relationships). Additionally, the symptoms must be present in a persistent and enduring pattern.

1.1.1 The concept of ADHD

Since its initial inclusion in a psychiatric diagnostic manual in the 1960s, the conceptualisation of the condition now known as ADHD has been in continuous development.

Over the decades, much research has been conducted on ADHD, making it one of the most widely studied disorders in child and adolescent psychiatry.[3] It has been increasingly recognised that many children do not grow out of ADHD as they reach adulthood.[4]

ADHD can present itself clinically heterogeneous, and with varying levels of impairment. While it is conceptualised as a categorical disorder in the diagnostic manuals, evidence from population-based taxometric studies do not support this

assumption. Rather, the data point to an understanding of ADHD as an extreme expression of complex and dimensional traits.[5,6] Depending on the environment, those traits may be considered useful. However, when they exceed a certain threshold, and are mismatched to the demands of the environment, they could be a contributing factor to impairment and suffering.

The question of whether ADHD is associated with personal strengths and societal benefits, has rarely been explored.[5] Proponents of the neurodiversity paradigm have advanced this idea, and some efforts have recently been made to study the potential positive aspects of ADHD.[5] For instance, the association of ADHD with creativity has been investigated, but there is no conclusive evidence yet.[7] A qualitative survey study, in which adults diagnosed with ADHD were asked to report their own strengths, using open-ended questions, revealed some common themes.[8] Commonly reported strengths included high creativity and curiosity, the aspect of resilience (eg not giving up easily), empathy (understanding others who are struggling), high energy levels, the ability to hyperfocus, and spontaneity.

1.1.2 History of ADHD

The following timeline 1.1 gives an overview of key events in the conceptualisation, scienctific research, diagnosis and treatment of ADHD.

Descriptions pre-diagnostic manuals

Descriptions of conditions similar to ADHD have been published since the 19th century. Notable examples include those of the Scottish physician Alexander Crichton in the late 1800s, and the British paediatrician George F Still at the beginning of the 20th century.[9]

In 1902, Still published case histories of children and adolescents in a scientific journal, some of which described symptoms resembling ADHD.[10] His publication is often considered to be a starting point in the history of ADHD.[9]

In German-language psychiatric literature during the late 19th and the early 20th century, the concept of chronic mania was discussed, which shows strong similarities to the modern concept of adult ADHD. Participants in these discussions included prominent psychiatrists, for example Emil Kraepelin and Carl Gustav Jung.[11]

In the 1930s, the concept of minimal brain damage developed, as it was assumed that hyperactive behaviour was caused by brain lesions. This idea was influenced by reports of behavioural disorders in children who had suffered from encephalitis (a common occurrence during the encephalitis epidemic from 1917 to 1928), as well

as in children with a history of head injury or other infectious diseases, such as measles.[9]

The concept was questioned in the late 1950s and in the 1960s, as it was demonstrated that a neurological cause could not be detected in many children who showed typical behaviour such as hyperactivity or inattention. This led to the change of terminology from minimal brain damage to minimal brain dysfunction in the 1960s.[9]

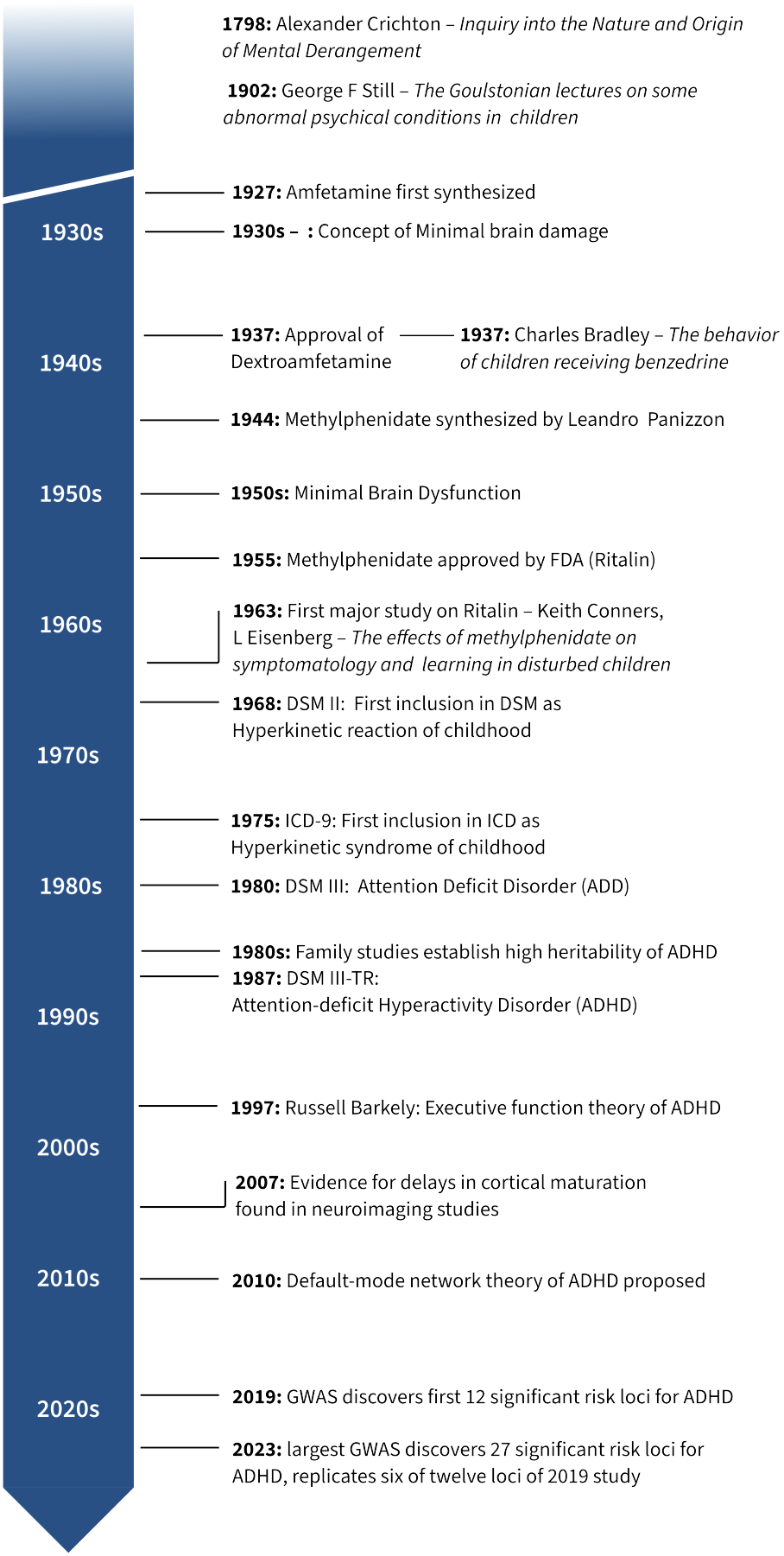

Figure 1.1: Timeline of key events in the history of ADHD

1.2 Diagnosis and classification

ADHD is a purely clinical diagnosis. It is based on an assessment of the core symptoms, as defined in diagnostic manuals, and the extent of impairment. No valid and reliable biomarkers are known that could be used for diagnosis.[10]

However, the clinically established diagnosis of ADHD has been found to be reliable and valid.[12]

The conceptualisation and diagnostic criteria of mental disorders are greatly influenced by, and defined in the two most influential diagnostic manuals. First, there is the International Classification of Diseases (ICD), currently in its 11th edition and published by the World Health Organization (WHO).[13] Secondly, the Diagnostic and Statistical Manual of Mental Disorders (DSM), currently in its revised fifth edition (DSM-V-TR), and published by the American Psychiatric Association.[2] The diagnostic criteria for ADHD are largely similar in both manuals. The following section provides an outline of the historical development of diagnostic criteria for ADHD.

1.2.1 Historical development of the diagnostic criteria

DSM-II

After not being in included in the first edition of the DSM in 1952,[14] a similar disorder was included in the DSM-II in 1968 under the name hyperkinetic reaction of childhood (or adolescence). It was defined as follows:

”This disorder is characterised by overactivity, restlessness, distractibility, and short attention span, especially in young children; the behaviour usually diminishes in adolescence. If this behaviour is caused by organic brain damage, it should be diagnosed under the appropriate non-psychotic organic brain syndrome (q.v.).”[15]

ICD-9

The first inclusion in the ICD occurred in its 9th revision in 1975[16] under the name hyperkinetic syndrome of childhood.

DSM-III

The term attention deficit disorder was first used in the DSM-III in 1980. It was also the first diagnostic manual to include quantitative symptom criteria for diagnosis, in an effort to enhance the reliability of diagnosis and provide a better basis for research.[17] Three symptom clusters were defined: inattention, impulsivity and hyperactivity.

For each cluster, three or more of six symptoms are required for diagnosis. The symptom descriptions in the DSM-III were focused on children and adolescents. Additionally, an age criterion was introduced: symptom onset must occur before the age of seven. Also, three subtypes were defined: ADD with hyperactivity, ADD without hyperactivity, and ADD, residual type.

DSM-III-R

In the revised edition of the DSM-III (1987), the list of diagnostic criteria was modified. Instead of 18, there were now 14 criteria, eight or more of which were required for a diagnosis. There were no subtypes in this edition.

DSM-IV

The DSM-IV (1993) is of particular importance to the history of adult ADHD, as it was the first manual to include descriptions of symptom manifestations in adults. The diagnostic criteria were again split into categories – six or more (of nine criteria) for inattention and six or more (of nine criteria) for hyperactivity/impulsivity were required for a diagnosis. Subtypes were introduced again: predominantly inattentive, predominantly hyperactive/impulsive, and combined type.

DSM-V

In the DSM-V (2013), ADHD was classified as a neurodevelopmental disorder for the first time. It also introduced two changes of diagnostic criteria that lower the threshold for diagnosing ADHD in adults:

1. If a person is 17 years of age or older, instead of six, only five or more criteria must be fulfilled for diagnosis, both for inattention and for hyperactivity/impulsivity category.
2. The required age of symptom onset was raised from before 7 to before 12 years.

The three subtypes from the DSM-IV remain, but are now referred to as presentations. This change emphasises potential changes in the manifestation of ADHD symptoms as the affected person grows and develops.[18] The revised DSM-V-TR from 2022 contains no major changes to the diagnostic criteria.

ICD-11

The diagnostic criteria from the 11th edition of the ICD (2022) are mostly similar to those of the DSM-V. Again, similar to previous editions of the ICD, absence of

quantitative symptom criteria is one major difference to the DSM. Instead, the ICD emphasises its focus on the judgement of the individual clinician in the diagnostic process.[1] One other notable difference was the addition of a new symptom criterion for impulsivity:

'having a tendency to act in response to immediate stimuli without deliberation or consideration of risks and consequences (eg engaging in behaviours with potential for physical injury; impulsive decisions; reckless driving).'[1]

1.2.2 Methods for diagnosis

The diagnosis of ADHD is based on a clinical interview, in which the symptoms according to the diagnostic criteria of the ICD or the DSM are evaluated in detail.

Diagnosing ADHD in an adult requires the following steps:

1. determinig that the adult meets ADHD diagnostic criteria in childhood (before age 12) and
2. determinig that the adult meets ADHD diagnostic criteria now.[19]

This process can be complicated by the problem that memory recall of childhood symptoms can be difficult or distorted in various ways - both when interviewing the adult patient or someone who knew the patient as a child, ie a parent. An additional aspect that can be an important addition to the diagnostic interview is taking a familiy history, as there are often other family members or close relatives with typical symptoms.[20]

1.2.3 Assessment instruments for diagnosis and research

A large number of assessment tools are available to assist with the diagnosis of ADHD and the assessment of the severity of symptoms. Many of them can be used both for clinical practice and research.[21] Table 1.1 provides an overview of some the most commonly used outcome assessment instruments and neuropsychological tests – many of them are used as measure of outcome of the studies included in this review.

Table 1.1 Tools for clinical outcome assessment (COA) commonly used for diagnosis and research

Assessment instrument		Measure of	Items	COA category
WURS	Wender-Utah-Rating-Scale SR	ADHD Symptoms; retrospective evaluation of childhood ADHD symptoms	25	PRO
WURS-k	Wender-Utah-Rating-Scale-Kurzform	ADHD Symptoms; Similar to WURS, but short version		PRO
DIVA	Diagnostic Interview for ADHD in Adults	ADHD Symptoms; Complete diagnostic assessment of adult ADHD		
ADHD-RS	ADHD Rating Scale	ADHD symptoms	18	PRO, ClinRO
ADHD-SR	ADHD Self-Rating Behaviour Questionnaire	ADHD symptoms	22	PRO
AISRS	Adult ADHD Investigator Symptom Rating Scale	ADHD Symptoms		ClinRO
ASRS	Adult ADHD Self-Report Scale	ADHD Symptoms	18	PRO
BADDS	Brown ADD Scales	ADHD Symptoms	40	PRO
CAARS	Conner‘s Adult ADHD Rating Scales	ADHD symptoms		PRO, ClinRO
CSS	Adult Barkley Current Symptoms Scale	ADHD symptoms		PRO, ClinRO
K-SADS	Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS-PL), ADHD Section	ADHD symptoms	18	ClinRO
WRAADDS	Wender-Reimherr Adult Attention Deficit Disorder Scale	ADHD Symptoms	28	ClinRO
CGI	Clinical Global Impression Scale	Severity of illness	1	ClinRO
AAQoL	Adult Attention Deficit/Hyperactivity Disorder Quality of Life Scale	QoL	29	PRO
Q-LESQSF	Quality of Life Enjoyment and Satisfaction Questionnaire - Short Form	Mindfulness	93	
FFMQ	Five Facet Mindfulness Questionaire	Mindfulness		
SCS-SF	Self-Compassion Scale - Short Form	Self-Compassion		
BAI	Beck Anxiety Inventory	Anxiety symptoms	21	PRO
BDI	Beck Depression Inventory	Depression symptoms	21	PRO
BRIEF-A	Behaviour Rating Inventory of Executive Function - Adult Version	EF	75	PRO
CVLT	California Verbal Learning Test	EF		PerfO
WCST	Wisconsin Card Sorting Test	EF		PerfO
TOVA	Test of Variable Attention	EF		PerfO
TMT	Trail-Making-Test	EF		PerfO
ST	Stroop Test	EF		PerfO
ANT	Attentional Network Test	EF		PerfO
CPT	Continuous Performance Task	EF		PerfO

1.3 Epidemiology

1.3.1 Prevalence and demographics

The prevalence of ADHD is estimated to be about 5% in children and adolescents, as was found in a large systematic review by Polanczyk et al in 2007, including 102 studies conducted in countries across the world.[22] The prevalence of ADHD in adults is estimated to be about 2.5%.[23]

In childhood, the male-to-female ratio of ADHD in the general population is about 2–2.5:1. This ratio moves closer to equal by adulthood.[24]

There has been controversy about the high variability of prevalence rates of ADHD found by different studies. However, this variability can be explained by differences in the methodology of studies, for example which diagnostic critera were used, the source of information, and the requirement of impairment for a diagnosis.[22]

When comparing prevalence studies with standardised procedures, there is no evidence of rising prevalence of ADHD in the last decades.[22]

Since ADHD is thought to be a childhood-onset neurodevelopmental disorder, it could be assumed that most adults with ADHD have a history of childhood ADHD. A four-decade longitudinal cohort study surprisingly found that 90% of adults with ADHD didn't have a history of ADHD in childhood.[25]

This finding raised new questions about the nature and the causes of adult ADHD. It has led some researches to hypothesise that apart from persisting childhood-onset ADHD, there exists a seperate, adult-onset syndrome, calling into question the prevailing concept of adult ADHD. These questions have not yet been answered conclusively.[26]

1.3.2 Comorbidity and morbidity

ADHD frequently co-occurs with other psychiatric disorders. It is estimated that up to 70 to 80% of individuals diagnosed with ADHD have at least one other psychiatric disorder over the course of their lifetime. The most common comorbidities, as identified in meta-analyses based on large general population studies, include anxiety disorders, major depressive disorder, bipolar disorder, and substance use disorder.[12]

The pooled odds ratios for different disorders have been calculated based on meta-analyses. These can be interpreted as estimates of the relative risk of having a disorder when comparing adults with ADHD to adults without ADHD. The pooled odds ratio has been found to be 5.0 for anxiety disorders, 4.5 for major depressive disorder, 8.7 for bipolar disorder, and 4.6 for substance use disorders, indicating highly increased risks.[27] Moreover, ADHD has been shown to frequently co-occur with autism spectrum disorders and eating disorders.[28] The suicide rate has been found to be increased in individuals with ADHD.[29]

Individuals diagnosed with ADHD are almost three times as likely to be nicotine dependent. They have a lifetime prevalence of up to 43% of developing any alcohol use disorder (AUD), and a lifetime prevalence of 3-11% of developing an alcohol dependence (ie moderate or severe AUD).[30] A moderate association has been found between ADHD and Internet addiction in a systematic review and meta-analysis.[31]

There is an association between sleep problems and ADHD.[32] ADHD has also been demonstrated to be associated with a threefold increased risk of obesity.[28] A population-based cohort study using Swedish register data found an association between ADHD and an increased risk of any cardiovascular disease. After adjusting for sex and year of birth, a hazard ratio (HR) of 2.05 was observed. After adjusting for other relevant factors such as education level, obesity, smoking, and psychiatric comorbidities, the HR was reduced to 1.65, which remained significant.[33]

A Danish nationwide cohort study found an increased mortality rate for children, adolescents, and adults with ADHD, compared to individuals without ADHD. The study found that ADHD was associated with decreased life expectancy and a more than doubled risk of death.[34]

ADHD is also associated with highly elevated levels of emotional dysregulation.[35]ADHD has been shown to be associated with a reduced quality of life and impairments in social functioning. Research has demonstrated ADHD to have a negative impact on relationships with peers and siblings. This has been observed across different cultures.[5] ADHD is associated with highly reduced academic performance, and higher dropout rates at school and universities. It is also associated with lower employment and poorer financial outcomes.[36]

1.4 Mechanisms/pathophysiology

Since the 1980s, much research in the fields of neuroscience and genetics has been conducted on ADHD - various theories on the biological causes of ADHD have developed. This section provides an overview of some of them. Two ways mechanisms can be categorised are by functional domain (eg arousal, reward respone, attention), or by levels of biological organisation (eg molecules, individual neurons, brain networks). Both approaches overlap, as a complex phenomenon such as ADHD affects many different levels of organisation at once.

1.4.1 Functional domains affected by ADHD

Arousal

The concept of arousal can be difficult to define. It describes both psychological and physiological states on a spectrum ranging from excessive sleepiness, inattention, and cognitive dysfunction to hypervigilance, overstimulation, and panic. At the centre lies a state of activation that is characterised by wakefulness, alertness and the ability to engage with environmental demands. Historically, the concept of arousal

has been closely linked to that of stress.[37]

Neurobiologically, the arousal system is closely linked to the Locus coeruleus-norepinephrine system of the brain.[37] One common theory of ADHD, which has a long history, assumes that there is a failure to maintain a state of optimal arousal of the cortex. It has been hypothesised that ADHD is characterised by chronic hypoarousal, leading to deficits in sustained attention and reduced vigilance.[38] Hyperactivity and sensation-seeking could then be seen as attempts to compensate for hypoarousal.[38]

Executive functions

Another theory of ADHD focuses on deficits in executive funcion. Executive function (also sometimes equated with the term cognitive control) refers to higher-level cognitive processes such as working memory, inhibitory and attentional control, cognitive flexibility, and goal-directed behaviour.[38]

The executive function theory of ADHD was proposed by Russell Barkley in 1997.[39] It suggests that a deficiency in inhibition leads to executive function (EF) deficits, which are assumed to be central to ADHD.

A large meta-analysis by Willcut et al[40] investigated the validity of the executive function theory of ADHD. The analysis revealed that ADHD, at a group level, was associated with significant deficits in all EF tasks, with medium effect sizes (Cohen's d 0.43 to 0.57; range of weighted mean ES). The strongest and most consistent effects were reported on working memory, response inhibition, planning and vigilance. However, these deficits were neither necessary nor sufficient for ADHD to manifest at the level of an individual.[40] It was concluded that, although EF deficits play an important role in the neuropsychology of ADHD, they are not the sole underlying cause that could explain all cases of the condition.

Emotional regulation

Emotional regulation can be defined as the ability of an individual to modify their emotional state, to promote behaviours that are adaptive and goal-directed.[35] Emotional dysregulation, on the other hand, can be defined as impairments of these adaptive processes, which can result in to behaviours that run against the interests of the individual.

It can be characterised as

"1) emotional expressions and experiences that are excessive in relation to social norms and are context inappropriate;

2) rapid, poorly controlled shifts in emotion (lability); and
3) the anomalous allocation of attention to emotional stimuli."[35] Clinically, emotional dysregulation manifests as irritability, and is often linked to temper outbursts and reactive aggression.[35] It has been demonstrated to be commonly associated with ADHD, with 34 to 70% of adults with ADHD having been found to be affected by impairing emotional dysregulation.[35]

Sleep and circadian rhythms

Another area of scientific investigation related to ADHD has focused on whether differences or dysfunctions in sleep and circadian rhythms explain ADHD. Studies have found that up to 80% of adults with ADHD experience sleep disturbances. Alterations in circadian rhythm biology, such as delayed sleep-waking time, have also been identified. Some researchers have therefore proposed that ADHD could be viewed as a circadian rhythm disorder, and have suggested treatments such as melatonin or bright light therapy.[41]

1.4.2 ADHD and functional brain networks

Several functional brain networks have been described over the last two decades, based on large resting-state functional connectivity MRI studies.[42] The term functional connectivity was coined by Karl Friston, who defined it as "temporal correlations between remote neurophysiological events".[42] Multiple networks of functionally coupled brain regions have been identified, and these findings have been replicated in multiple studies.[42–44] Some of the networks that have been implicated to play a role in ADHD are:[12]

- Default-mode network
- Fronto-striatal network
- Fronto-parietal network
- Attention networks

ADHD and the default-mode network

One theory, the interference hypothesis, suggests that a reduced ability to sustain attention is at the core of ADHD.[38] It asserts that in ADHD, there is a higher rate of interference of the default-mode network, resulting in the interruption of brain networks that are active during focused attention on a task.

The default mode network (DMN) is a functional brain network that was first described by Raichle et al in 2001.[45] It consists of a set of defined anatomical re-

gions, including the ventromedial prefrontal cortex, the precuneus, and the anterior and middle hippocampus. The DMN shows increased activity during periods when outward-oriented and goal-directed tasks are not being performed.[44] DMN activity is associated with self-referential and emotional processing, as well as the recollection of past experiences.[44] A defining feature of the DMN is that its activity is anti-correlated with that of brain networks typically active during outward-oriented and goal-directed tasks.[44]

There is evidence to suggest that the anti-correlation between the DMN and such networks, like the task-positive dorsal and ventral attention networks, is reduced in individuals with ADHD compared to controls.[12]

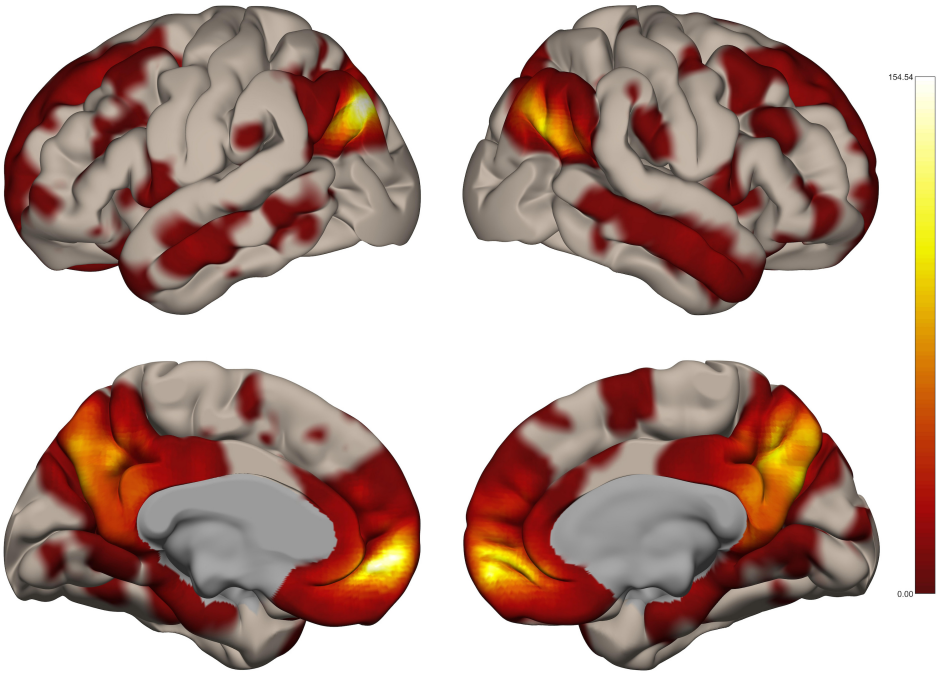

Figure 1.2: Heatmap visualisation of default-mode network resting state functional connectivity.
Created using the CONN functional connectivity toolbox (v.22.v2407),[46] using the NYU TRT fMRI dataset.[47]

In a meta-analysis of fMRI studies, a hypoactivation in the frontoparietal system has been found in adults with ADHD – this is consistent with executive function deficits. In addition, a hyperactivation of the visual and dorsal attention systems has been found, which can be interpreted as compensatory activity.[48]

A large systematic review and meta-analysis of functional magnetic resonance imaging (fMRI) studies by Cortese et al (2021) examined 30 resting-state fMRI studies on individuals with ADHD compared to typically developing controls. A statistical analyis on ADHD-specific hyper- and hypoconnectivity patterns of the individual

studies was done, using voxelwise meta-anlysis. No significant spatial convergence of the ADHD-related hypo- or hyperconnectivity was found across the studies.[49] The authors conclude that this could be explained, among other things, by the heterogeneity of ADHD and its pathophysiology.

1.4.3 Other neurobiological findings

Several neurobiological alterations have been found to be associated with ADHD. While different brain regions have been implicated, many of these findings have not been replicated.[38]

Examples for brain regions that are often implicated in ADHD are the dorsolateral prefrontal cortex, the inferior frontal cortex, and the parietal cortex.[12] The dorsolateral prefrontal cortex can be described as being responsible for multiple executive functions. These include, among others, working memory, temporal foresight, processing speed and selective attention, as well as attention switching.[12] The inferior frontal cortex is considered to play an important role in inhibition, sustaining attention and timing.[12]

Differences in white matter tracts in ADHD have been investigated using diffusion tensor imaging (DTI) techniques. A large systematic review and meta-analysis of 129 DTI studies highlighted several white matter alterations in individuals with ADHD. These alterations were found to be correlated with symptom severity and cognitive deficits. However, the authors also noted low quality of more than two thirds of the included studies as a major limitation.[50]

Brain dopamine systems, reward response and ADHD

Several forms of reward system dysregulation have been found in ADHD, including, for example, a reduced ability to delay gratification. For example, children with ADHD have been found to be more likely to choose small immediate rewards over larger delayed ones.[38] The major brain system involved in reward and motivation is the mesolimbic dopamine pathway. There is research suggesting that alterations in the synaptic dopamine processing of this pathway are aossociated with reward system dysregulations.[51]

In the brain, dopamine acts as an important neurotransmitter/neuromodulator. It plays a key role in processes such as reward and motivation, learning, cognition and motor control.[52] Two main dopamine pathways have been described – the nigrostriatal pathway, which is best known for its role in control of voluntary movements and the aetiology of Parkinson's disease, and the mesocorticolimbic pathway. The

mesocorticolimbic pathway consists of a small number (about 5,000) dopaminergic neurons located in the ventral tegmental area (VTA). Their axons project mostly to the ventral striatum (including the Ncl accumbens) and the prefrontal cortex (PFC) and cingulate cortex. There have been alterations found in this pathway in ADHD.[38]

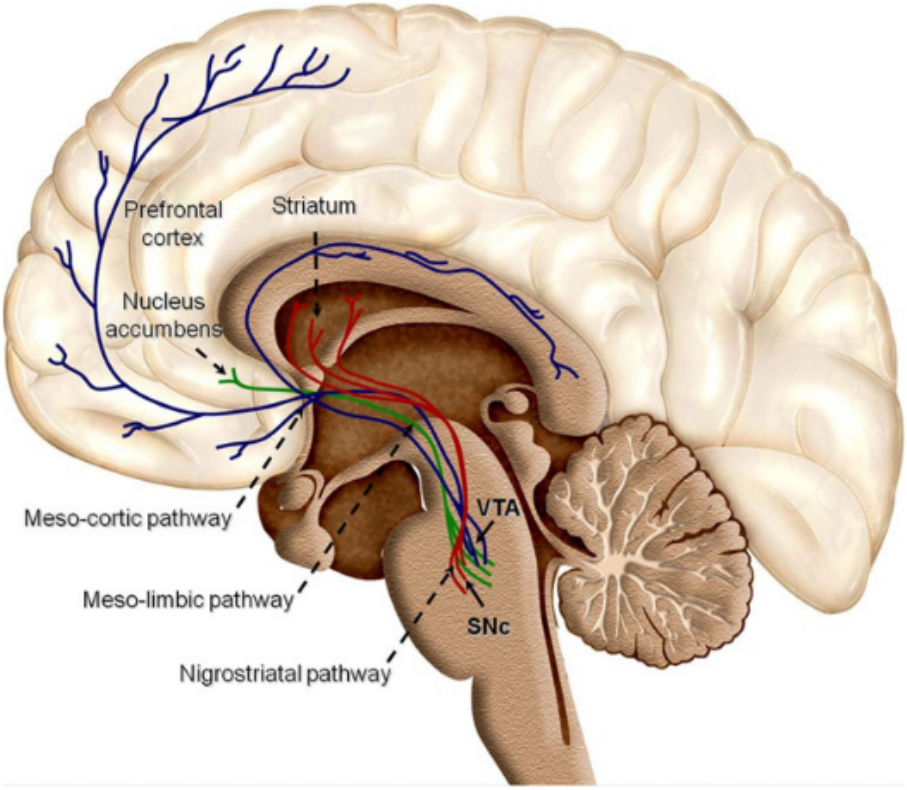

Figure 1.3: Overview of the dopaminergic systems in the human brain[52]

Important contributions to the research on the importance of the dopaminergic neurotransmitter system in the brain for the neurobiology of ADHD have been made by the team around Nora D Volkow.[51,53,54] For example, in one study using positron emission tomography they found that in medication-naïve adults with ADHD, the levels of dopamine transporters in certain brain areas (the left caudate and the left nucleus accumbens) were lower compared to controls without ADHD. The dopamine transporter levels in the putamen did not differ between the two groups, but levels were correlated with higher scores on inattention in both groups.[53]

While there is evidence for some involvement of the dopamine system in ADHD, only very limited evidence suggests that it is lower dopamine levels that define ADHD.[55] Evidence was found for an increase, but also for a decrease, as well as for no change in extracellular frontostriatal dopamine in individuals with ADHD compared to healthy controls. No consistent pattern of research results on the dopamine hypothesis on ADHD has been identified.[55]

Neurodevelopmental model

This model focuses on possible mechanisms in neural development that could explain ADHD symptoms, which has led to many studies looking at differences in brain maturation.[12,56] A delay in cortical maturation was found in children with ADHD, being most prominent in prefrontal regions of the brain.[57]

1.4.4 Genetics

ADHD has been found to have a high heritability estimate (h2) of 0.74 to 0.80 – the highest of eight common psychiatric conditions studied in a large sibling cohort study. This means that the contribution of genetic variance to trait variance is 80%.[58,59]

Twin studies suggest that the diagnosis of ADHD represents the extreme end of continuous traits, and that ADHD symptoms are continuously distributed in the population.[59]

Beginning with 1999, a research cluster around the genetics of ADHD was identified, with an important topic in the 2000s being genetic polymorphisms. Another large research cluster spans the 2010s, with genome-wide association studies (GWAS) and polygenic risk scores (PRS) being topics of interest.[3] Genetic polymorphisms are single gene variants; large studies have found very small effect sizes for single genes.

Family-based linkage analyses have been conducted, in which broad sections of the genome are screened. No evidence of single genes with large effect sizes on ADHD has been found.[38]

Genome-wide association study and polygenic risk scores

Genome-wide association studies (GWAS) have been conducted. These studies look for associations between a disorder and a large number (up to millions) of single nucleotide polymorphisms (SNPs) across the entire genome.

A large GWAS from 2019 identified twelve genome-wide risk loci for ADHD (for example FOXP2).[60] According to the analysis, a much larger proportion of the heritability of ADHD can be attributed to all common gene variants than to risk loci. This finding suggests a highly polygenic aetiology of ADHD.[60] This can be seen as evidence for ADHD as a dimensional phenomenon, describing the extreme end of a spectrum of traits, that manifest as ADHD symptoms.

Another large GWAS from 2023 identified 27 genome-wide risk loci for ADHD. However, of the 12 risk loci identified in the 2019 study, only six have been replicated

by this study.[61] This could indicate various issues – for example, it could be a sign of low statistical power, leading to false positives.[38]

1.4.5 Risk factors

Many environmental factors have been investigated as possible risk factors for developing ADHD.

Prenatal toxin exposure

Three large population-based birth cohort studies found associations between maternal use of acetaminophen (paracetamol) in pregnancy and the risk of the child developing ADHD. The more recent of these two studies, which used data from the Norwegian Patient Registry, found a hazard ratio of 2.20 (95% CI 1.50 to 3.24) for more than 29 days of maternal acetaminophen use and ADHD in offspring. This study adjusted for several cofounders like familial ADHD risk, and acetaminophen use before pregnancy.[62] However, a 2026 systematic review and meta-analysis on paracetamol exposure and child neurodevelopment calls that association into question. It focuses on sibling-comparison studies, and found that, when including only studies with low risk of bias in the analysis, there was no association beween paracetamol use during pregnancy and AHD (OR=0.97, 95% CI 0.89 to 1.05; P=0.49).[63]

An association between maternal phtalate metabolite levels and a increased risk of ADHD was found in another Norwegian cohort study. Children from mothers in the highest quintile of urine phtalate metabolites had about three time the odds of an ADHD diagnosis compared to those in the lowest quintile (OR=2.99, 95% CI 1.47 to 5.49).[64]

A large population-based cohort study, using data from 913,000 children in the Danish national registers, found an association between prenatal exposure to the antiepileptic drug valproate and an about 50% increased ADHD risk (adjusted hazard ratio=1.48, 95% CI 1.09 to 2.00) compared to children not exposed to valproate.[65]

Environmental toxins

Exposure of children to organophosphate pesticides, which have neurotoxic properties, has been shown to be associated with higher rates of ADHD.[66]

High blood lead levels in childhood have been consistently shown to be associated with a higher likelihood of developing ADHD. A meta-analysis of 14 studies reported the odds of ADHD being increased 4-fold for higher blood lead levels. As an example, one study, using data from 4700 youths of cross-sectional sample of the US population,

found that those with blood lead levels in the highest fifth had a four times increased odds of developing ADHD compared to those in the lowest fifth.[28]

An association between maternal smoking during pregnancy and with second-hand smoke exposure in childhood and likelihood of ADHD has been found. In the first case, the association disappeared after adjustments for familiy history of ADHD were made. In the second case, it is not clear wether the association is causal or due to confounders.[28]

No association between sugar consumption[67] and ADHD, and between perfluoroalkyl substances (PFAS)[68] and ADHD has been found.

1.4.6 Summary: mechanisms of ADHD

In summary, the neurobiological research on ADHD has produced a large number of heterogeneous findings, but until now, no clear integrated picture has been found.

There are multiple biological features (eg neurotransmitters, brain regions, brain networks, genes) which have been implicated in ADHD. A common characteristic of these findings are its small effect sizes. Koirala et al (2024)[38] suggest several possible reasons for this situation.

Firstly, ADHD is a heterogeneous condition, and as such, it can be assumed to have multiple aetiologies and mechanisms. The highly polygenic genetic aetiology of ADHD supports this idea. The diagnostic construct of ADHD as a categorical, binary disorder can be assumed not to reflect this complex reality.

Another reason for the limitations of neurobiological insights on ADHD could be that many studies have lacked the statistical power to detect small effect sizes reliably. One example is the small sample sizes that have been often seen in brain imaging studies.

The effect of biases, such as p-hacking, or publication biases, can be a another explanation for a large number of studies with highly significant findings that are not generalisable.[38]

In summary, ADHD can be understood as a fuzzy phenotype with multiple, different and overlapping aetiologies. It is highly heritable and associated with numerous subtle neurobiological alterations. These findings are consistent with the clinically heterogeneous presentations of ADHD.[38]

1.5 Treatment of ADHD

This section summarises the treatment recommendations in guidelines, followed by an overview of pharmacological and some non-pharmacological therapies.

1.5.1 Guideline recommendations

The German S3 guideline from 2018[69] recommends a multimodal therapeutic concept, which should be individualised to the needs of the patient. According to the guidelines, for all patients, extensive psychoeducation about ADHD should be offered. The first-line therapy recommended for adults is pharmacotherapy.

Psychosocial interventions can be integrated in the treatment plan alongside the pharmacological treatment. The guidelines recommend that they should be offered if residual ADHD symptoms that warrant treatment persist. Also, if the pharmacotherapy is not tolerable or acceptable to the patient, psychotherapy (based on CBT) is recommended,either in single or in group sessions.

The National Institute for Health and Care Excellence (NICE) guidelines (England, 2018)[70] recommend offering medication as a first-line treatment for adults with ADHD, with the recommendation being to start with either methylphenidate or the amfetamine formulation lisdexamfetamine.[18] Further, the NICE guidelines recommend that non-pharmacological treatments should be considered for adults with ADHD who have made the informed decision not to take medication or have found it to be ineffective or not tolerable, and as well if they have difficulty adhering to it.[71]

1.5.2 Pharmacological treatments

Medications that have been shown to be effective for treating ADHD mostly act on the dopamine, and to a lesser degree the noradrenaline systems of the brain. They can be grouped into stimulants and non-stimulants.

Stimulants (including amfetamine or methylphenidate formulations) are being generally recommended by guidelines before non-stimulants (eg alpha-2-adrenergic agonists such as clonidine or guanfacine, or selective noradrenaline reuptake inhibitors, for example atomoxetine or viloxazine).

The safety and efficacy of stimulants for treating ADHD symptoms has been demonstrated by many randomised controlled trials, which typically examine a treatment duration of several weeks.[28]

The efficacy of stimulants for treating ADHD symptoms in adults in those short-term trials has shown to be high. For example, a 2018 large systematic review and meta-analysis of randomised controlled trials (RCTs) found stimulants to be more effective than placebo on the outcome of ADHD symptoms. The effect sizes found were in the medium-to-high range, with a standardised mean difference (SMD) of −0.49 (95% CI −0.64 to −0.35) for methylphenidate and a SMD=−0.79 (95% CI −0.99 to −0.58) for amfetamines. The outcomes were rated by clinicians at the endpoint of the studies closest to 12 weeks.[72]

Table 1.2 Overview of ADHD medications

Substance	Mechanisms[73]	Duration of response (h)[12]
Stimulants		
Lisdexamfetamine	Prodrug of dexamfetamine	13
D/L-Amfetamine	DAT- and NET-inhibition; VMAT2- and MAO-Inhibition	4-6
Dexamfetamine		4-6
Methylphenidate	DAT- and NET-Inhibition; alpha-2-agonist	4 (IR tablets)
Non-stimulants		
Atomoxetine	Selective noradrenaline reuptake inhibitor	Not specified
Guanfacine	Alpha-2-adrenergic agonist	Not specified
Clonidine	Alpha-2-adrenergic agonist	Not specified

Source: Adapted from Faraone et al,[12] modified.

History and pharmacology of stimulants

Psychostimulant medications mostly act by increasing synaptic DA and NE concentrations. The two most important stimulants used for the therapy of ADHD are amfetamine and methylphenidate and its derivates.

Racemic amfetamine was first synthesised in 1927 by the chemist G A Alles, who was looking for a cheaper and more easily synthesizable alternative to ephedrine.[74] Starting in 1935, it was marketed under the brand name 'Benzedrine' by the pharmaceutical company Smith, Kline and French, for conditions like narcolepsy and mild depression.[74] In 1937, Benzedrine was suggested by Bradley as a treatment for children who would now probably be diagnosed with ADHD.[75] In 1937, Smith, Kline and French started marketing dexamfetamine (the dextro-enantiomer, one of two mirror-like variants of the amfetamine molecule) as Dexedrine.[74]

Amfetamines are part of the group of biologically active ß-phenylethylamines, and share this molecular structure with norepinephrine and dopamine.

Methylphenidate was first synthesised by Leandro Panizzon in 1944, marketed as Ritalin (named after Panizzon's wife Marguerita), and approved by the US Food and Drug Administration in 1955. The first major study of methylphenidate for the

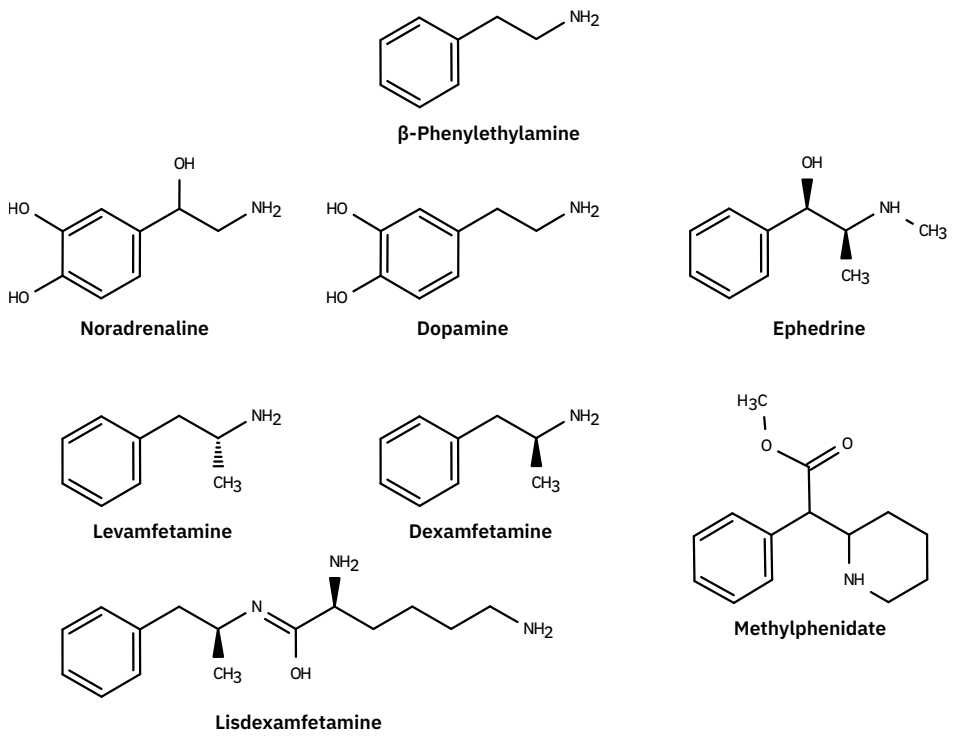

Figure 1.4: Molecular structures of phenylethylamine derivates.
(Image created with ketcher (v3.4.0)[76] and inkscape (v1.4.3)[77])

treatment of an ADHD-like condition in children was conducted in 1963 by Conners et al.[38]

Over the decades, many different variations and formulations of amfetamines and methylphenidate have been developed, including various extended-release formulations.

An example is the prodrug lisdexamfetamine dimesylate (marketed under the brand names Vyvanse and Elvanse). As of December 2025, it is the only amfetamine approved for adult ADHD in the EU. The molecule is constituted of D-amfetamine, with the amino acid L-lysine covalently bound to it. Following absorption into the bloodstream, the substance is metabolised by enzymes in red blood cells to D-amfetamine and L-lysine, which is the rate-limiting step in its metabolism.[74]

Because of this, peak plasma concentrations are reached slowly and independently of the route of administration. Therefore, lisdexamfetamine is a viable option for individuals with ADHD who are at risk of, or suffering from, substance use disorders or amfetamine abuse.[74]

Drug mechanisms

Both amfetamine and methylphenidate lead to an increase in the extracellular DA and NE concentration in the brain.

They both accomplish this by inhibiting the dopamine transporter (DAT) and the norepinephrine transporter (NET), which are responsible for the reuptake of DA and NE from the synapse into the presynaptic nerve terminal.

Amfetamine additionally inhibits the vesicular monoamine transporter 2 (VMAT-2), which leads to release of DA from cytosolic storage vesicles into the cytosol of the presynaptic nerve ending, and then to the reverse transport into the synapse via DAT.[73] Amfetamine is also a (relatively weak) inhibitor of the cytosolic enzyme monoamine oxidase (MAO). The inhibition of MAO leads to a decreased breakdown of DA.[74]

The brain regions that are most affected by AMP are the striatum (the location of most DATs), but also the cortex and the VTA.

Methylphenidate, apart from its action as DAT- and NET-inhibitor, acts as an alpha-2-adrenergic agonist, which could be a reason for its possible procognitive effects. It also has agonist activity at the 5-HT1A (serotonin) receptor.[73]

A large 2025 fMRI study by Kay et al[78] suggests that stimulants mostly affect functional connectivity in brain networks associated with arousal and reward. The study also found no effects of stimulants on established attention networks. This suggests that stimulants may work by increasing motivation and arousal. Also, effects were shown that could be interpreted as reversing the effects of sleep deprivation. The authors conclude that the ”combined noradrenergic and dopaminergic effects of stimulants may drive brain organization towards a more wakeful and rewarded configuration, improving task effort and persistence without effects on attention networks.”[78]

Evidence base

A large systematic review and component network meta-analysis[79] of RCTs showed amfetamines, methylphenidate and atomoxetine to be more effective than placebo in reducing ADHD core symptoms in adults both in self-based and clinician-based ratings at timepoints closest to 12 weeks.

Few RCTs that study medication effects for longer timespans than 12 weeks have been conducted.[79]

A Cochrane review (systematic review) of amfetamine for the treatment of adult ADHD analysed 19 RCTs including over 2500 participants treated with different amfetamine formulations. The review found a reduction of ADHD symptoms, both when assessed by clinicans, and when assessed by the patients. However, the quality

of evidence was rated as low to very low according to the GRADE Working Group grades of evidence.[80]

A 2024 large case control study investigating at cardiovascular disease (CVD) risk associated with long-term ADHD medication use found a 4% increase of CVD risk for each year of cumulative use.[81]

Current limitations of the evidence of pharmacological treatments

There is little data available on the long-term efficacy and tolerability of stimulant therapy for time spans longer than one or two years.

There is evidence of poor long-term adherence to stimulant medications. A retrospective observational study using population-based databases found that one year after initiation of medication, 39% of young adults (18–24 years) and 48% of adults ($\geq$25 years) remained on treatment. At the 5-year follow-up, only 10% of young adults and 15% of adults remained on treatment.[82]

Another possibly related topic is the loss of medication efficacy over time due to the formation of tolerance. Research has identified some physiological mechanisms of neuroadaptations to stimulants. However, few clinical studies on tolerance to stimulant medications have been conducted.[83]

In a positron emission tomography (PET) study, Volkow et al investigated a possible mechanism of tolerance formation during long-term stimulant treatment. Dopamine transporter availability in the brains of adults with ADHD who had never been on medication was compared before and after twelve months of treatment with methylphenidate, as well as with a control group without ADHD who were not taking stimulant medication. An increase in striatal dopamine transporter availability of 24% after 12 months of stimulant treatment was found, while the control group showed no change after 12 months. The authors hypothesised that this upregulation of dopamine transporters is a possible mechanism of tolerance formation, which may result in decreased efficacy of the medication, while leading to an exacerbation of ADHD symptoms when it is stopped.[54]

A 2018 Cochrane review found that the available evidence showed amfetamines to be effective in improving the severity of ADHD symptoms in adults. However, the quality of the evidence from the 19 included studies was graded as low to very low. Possible issues noted were the short duration of the studies, restrictive inclusion criteria, and multiple potential biases, eg due to funding. Of the 19 included studies, 16 studies were funded by the manufacturer, two did not specify their funding, and one study was government-funded. Another limitation noted by the review was

the overall low number of studies and included patients.[80] The review sparked a controversial scientific debate, as expert consensus papers and guidelines tend to reach much more positive conclusions about the quality of evidence for stimulant treatment for ADHD.[84]

1.5.3 Non-pharmacological interventions

This section gives a brief overview of the non-pharmacological interventions that are the focus of this review.

Cognitive behavioural therapy (CBT)

Cognitive behavioural therapy (CBT) is a form of psychotherapy encompassing many different methods, techniques, and historical influences. It is a very widely practiced method, and backed by a large volume of research spanning multiple decades.

CBT originated in the 1960s as an attempt to integrate behaviour therapy and cognitive therapy. Aaron Beck is considered a central figure.[85] Behaviour therapies were based on behaviourism, which focused solely on observable behaviours. The methods of behaviour therapy were later augmented by exposure and response prevention (ERP), a therapeutic strategy formalised by Edna Foa, and recognised as a central therapeutic technique for treating obsessive-compulsive disorder (OCD).[85,86]

Cognitive therapy was strongly influenced by the emerging field of cognitive psychology in the 1960s. One of the most influential figures associated with cognitive therapy was Albert Ellis, the founder of rational-emotive therapy (RET). Ellis was heavily influenced by Stoic philosophies, the analytic philosophy of Russell, as well as by psychoanalysis. His therapeutic strategies included cognitive strategies like challenging dysfunctional beliefs, as well as help developing clients develop unconditional self-acceptance.[85,87] "In Beckian CT, patients are trained to notice and respond more rationally to negative automatic thoughts, first by labeling various cognitive distortions, and then engaging cognitive restructuring with the therapist and in journalling exercises as homework."[85] Beginning in the 1990s, a so-called third wave of CBT integrated influences of mindfulness and acceptance. Influential forms of therapy belonging to this third wave are Dialectical Behavioural Therapy (DBT) by Marsha Linehan and Acceptance and Commitment Therapy (ACT) by Steven Hayes. DBT has been shown to be an effective treatment for borderline personality disorder (BPD) in multiple studies. However, as a systematic review and meta-analysis pointed out, the effect sizes were small, and many of the studies had a substantial risk of bias.[88] As BPD and ADHD can exhibit several similar features, such as emotional dysregulation and impulsivity, DBT in the form of group skills training has been

suggested for the treatment of ADHD.[89]

There is an overlap with the mindfulness-based therapies described in the following section, which could also be categorised as variants of third-wave CBT. For the purpose of this thesis, mindfulness-based interventions are placed in their own category.

Mindfulness-based cognitive therapy (MBCT) and other mindfulness-based interventions

The practice of mindfulness involves as core elements the cultivation of nonjudgmental awareness in the present moment. This is reflected in the definition of mindfulness by Jon Kabat-Zinn, who describes it as ”paying attention in a particular way: on purpose, in the present moment, and nonjudgmentally”.[90]

Drawing inspiration from Eastern contemplative traditions and religions such as Buddhism, he developed Mindfulness-Based Stress Reduction (MBSR), which was the first method to incorporate mindfulness into Western medicine. It is an eight-week programme designed for group settings, and was originally developed to help manage chronic pain.[91]

Mindfulness-based cognitive therapy (MBCT) was created by the Zindel Segal, John Teasdale and Mark Williams in the 1990s. It was originally developed as an intervention to prevent relapse in individuals with major depression. It aimed to integrate elements of CBT for depression with components of MBSR.[92]

Dialectical Behavioural Therapy also includes elements of mindfulness, and numerous other mindfulness-based programs have emerged.[91]

Mindfulness interventions typically involve the systematic cultivation of a mindful attitude. This involves practising intentional awareness of different aspects of one’s experience, such as thoughts, emotions, or bodily sensations. It can involve both formal mindfulness meditation exercises and informal exercises in daily life.

Exercise

A commonly used definition of physical activity was created by Caspersen et al in 1985, who defined it as ”any bodily movement produced by skeletal muscles that results in energy expenditure.”[93] The same paper also defined Exercise, or exercise training, as a planned, structured and repetitive subset of physical activity done with the intermediate or final goal of improving or maintaining physical fitness.[93] A single session of exercise is often referred to as acute exercise.[94]

A possible way to categorise physical activity is to divide it into three groups: lifestyle physical activity, aerobic exercise, and resistance or strength exercise.[95] Lifestyle physical activity includes activities of daily life that lead to energy expenditure, without necessarily being planned or structured. Examples include activities in daily routines, such as walking, doing household chores or gardening. Aerobic exercise is characterised by rhythmic and repetitive movements that increase heart rate and lead to improvements in cardiovascular fitness. Examples of such activities include running or cycling. Strength or resistance training involves exercises that lead to muscle contractions against a resistance, which leads to increased muscular strength and also increases functional capacity and endurance. Examples include weightlifting, exercises with resistance bands, and bodyweight strength exercises.[95]

A 2025 meta-review of Vancampfort et al highlights that evidence synthesis has yet to establish a clear outline of the differential effects of these three categories of physical activity on different psychiatric disorders.[95]

Exercise has been found to be an effective treatment for major depression, and is now considered to be non-inferior to first-line treatments like antidepressants and psychotherapy.[96] Both 2022 NICE guidelines[97] and WHO guidelines[98] on depression recommend exercise or physical activity as an adjunct treatment.

More broadly, the WHO provides recommendations on physical activity for adults of all ages. Among the numerous health benefits cited are reduced anxiety and depression symptoms, and improved cognitive health.[99] In their 2020 guidelines on physical activity and sedentary behaviour, they recommend a weekly minimum of 150–300 minutes of aerobic physical activity of moderate intensity, or 75–150 minutes of aerobic activity of vigorous intensity, or an equivalent combination of both.[99]

1.5.4 Hypothesised mechanisms of included interventions

The range of hypothesised mechanisms of the three categories of intervention included is very broad. The following section provides an overview of therapeutic components that could be responsible for the effects of the three included interventions.

CBT

The factors that can lead to the effects of psychological interventions can be divided into different components. Regarding CBT, Matsumoto et al suggested one possibility in a component meta-analysis..[100] Nine different components were defined (listed in Table 1.3).

Table 1.3 Components of CBT

Component	Definition and description
Psychoeducation	Providing the client with information about ADHD.
Cognitive restructuring	Technique that involves challenging and modifying irrational or maladaptive beliefs, for example using tools such as thought recording or journalling exercises.
Problem-solving techniques	Assisting the client in breaking problems into smaller parts, and to develop specific solutions.
Organisational techniques	Techniques such as behavioural analysis, developing strategies for organisation, planning and time management
Supportive components	Positive regard, support and attention directed toward the patient.
Third-wave components	Elements such as mindfulness, acceptance, identifying and aligning oneself to values.
Relaxation techniques	Techniques such as progressive muscle relaxation of breathing exercises
Placebo components	Positive expectancy inducing positive psychological effects.
Nocebo components	Negative expectancy or disappointment inducing negative psychological effects (for example by being assigned to TAU group of an intervention study)

Source: Adapted from Matsumoto et al,[100] modified.

Many of these components are potentially valuable for treating ADHD or its comorbidities. For instance, it can be argued that practising organisational skills could help with the executive dysfunction often associated with ADHD. Third-wave elements, such as mindfulness and acceptance, could potentially be helpful in dealing with emotional dysregulation. They could also help to develop a positive self-concept. This could be particularly beneficial, given that an association between ADHD and low self-esteem has been shown.[101]

Mindfulness-based interventions

The mindset cultivated through mindfulness practices often involves disengagement from unhelpful patterns and thoughts, and the development of meta-awareness.[102] Another component of mindfulness is adopting an open and accepting attitude towards one's own experience.

The emphasis on training attention and on fostering a non-reactive attitude towards difficult impulses and emotions lends itself to hypotheses about how mindfulness interventions could help with ADHD. For instance, these interventions could address the core symptoms of inattention and impulsivity, as well as the frequently co-occurring emotional dysregulation and executive dysfunction.

Exercise and physical activity

There are several commonly discussed hypotheses and explanations in the exercise and physical activity literature as to why exercise could be helpful in treating psychiatric disorders. These include neurobiological, behavioural, psychological and social effects.

Several neurobiological mechanisms have been widely studied. For instance, it has been demonstrated that exercise increases neuroplasticity. The term neuroplasticity refers to both the growth of new neurons (neurogenesis) as well as the formation of new connections within existing neural networks (synaptogenesis). Subjects that are commonly studied include changes in various brain areas, such as the hippocampus. These include potential exercise-induced volumetric changes, as well as neurogenesis.[103] Another widely studied neurobiological mechanism is the release of neuroplasticity facilitators. The most prominent example of these is brain-derived neurotrophic factor (BDNF). BDNF levels have been shown to be increased following exercise.[104] Another proposed mechanism is changes in inflammatory biomarkers.

The behavioural and psychosocial mechanisms discussed include an increased sense of accomplishment and self-efficacy, as well as improved self-regulation and self-esteem.[104,105] Positive socially mediated effects, especially of group exercise activities, have also been studied, such as increased social support. Access to green and blue spaces is another potential mechanism for achieving positive mental health outcomes. For example, some meta-analytic evidence suggests that physical activity in nature leads to more beneficial psychological outcomes than physical activity in urban environments.[95]

1.6 Research questions and objectives of the review

The following review questions are adressed:

1. What is the evidence for cognitive-behavioural therapy (CBT) as an intervention for adults with ADHD regarding ADHD symptoms and other outcomes, such as comorbidites, QoL and executive functions?
2. What is the evidence for mindfulness-based interventions for adults with ADHD regarding ADHD symptoms and other outcomes, such as comorbidites, QoL and executive functions?
3. What is the evidence for exercise and physical activity interventions for adults with ADHD, regarding ADHD symptoms and executive functions?

The review will include evidence for these three intervention types, both as an adjunct to and as an alternative for ADHD medication. Due to the limited volume of available evidence, question three will be adressed in a more exploratory manner, with broader inclusion criteria.

Due to of the increased recognition and diagnosis of ADHD in adults, there is a high demand for a wider range of effective, evidence-based long-term treatments.

Pharmacological treatments have been studied extensively, and there is expert consensus on their effectiveness. However, there are still many areas of uncertainty surrounding the evidence, especially with regard to long-term efficacy and adverse events. This could be another argument for why non-pharmacological treatments could be particularly interesting for an early-onset and often chronic condition like ADHD.

The objective of this review is to summarise the current state of evidence on three selected non-pharmacological treatments, identify limitations in the evidence, and highlight areas in which further research could be warranted.

The intent is to contribute to the development of an evidence-based multimodal therapy concept for the treatment of adult ADHD.

Chapter 2

Methods

This chapter summarises the methods used for this review, including the inclusion and exclusion criteria, the process of data collection and analysis, and the synthesis of the data.

2.1 Description of methods

The review method selected was a narrative literature review. Where possible, components of the approach used in systematic reviews were integrated. The review methods were loosely based on the PRISMA 2020 guidelines, as described in the Cochrane Handbook for Systematic Reviews of Interventions.[106] However, due to the narrative design of this review, some of the recommended steps in the guideline have been omitted or simplified.

2.2 Criteria for considering studies for this review

The papers fitting for inclusion have been assessed for the following criteria:

2.2.1 Population

In order to obtain a sufficient number of studies for each of the three interventions of interest, two differently broad inclusion criteria had to be defined.

1) and 2) CBT and mindfulness-based interventions Only randomised controlled trials (RCTs) on adults (aged at least 18) with a formal diagnosis of ADHD were included.

3) Physical activity and exercise Preferrably, randomised controlled trials (RCTs) on adults (aged at least 18) with a formal diagnosis of ADHD were included. Observational studies, and broader populations (studies including both adults and adolescents, and studies on participants who screened positive for ADHD (but did not have a formal diagnosis)) were included as additional evidence. The included studies were limited to studies published in the time period from 2010 to December 2025.

2.2.2 Intervention

The included non-pharmacological interventions were cognitive-behavioural and mindfulness-based therapies, as well as physical exercise interventions. Of particular interest were chronic physical exercise interventions, and studies including these were preferred over studies of acute exercise interventions.

Studies with the following types of control group were included: no treatment, waitlist, different existing practice control groups (eg treatment as usual (TAU), standard clinical management (SCM)), and active control interventions with different levels of assumed specificity (eg relaxation, support group, psychoeducation).

Special attention was given to identify the type of control group employed by the studies, particularly existing practise control groups and active control groups. This was done as control group stringency can have a major impact on effect sizes, with studies with more active control groups often finding smaller between-group differences in treatment effects.[107] In addition, terms commonly used to describe control groups, such as TAU, are sometimes used inconsistently in the literature.[108]

Regarding medication, studies involving both medicated and unmedicated adults were included. Attention was given to the type of medication, whether it was newly started or pre-existing, and on stratification of medicated individuals between groups.

2.2.3 Outcome

Primary outcomes that were of particular interest were ADHD core symptoms. Secondary outcomes included QoL, and executive functioning, as measured by various neuropsychological tests. If assessed by the studies, outcomes such as comorbidities and functional outcomes were also investigated as secondary outcomes.

Additional emphasis was placed on evaluating the types of clinical outcome assessments (COAs) used by the studies. These COAs were categorised using the taxonomy of the Report of the ISPOR Clinical Outcomes Assessments.[109] It defines four different types of COAs:

1. PRO (patient-reported outcome): This refers to assessment instruments in which the patient themselve rates their symptoms. A typical example is the Beck Depression Inventory (BDI), which is widely used to measure outcomes on depressive symptoms.
2. ClinRO (clinician-reported outcome): In ClinROs, the assessment of the outcome is carried out by a member of the investigator team of the study, who is clinically trained. Often, this type of COA is also referred to as clinician-rated; sometimes also as investigator-rated.
3. ObsRO: observer-reported outcome: This type of COA involves a person who is not required to be professionally trained, and who typically knows the patient well. For example, this could be a parent or partner, who is instructed to rate the patient using an assessment tool. This type of rating is sometimes also referred to as observer-rated or informant-rated.
4. PerfO: performance outcome: PerfO refers to assessment tools which use objective measures, which cannot be influenced by the judgement of a rater. The performance of the patient on a defined, standardised task is quantified using predefined, objective criteria. Relevant examples are the neuropsychological tests commonly used to measure executive functioning.

In addition to those four categories, another possible outcome category is biomarkers, which is also sometimes used in ADHD intervention studies. Examples include fMRI scans or EEG measurements, typically conducted while study participants complete neuropsychological tests.

When reporting the time points of assessments in tables, the following terminology is used:

1. pre: pre-treatment: assessment was conducted at baseline, shortly before the start of the interventions.
2. post: post-treatment: assessment conducted shortly after completing all treatment sessions.
3. Xm: X-month follow-up: assessment conducted X months after the post-treatment time point.

The time specifications for the follow-up period always refer to the time point post-treatment. For example, 3m refers to three months after post-treatment. Additionally, the number of different hypotheses tested for the primary and secondary outcomes was noted, as was whether a statistical correction for multiple comparisons was made or discussed.

2.3 Search methods for identification of studies

A search in literature databases, including PubMed and Google Scholar, was conducted in order to identify relevant articles. Additionally, the reference sections of systematic reviews and other relevant articles were manually screened to identify any further relevant articles. Various search terms were used in different combinations as part of the search strategy. Examples include ”ADHD”, ”adult”, ”non-pharmacological”, ”treatment”, ”psychotherapy”, ”CBT”, ”mindfulness”, ”MBCT”, ”exercise” and ”physical activity”. The time of publication was limited to the period from 2010 to December of 2025. The papers that were found were manually reviewed to ascertain whether they met the inclusion criteria. This process involved screening the titles and abstracts, and the full text where necessary. Relevant articles were collected using the reference management software Zotero.[110]

65 publications were selected as candidates for inclusion after using the search strategies described. Of those, 39 were excluded after further investigation, because they either did not meet the inclusion criteria, or were duplicates. In the end, 26 publications remained that were included in the review. There were two cases in which two publications reporting on the same group of participants were included (Mehren et al (2019),[111,112] Philipsen et al (2015),[113] Lam et al.(2019)[114]) These were counted as one single study each, thereby reducing the number of included studies to 24. Nine publications investigating dialectical behavioural therapy (DBT) for ADHD and one publication about internet-based CBT interventions were excluded. Since both of those categories fall under the category of CBT, this was a somewhat arbitrary decision to limit the scope of the review.

2.4 Data collection and analysis

Data from the included studies were extracted and entered into a spreadsheet software for further analysis.

The following data were collected on the outcome:

- assessment tools used
- types of outcome measured (as primary and secondary outcome)
- number and timing of assessments
- most relevant results of assessments
- measure and magnitude of effect size, if reported, as well as p-values and confidence intervals

The following other data were collected on:

- the report: authors, year, source of publication
- the participants: age, sex, diagnosis, ADHD medications (including medication type; also if medication was preexisting or newly established).
- the research design: sampling mechanism, treatment assignment mechanism, adherence, length of follow-up.
- the intervention: type, duration, timing, mode of delivery; also collected on control group, if applicable.

2.4.1 Data synthesis

A narrative synthesis of study results was carried out – some recommdations of the SwIM (synthesis without meta-analysis) guidelines were incorporated.[115] The studies were grouped by intervention type, and by control group stringency as secondary grouping. The effect measures with confidence intervals were used as a metric for synthesis. If those were not reported by a study, the stated direction and magnitude of effect was used. The synthesis was presented as narrative summary. Key characteristics of the included studies were summarised in tabular form.

Chapter 3

Results

3.1 Description of studies

This section provides an overview of all included studies, sorted by type of intervention and study design. Basic information extracted from the included studies is summarised in tables. A total of 24 studies were included: ten RCTs on CBT, six RCTs on mindfulness-based interventions, and eight studies of different designs on exercise and physical activity. Studies that were conducted on the same sample, but whose results were reported in several articles, were counted as a single study.

To improve comparability, the studies were grouped by stringency of control condition. A classic hierarchy of control group stringency ranges from low to high, in the following order: no treatment, wait list, existing treatment conditions to active control groups (such as unspecific therapy conditions and alternative treatment protocols). As the control group stringency increases, the effect size of an intervention can be expected to decrease, provided that the intervention is effective.[108]

The boundaries between the various types of control group conditions are often blurred. For example, there can be overlap between wait list and different kinds of existing practice control groups, such as treatment as usual (TAU).[108] Therefore, a simplified categorisation was used:

1. Control groups with lower stringency: No treatment, wait list, and existing practice conditions (eg treatment as usual (TAU))
2. Active control groups, for example therapy protocols with less specific therapeutic strategies

3.1.1 CBT intervention studies

Ten RCTs investigating CBT interventions were included.

Table 3.1 Overview of included studies on CBT interventions

First author	Year	Country	n	age (mean)	female (%)	Med (%): I/C	Intervention	Control	Primary outcome
Emilsson[116]	2011	Iceland	54	33,9	63,0	1i00/100	CBT + M	TAU + M	ADHD symptoms
Young[117]	2015	Iceland	95	35,2	65,3	100/100	CBT + M	TAU + M	ADHD symptoms, Sev
Dittner[118]	2018	UK	60	35,9	31,7	63,3/86,7	CBT + TAU	TAU	ADHD symptoms; Func imp
Anastopoulos[119]	2021	USA	250	19,7	66,0	53,3/41,7	CBT	wait list	ADHD symptoms, EF, D, A; func OC
Pan[120]	2021	China	98	25,8	40,8	100/100	CBT + M	CM + M	ADHD symptoms
Corbisiero[121]	2017	Switzerland	43	31,9	44.2	100/100	CBT + M	SCM + M	ADHD symptoms
Solanto[122]	2010	USA	88	41,7	65,9	42,2/46,5	CBT	Supportive therapy	ADHD symptoms
Safren[123]	2010	USA	86	43,2	44,2	100/100	CBT + M	Relax+educ support + M	ADHD symptoms
Vidal[124]	2013	Spain	32	39,5	53,1	100/100	CBT + M	Psychoed group + M	ADHD symptoms
Philipsen;[113] Lam[114]	2015; 2019	Germany	419	35	49,9	210 M, 209 P	2 x 2 factorial: CBT + M, CBT + P, ICM + M, ICM + P		ADHD symptoms

Med (%): I/C percent of participants on ADHD medication in intervention group/control group
abbreviations: A, anxiety; CM, clinical management; D, depression; EF, executive functioning; Func imp, functional impairment; Func OC, functional outcomes; ICM, individual clinical management; M, medication; P, placebo; Relax+educ supp, Relaxation and educational support; SCM, standard clinical management; Sev, severity of illness;

3.1.2 Mindfulness-based interventions

A total of six RCTs were included in the review. Of those, four used preexisting treatment or wait list controls, and two used a more stringent active control group (psychoeducation interventions).

Table 3.2 Overview of included studies on mindfulness-based interventions

First author	Year	Country	n	Age (mean)	female (%)	Med (%): I/C	Intervention	Control	Primary outcome
Gu[125]	2018	China	54	20,3	44,4	64,3/76,9	MBCT	Wait list	ADHD symptoms, A, D, academic performance
Hepark[126]	2019	Netherlands	103	35,9	54,4	60,0/54,2	MBCT	Wait list	ADHD symptoms
Janssen[127]	2019	Netherlands	120	39,4	53,3	60,0/48,3	MBCT + TAU	TAU only	ADHD symptoms
Schoenberg[128]	2013	Netherlands	50*	52,3*	37,0	48,3/61,6	MBCT	Wait list	EF (+EEG)
Bachmann[129]	2018	Germany	74	40,1	55,0	0/0	MBCT	Psychoeducation group	EF, ADHD symptoms
Hoxhaj[130]	2018	Germany	81	39,5	51,2	0/0	MI	Psychoeducation group	ADHD symptoms

Med (%): I/C; percent of participants on ADHD medication in intervention group/control group
Abbreviations: A, anxiety; D, depression; EF, executive functioning; MI, mindfulness intervention

3.1.3 Physical exercise

Table 3.3 Overview of included studies on physical activity and exercise

First author	Year	Country	n	age (mean)	female (%)	Med (%): I/C	Study design	Primary outcome
Fritz and O'Connor[131]	2021	USA	32	20,1	100,0	0,0/0,0	RCT: chronic exercise (Yoga)	EF
Kouhbanani[132]	2023	Iran	52	35,3	100,0	Not clearly reported	RCT: chronic exercise (Pilates)	EF
Svedell[133]	2025	Sweden	63	36,1	76,8	62,8/65	RCT: chronic exercise vs TAU	ADHD symptoms
Mehren*[111,112]	2019	Germany	46	29,5	22,5	20,0/0,0**	RCT: acute exercise	EF (+ fMRI)
Dinu†[134]	2023	UK	159	26,6			RCT: acute exercise: (10 min aerobic vs 10 min Yoga)	EF
Mayer†[135]	2024	Germany, UK, Netherlands, Spain	207	26,0	55,1	BLT (64,3), EI (72,5), TAU (66,2)	RCT: chronic exercise: EI vs BLT vs TAU	Depression symptoms
Berger†[136]	2014	Germany	1615	43,3	53,7	Not assessed	Observational study	Excessive exercising
Koch†[137]	2022	Germany, UK, Spain	185				Observational study	Affect (e-diary)

*two separate study reports, summarised as one study
†broader inclusion criteria, included as lower-priority additional evidence
Med (%): I/C; per cent of participants on ADHD medication in intervention group/control group
Abbreviations: BLT, bright light therapy; EI, exercise intervention

3.2 Presenting results of studies

3.2.1 CBT

A first group of studies compared a CBT intervention with an unspecific control condition, such as treatment as usual (TAU) or wait list.

Group 1: CBT vs wait list or prexisting treatment conditions

Emilsson et al (2011).[116] This RCT compared a group of CBT+Medication with the control condition TAU+Medication, and reported changes in ADHD symptoms (PRO and ClinRO) as primary outcome. Severity of illness (ClinRO) was assessed via CGI, but it was not reported if this was considered a primary or secondary outcome. Additionally, comorbidities (anxiety and depression) were assessed as secondary outcomes (PRO). The time points of the assessments were at baseline, post-treatment and 3-month follow-up. The outcome reporting included multiple hypothesis tests (five on the primary, seventeen on the secondary outcomes), and did not discuss statistcal corrections for type I errors.

The results comparing pre-post showed medium to large effect sizes of CBT+M vs

Table 3.4 Details on included studies: CBT vs wait list or preexisting treatment condition

Study	Intervention	Control group	AT (Primary OC)	AT (Secondary OC)	Assessments
Emilsson et al (2011)[116]	15×90 min grp CBT, 2/wk; +1×30 min ind/wk; + Med	TAU + Med (group received psychopharmacological treatment only)	CSS (PRO), K-SADS (ClinRO), CGI (ClinRO)	BAI (PRO), BDI (PRO), RATE-S (PRO)	Pre, post, 3m follow-up
Young et al (2015)[117]	15×90 min grp CBT, 2/wk; +1 session with mentor/wk, at least 30 min	TAU + Med (psychopharm and other non-pharm interventions; but not systematically provided or recorded)	K-SADS (ClinRO), CGI (ClinRO), CSS (PRO)	BAI (PRO), BDI (PRO), QOLS	Pre, post, 3m follow-up
Dittner et al (2018)[118]	15×90 min ind CBT over 30wk; + 1 session (wk 42)	TAU (visits to doctor, specialist ADHD service, etc, with focus on medication management)	CSS (ClinRO), WSAS (ClinRO)	HADS (PRO), CORE-OM (PRO), CGI - binary recoded version (PRO and ClinRO), CSS (ObsRO)	Pre, post
Anastopoulos et al (2021)[119]	Semester 1: 8×90 min grp CBT, 1/wk; +8×30 min ind mentoring sessions, 1/wk Semester 2: 1×90min grp booster session; 6×30 min ind mentoring sessions	Wait list	CAARS-S:L (PRO), BRIEF-A (PRO), BDI-II (PRO), BAI (PRO)	3 newly created questionaires evaluating clinical change mechanisms and service utilisation	Pre, Post, follow up (end of maint. semester)
Pan et al (2021)[120]	12×120 min grp CBT, 1/wk	CM + MED (basic clinical management and consultation)	ADHD-RS (PRO)	CAARS (PRO), SAS (PRO), SDS (PRO), STAI (SR), SES, ATQ, DAS, WHOQOL-BREF, BRIEF-A, TMT (PerfO), Stroop test (PerfO)	Pre, post, 3m and 6m follow-up

AT (Primary/Secondary OC): assessment tools used for primary/secondary outcome; Assessments: time points of assessments
Abbreviations: ADHD-RS, ADHD Rating Scale; ATQ, Automatic Thoughts Questionnaire; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BRIEF-A, Behaviour Rating Inventory of Executive Function - Adult Version; CAARS-S:L, Conner‘s Adult ADHD Rating Scales; CGI, Clinical Global Impression Scale; CORE-OM, Clinical Outcomes in Routine Evaluation Outcome Measure; CSS, Adult Barkley Current Symptoms Scale; ClinRO, clinician-rated outcome; DAS, Dysfunctional Attitudes Scales; HADS, Hospital Anxiety and Depression Scale; K-SADS, Kiddie-Schedule for Affective Disorders and Schizophrenia; MED, medication; ObsRO, observer-rated outcome; PRO, patient-rated outcome; QOLS, Quality of Life Scale; RATE-S, R&R2 ADHD Training Evaluation Self-report Scale; SAS, Self-Rating Anxiety Scale; SDS, Self-Rating Depression Scale; SES, Self-Esteem Scale; STAI, State-Trait Anxiety Inventory; TAU, treatment-as-usual; TMT, Trail-Making-Test; WHOQOL-BREF, World Health Organization Quality of Life-Brief Version.

TAU+M on ADHD symptom scores (ClinRO). Symptoms improved at post-treatment (d=1.03; P<0.01) on K-SADS. The effects persisted on follow up. In addition, medium to large effect sizes on self-rated ADHD symptoms were found (d=0.76; P<0.01), with a larger effect at follow-up (d=1.08; P<0.001). Improvements on comorbidities (for example anxiety, depression) were not statistically significant at post-treatment, but at 3-month follow-up (showing large effect sizes).

No confidence intervals for outcomes were reported. Regarding handling of missing data, the authors state: ”Thus intention to treat analysis (ITT) was conducted. Missing values were not imputed because the ANCOVA calculates outcome whilst adjusting for all baseline data.”[116] This can be interpreted as a methodological error, as not performing imputation for missing values because of ANCOVA contradicts the statement that ITT has been done, thereby increasing risk of bias.

Young et al (2015).[117] This RCT compared already medicated adults with ADHD randomised to a CBT+Med and a TAU+Med group. The CBT intervention consisted of 15 sessions of CBT (both group and individual setting). The three primary outcomes were ADHD symptoms (ClinRO as well as PRO) and severity of illness (ClinRO). Secondary outcomes were anxiety (PRO), depression (PRO) and QoL (type of COA not clearly reported). All COAs were conducted at baseline, at end of treatment, and at 3-month follow-up.

The outcomes were reported as between-group differences in treatment effects. The data were analysed using linear mixed-model analysis, and the post-treatment and 3-month follow-up time points were combined for each outcome.

Statistically significant effects of CBT+Med compared to TAU+Med were found on the primary outcomes (reported as seven different scales), with medium effect sizes. These included improvements in clinician-rated ADHD symptoms (K-SADS; total score and two subscales; d=0.51 to 0.65; all P<0.001), self-rated ADHD symptoms (CSS; total score and two subscales; d=0.42 to 0.46; all P<0.001) and severity of illness (CGI; d=0.64; P<0.001). A statistically significant effect on self-rated depression symptoms was found (BDI; d=0.31; P<0.001), while no statistically significant effects were found on anxiety symptoms and QoL.

A high dropout rate of up to 50% of participants at 3-month follow-up was reported.

Dittner et al (2018).[118] This RCT included 60 adults with ADHD, who were randomly split into an CBT+TAU group vs a TAU group.

The CBT intervention consisted of 15 90-minute sessions, which were spread out over 30 weeks; another session was done at week 42, which was the time point of the primary outcome assessment. The TAU sessions were focused on medication management, and didn't include information or advice regarding managing ADHD symptoms.

The results favoured the CBT group with large effect sizes - it showed a larger decrease in clinician-rated ADHD symptoms (measured with Barkley's Current Symptoms Scale; standardised ES=−1.31; P<0.001), and clinician-rated functional impairment (measured with WSAS, standardised ES=−0.82; P=0.003) in the CBT+TAU compared to the TAU group.

Anastopoulos et al (2021).[119] This multi-site RCT included college students with ADHD (n=250), randomised to either a CBT group (with group and individual sessions)

or a waiting list control group. The intervention consisted of an active treatment period with eight weekly group sessions (90 minutes each), and eight weekly individual mentoring sessions (30 minutes each). This was followed by a one semester-long maintenance phase with one 90 minute group booster session and up to six 30 minute individual mentoring sessions. Primary outcomes were ADHD symptoms, executive functioning, depression and anxiety symptoms (all self-reported). The assessments were carried out pre-treatment, post-treatment, and post-maintenance.

The data were analysed using latent growth curve modeling (LGCM); the change in symptoms over time were compared between both groups.

The results favored CBT vs wait list on ADHD symptoms (CAARS total score), with an effect size of d=0.39 (95% CI 0.15 to 0.65). Also, there was a statistically significant improvement in executive functioning outcomes in CBT compared to WL, showing medium effect sizes.

The study's CONSORT flow chart reports a number of 280 randomised, of which 30 were exluded from the immediate CBT group because of scheduling conflicts. Inconsistent with this statement, the abstract reports a number of 250 randomly assigned. The baseline characteristics are reported for the group after the post-randomisation exclusions, not for the complete randomised sample.

Pan et al (2021).[120] This RCT on medicated adults with ADHD compared a 12 week CBT group (CBT + Medication) with a control group of Medication only. Primary outcome was ADHD symptoms at post-treatment time point (12 weeks), reported as three scores (total score, and two subscales). Multiple secondary outcomes were assessed. In total, 57 different outcomes were reported (19 scales, subscales or scores, each for three time points). Multiple comparisons were done (three hypotheses tested for primary, and 54 for secondary outcomes); it was reported that "Bonferroni-adjusted post hoc pairwise comparisons" were used.

Results for the primary outcome were an improvement on total ADHD-RS post-treatment (primary outcome) not statistically significant (d=0.34; P=0.096) and statistically significant effect only on inattention-subscale (d=0.453; P=0.026).

Group 2: CBT vs enhanced usual care or active control conditions

Corbisiero et al (2017).[121] This RCT compared a included 43 adults with ADHD, which were randomised to a CBT+Med group and a standard clinical management (SCM)+Med group. The CBT intervention consisted of ten to twelve weekly 2-hour sessions of individual psychotherapy, while the SCM was comprised of 10–12 weekly 30

Table 3.5 Details on included studies: CBT vs enhanced usual care or active control group

Study	Intervention	Control group	AT (primary OC)	AT (Secondary OC)	Assessments
Corbisiero et al (2017)[121]	10-12×120 min ind CBT, 1/wk; +Med	SCM ; +Med (SCM consisted of 30min medication counseling sessions with a psychiatrist, at same frequency as intervention group); +Med	CAARS-S:S, O:L (PRO, ClinRo), WRAADDS, ADHD-SR (PRO), SDS (PRO), AAQoL (PRO), RSES	CAARS subscales (ObsRO and PRO), ADHD-DC (OR), CGI subscales (OR), BDI (SR)	Pre, post, 9m follow-up
Solanto et al (2010)[122]	12×120 min grp CBT, 1/wk	Supportive therapy: group intervention of same duration, frequency and therapy attention, elements of psychoeducation; but no specific strategies of metacognitive therapy	AISRS (ClinRO), CAARS-S inatt./mem. Subscale (PRO)	BADDS (PRO), BDI (PRO), BRIEF-A (PRO), RSEI (PRO), CAARS-OR (ObsRO), OTMOPS (PRO), HAM-A (ClinRO)	Pre, post
Safren et al (2010)[138]	12×50 min ind CBT	Relaxation + educational supprt + M	ADHD-RS (ClinRO), CGI (ClinRO)	CSS (PRO)	Pre, post, 3m and 9m follow-up
Vidal et al (2013)[124]	12×120 min grp CBT, 1/wk	Psychoeducation group	ADHD-RS (PRO), CAARS (PRO), CGI-S (ClinRO and PRO)	BDI (PRO), STAI, QLESQ	Pre. post
Philipsen et al (2015),[113] Lam et al (2019): (follow-up report)[114]	GPT: 12×100 min grp PT, 1/wk; then 9×100 min grp PT, 1/month over 52wk	ICM: 12×15–20 min ind PT, 1/wk; then 9×15–20 min ind PT, 1/month over 52wk	CAARS (ObsRO) at 12w	CAARS subscales (ObsRO and PRO), ADHD-DC (OR), CGI subscales (OR), BDI (SR)	Pre, after intensive treatment (12w), during maintenance (24w), post (52w), 1,5y follow-up

AT (Primary/Secondary OC): assessment tools used for primary/secondary outcome; Assessments: time points of assessments
Abbreviations: AAQoL, Adult Attention-Deficit/Hyperactivity Disorder Quality-of-Life Scale; ADHD-DC, ADHD Diagnostic Checklist; ADHD-RS, ADHD Rating Scale; ADHD-SR, ADHD Self-Rating Behavior Questionnaire; AISRS, Adult ADHD Investigator Symptom Rating Scale; BADDS, Brown ADD Scales; BDI, Beck Depression Inventory; BRIEF-A, Behaviour Rating Inventory of Executive Function - Adult Version; CAARS, Conner‘s Adult ADHD Rating Scales; CGI, Clinical Global Impression Scale; ClinRO, clinician-rated outcome; HAM-A, Hamilton Anxiety Rating Scale; MED, medication; OTMOPS, On Time Management Organization and Planning Scale; ObsRO, observer-rated outcome; PRO, patient-rated outcome; QLESQ, Quality of Life Enjoyment and Satisfaction Questionnaire; RSEI, Rosenberg Self-Esteem Inventory; RSES, Rosenberg Self-Esteem Scale; SCM, standard clinical management; SDS, Self-Rating Depression Scale; STAI, State-Trait Anxiety Inventory; TAU, treatment-as-usual; WRAADDS, Wender-Reimherr Adult Attention Deficit Disorder Rating Scale.

minute medication counseling sessions with a psychiatrist. The medication used for all participants was initiated before the begin of the study, up-titrated, and stabilised at a final dosage for at least 2 weeks. The only medication type used was long-acting MPH formulations.

The outcomes included ADHD symptoms, impairment and quality of life, and attitudes to treatment and the quality of the therapeutic process. Many different assessment tools were used – it was not specified which outcomes were considered primary or secondary. The assessments were conducted at baseline, after treatment and at 9-month follow-up. The data were analysed using ANOVA; latent variable were extracted and composite scores from different symptom scales created and reported as outcome.

The results showed an improvement in ADHD symptoms in both groups over time

– however, no statistically significant difference between both groups was found.

The study reports its small sample sizes as one of its main limitations.

Solanto et al (2010).[122] This RCT compared a 12-month group intervention of Meta-Cognitive therapy vs a support group control. A group of 88 adults with ADHD was stratified by ADHD medication use, and then randomly allocated to the groups.

The CBT intervention used consisted of 12 weekly 2-hour sessions of Meta-Cognitive therapy in a group setting. The support therapy intervention was carried out in a similar setting (12 weekly 2-hour group sessions), and included factors of group support, therapist attention and psychoeducation, but none of the specific strategies and exercises of the Meta-cognitive therapy group.

Primary outcomes were ADHD symptoms, assessed with the AISRS (clinician-rated) and the CAARS-S inattention/memory subscale (self-rated). The assessments were conducted at baseline and a post-treatment time point.

Between-group differences were over time (pre-post) were compared, with general linear models as method of statistical analysis. The findings were a statistically significant effect of treatment vs controls (SMD=−0.56, 95% CI −1.01 to −0.12); (effect size calculated by a cochrane review[139]) in clinician-rated ADHD symptoms. No follow-up assessments were carried out.

Safren et al (2010).[123] This RCT compared a CBT intervention with an active control group of relaxation and educational support, in adults with ADHD already treated with medication. The CBT intervention consisted of 12 sessions of individual CBT. Primary outcomes were ADHD symptoms and severity of illness (both clinician-rated), and secondary outcomes were self-rated ADHD symptoms. In addition to a baseline asssessment, all outcomes were assessed at post-treatment and a 3-month and a 9-month follow-up. The results showed statistically significant effect of treatment vs control at post-treatment on ADHD symptoms (d=0.60; P=0.02) and CGI (d=0.53; P=0.03).

Vidal et al (2013).[124] This randomised controlled pilot study compared a psychoeducation group with a CBT group. Primary outcomes were ADHD symptoms (self-reported), and severity of illness (self- and clinician-rated); secondary outcomes included depression, anxiety, and QoL. The assessments were conducted at baseline and after treatment.

Results reported where statistically significant improvements in ADHD symp-

toms and depression, anxiety and QoL in both groups; no statistically significant differences between groups were found.

The small sample size (n=32 randomised) was reported as one main limitation of this study.

Philipsen et al (2015),[113] Lam (2019).[114] This large multicentre RCT used a 2x2 multifactorial design, and compared group CBT with individual clinical management (CM), as well as methylphenidate (MPH) with placebo. A 1:1:1:1 randomisation was done to four groups: CBT+Medication, CBT+Placebo, CM+Medication, CM+Placebo. The study compared CBT with CM and Methylphenidate with placebo.

The outcome assessments were conducted at five time points: at baseline, after 12 weeks of intensive treatment, during maintenance at 24 weeks, at post-treatment (at 52 weeks) and at a follow-up time point (1.5 years after post-treatment). Primary outcome was ADHD symptoms (described as observer-rated) at 12 weeks, with two comparisons being made: CBT vs CM, and MPH vs placebo. Secondary outcomes included ADHD symptoms subscales (observer-rated and PRO), ADHD-DC and CGI (described as observer-rated) and depression symptoms (self-rated). It was not specified who the observers carried out the ratings were. The description as blinded observer ratings points to clinicians, rather than observers as defined in the COA taxonomy (non-clinical observer who knows the patient).

The data were analysed using ANCOVA (adjusted for baseline measurements as covariates). The data were analysed as randomised (ITT), and missing data was replaced with multiple imputation, using LMCF (last mean carried forward). The results showed ADHD symptom reductions in all groups. The all-group baseline ADHD symptom score (CAARS) of 20.6 improved to adjusted means of 17.6 for CBT and 16.5 for CM at post-treatment. The adjusted mean of MPH was 16.2, that of placeboo 17.9. At the primary endpoint, methylphenidate was superior to placebo, but CBT was not superior to CM. No significant differences between groups were found on depression scores. The results remained stable at 1.5-year follow-up.

One explanation for why CBT may have not been more effective than CM was discussed by the authors. As CM included individual counseling, while the intervention in the CBT group was conducted in a group session, the authors hypothesised that the individual counseling may potentially be better able to respond to individual needs of participants..[113]

Table 3.6 Summary of outcomes on ADHD symptoms at end of treatment: CBT

Study	Ctrl	n	ADHD Symptoms (ClinRO)		ADHD Symptoms (PRO)	
Emilsson (2011)[116]	1	54		d 1.03, CI NR; P<0.01		
Young (2015)[117]	1	95	T IA HI	d 0.65; β −5.41 (−7.43, −3.38) d 0.56; β −3.22 (−4.6, −1.84) d 0.51; β −2.11 (−3.29, −0.93)		
Dittner (2018)[118]	1	60	T	adj ES=−1.52; AMD −10.2 (−14.25, −10.2);		
Anastopoulos (2021)[119]	1	250			T IN HI	d 0.39 (0.15, 0.65); P=0.02 d 0.50 (0.25, 0.76); P=0.001 d 0.16 (0.09, 0.41); P=0.220
Pan (2021)[120]		98	T		T IN HI	d 0.340; b 2.984 (0.074, 5.894); P=0.096 d 0.457; b 2,336 (0.645, 4.028); P=0.026 d 0.137; b 0.655 (−0.923, 2.232); P=0.498
Corbisiero (2017)[121]	2	43	T IA HI	SMD* −0.31 (−0.91, 0.29) SMD* −0.09 (0.69, 0.51) SMD* −0.41 (−1.02, 0.20)		
Solanto (2010)[122]	2	88	T IA	SMD* −0.80 (−1.24, −0.37) SMD* −0.46 (−0.88, 0.03)		
Safren (2010)[138]	2	86		SMD* −1.15 (−1.92, −0.38)		
Vidal (2013)[124]	2	32	T IA HI	SMD* 0.04 (−0.65, 0.73) SMD* 0.59 (−0.12, 1.31) SMD* 0.29 (−0.41, 0.99)		
Philipsen (2015)[113]	2	419				

Control: 1 non-active control group (waiting list, treatment as usual), 2 enhanced usual care of active control group
Abbreviations: AMD, adjusted mean difference; CI, 95% confidence interval; Ctrl, control group stringency; d, Cohen's d; ES, effect size; IA, inattention subscale; HI, hyperactivity/impulsivity subscale; NR, not reported; SMD, standardised mean difference; T, total score
* Data calculated by systematic review from Liu et al[140]

3.2.2 Mindfulness-based interventions

Gu et al (2018).[125] This RCT compared a 6-week individual MBCT intervention with a wait list control group. It was not reported if the primary outcomes were prespecified – outcomes were only labelled as primary in the results table of the study report. Those primary outcomes were ADHD symptoms (PRO), anxiety and depression (both PRO), and academic scores. Secondary outcomes were mindfulness (PRO) and attentional networks, which includes a executive function component (PerfO). All outcome assessments were conducted at pre-treatment, post-treatment, and at 3-month follow up. It was not precspecified which or if certain time points were considered to be primary.

The data were analysed with repeated-measures ANOVA.

The results reported were statistically significant reductions in ADHD symptoms, depression symptoms and anxiety, increases in mindfulness and better results in the EF test in the MBCT group compared to the wait list group. The effect size reported for between-group differences in ADHD symptoms (CAARS total score) after treatment was d=1.26 (confidence interval not reported; P<0.01), favouring MBCT.

Table 3.7 Details on included studies on mindfulness-based interventions

Study	Intervention	Control group	AT (Primary OC)	AT (Secondary OC)	Assessments
Gu (2018)[125]	6 individual sessions, 1/week, daily self-practice	WL	CAARS-S Inatt. (PRO), BAI (PRO), BDI-2 (PRO), GPA	MAAS (PRO), ANT (PerfO)	pre, post, 3m
Hepark (2019)[126]	12 sessions, 1/week + 1 guided silent practice session; daily self-practice	WL	CAARS-INV:SV (ClinRO)	CAARS-S:SV (PRO), BRIEF-A (PRO), OQ (3 subscales), KIMS (PRO), BDI-II (PRO), STAI (PRO)	pre, post
Janssen (2019)[127]	8 sessions of 2.5h, 1/week, 1 silent day (6h), daily self-practice (appr. 30min/day with guided exercise); groups of about 9 individuals/group	TAU only	CAARS-INV:SV (ClinRO)	CAARS-S:SV (PRO), BRIEF-A (PRO), FFMQ-SF (PRO), SCS-SF (PRO), MHC-SF (PRO), OQ (PRO)	pre, post, 3m, 6m
Schoenberg (2013)[128]	12 weekly group sessions for 3h; daily self-practice	WL	NPT + EEG, CAARS		pre, post
Bach-mann(2018)[129]	8 weekly group sessions for 2,5h; daily self-practise	psychoeducation group	NPT + EEG, CAARS (SR + OR), one-back letter task + fMRI		pre, post
Hoxhaj (2018)[129]	8 weekly group sessions for 2,5h; daily self-practise	psychoeducation group	CAARS (OR), inat-tention/memory subscale	Other CAARS subscales (OR and S), BSI, BDI-II, SF-36, FFMQ	pre, post, 6m

AT (Primary/Secondary OC): assessment tools used for primary/secondary outcome; Assessments: time points of assessments
Abbreviations: AAQoL, Adult Attention-Deficit/Hyperactivity Disorder Quality-of-Life Scale; ADHD-DC, ADHD Diagnostic Checklist; ADHD-RS, ADHD Rating Scale; ADHD-SR, ADHD Self-Rating Behavior Questionnaire; AISRS, Adult ADHD Investigator Symptom Rating Scale; BADDS, Brown ADD Scales; BDI, Beck Depression Inventory; BRIEF-A, Behaviour Rating Inventory of Executive Function - Adult Version; CAARS, Conner‘s Adult ADHD Rating Scales; CGI, Clinical Global Impression Scale; ClinRO, clinician-rated outcome; HAM-A, Hamilton Anxiety Rating Scale; MED, medication; OTMOPS, On Time Management Organization and Planning Scale; ObsRO, observer-rated outcome; PRO, patient-rated outcome; QLESQ, Quality of Life Enjoyment and Satisfaction Questionnaire; RSEI, Rosenberg Self-Esteem Inventory; RSES, Rosenberg Self-Esteem Scale; SCM, standard clinical management; SDS, Self-Rating Depression Scale; STAI, State-Trait Anxiety Inventory; TAU, treatment-as-usual; WRAADDS, Wender-Reimherr Adult Attention Deficit Disorder Rating Scale.

No statistically significant difference in academic performance was found between groups. Only self-report scales were used for outcome assessments.

The number randomized was reported as n=54 in the abstract - however, in the flow diagram of the study, the number randomised is reported to be n=56, with 54 being the number analysed (excluding two participants who dropped out due to scheduling conflicts).

Hepark et al (2019).[126] In this RCT, a MBCT group was compared to a waiting list control. The main outcome was between-group difference in ADHD symptoms (ClinRO). Three comparisons were reported for the main outcome (2 CAARS-subscales, and a total score). It was not prespecified if any of those scores was considered the primary result. Secondary outcomes were ADHD symptoms, executive functioning, anxiety, depression, mindfulness and patient functioning (all self-rated). The assessments were conducted at baseline and post-treatment. No follow-up outcomes were measured. The data were analysed using ANCOVA, adjusting for baseline symptoms as

covariate.

MBCT achieved greater reductions in the main outcome of clinician-rated ADHD symptoms compared to the wait list control group (CAARS Total score; d=0.78, P<0.01). Also, the differences between the groups favoured MBCT in self-rated ADHD symptoms (d=0.67; P<0.01), executive functioning (d=0.93; P<0.01), and mindfulness skills (d=0.86; P<0.05). The effect sizes reported are large. No significant between-group differences were found in depression (PRO), anxiety (PRO), and functional outcomes (PRO). The results were reported based on a per-protocol analysis. An ITT analysis with imputation of missing data (using LOCF) was done in addition, but reported in a less detailled manner.

Janssen et al (2019).[127] This RCT compared a MBCT+TAU group with a TAU control. Primary outcome was between-group changes in clinician-rated ADHD symptom from pre to post-treatment. Secondary outcomes were ADHD symptoms, executive functioning, mindfulness, self-compassion, positive mental health and general functioning (all self-reported).

Outcome assessments were conducted at pre-treatment, post-treatment, 3-month and 6-month follow-up. The data were analysed using ANCOVA, adjusting for baseline measurements. Missing data was handled using multiple imputation with the Last Observation Carried Forward (LOCF) method.

At post-treatment, the MBCT group showed a greater reduction in clinician-rated ADHD symptoms than the TAU group, with a medium effect size (d=0.41; P=0.004). In self-rated ADHD symptoms, the MBCT group also improved more than the TAU group (d=0.37; P=0.009).

Other outcomes like mindfulness skills, self-compassion and positive mental health also improved from pre- to post-treatment, with between-group differences favoring MBCT (effect sizes between 0.32 to 0.42). The treatment effects remained stable at follow-up. No statistically significant difference between groups was found on executive functioning at post-treatment.

Schoenberg et al (2013).[128] This RCT compared a 12-week MBCT group intervention to a wait list control. The intervention included 12 weekly 3 hour group sessions and daily mindfulness self-practise (30–45 minutes). There were two types of outcomes investigated: EEG + neuropsychological tests (main outcome), and clinical outcome assessments. The EEG + NPT outcomes were to measure subsets of EF were done via EEG measurements while performing a visual continuous performance task (CPT-X) (PerfO). Clinical outcomes assessed were ADHD symptoms, mindfulness, social

functioning and psychological distress (all self-rated). Outcome assessments were conducted at baseline and post-tretment.

The data were analysed using repeated-measures ANCOVA. No specific method of handling missing data, like ITT analysis, or multiple imputation was reported. Therefore it is not clear if the study used a per-protocol analysis. The paper also states in its results section that, "Due to the various findings analysed vs reporting length constraints, non-significant results are not explicitly reported in the following sections."[128]

The EEG measures showed an association of increased Pe and NoGo-P3 amplitudes in the MBCT group, which was interpreted as improved error awareness and inhibitory control.

Statistically significant changes for ADHD symptoms, measures of the outcome questionaire (OQ-45), and mindfulness skills were found in the pre-post comparison of the MBCT group, while no significant pre-post changes were found in the wait list group. No effect sizes or confidence intervals were reported on clinical outcomes.

Regarding the clinical outcomes, the trial found that specifically in the MBCT group, increased Pe amplitudes were correlated with a decrease in hyperactivity/impulsivity symptoms, and increased P3-amplitudes were correlated with decreased inattention symptoms.

Bachmann (2018).[129] This RCT compared a 8-week MBCT group intervention with a psychoeducation group intervention of similar duration and intensity. The main outcomes were executive functioning (using an n-back task investigating working memory, performed during an fMRI scan) and ADHD symptoms (ObsRO and PRO) after treatment. Time points of assessments were at baseline and post-treatment.

No significant difference between the intervention groups was found for any outcome at the main endpoint. Both groups showed a significant decrease in ADHD symptoms and an improvement in task performance at post-treatment. No follow-up assessments were conducted in this study.

Hoxhaj (2018).[130] This RCT compared a 8-week Mindfulness training program to a psychoeducation intervention of the same duration. Included were unmedicated adults with ADHD. The mindfulness intervention consisted of eight weekly 2.5-hour sessions, and mindfulness meditation and exercises as daily homework. Assessments were conducted at baseline, post-treatment, and a 6-month follow-up. The primary outcome was change in ADHD symptoms (inattention/memory-subscale) (ClinRO)

from pre- to post-treatment. Secondary outcomes were ADHD symptoms subscales and self-ratings, depression, QoL and Mindfulness. It is not stated if the primary outcome is between-group differences of treatment effects, or pre-post differences. Both of those differences are reported. The data were analysed using repeated measures ANOVA. Effect sizes were reported as partial η^2. The authors state that "Effect sizes less than 0.06 are considered small, values between 0.06 and 0.14 are medium, and values greater than 0.14 large."[130]

The results showed ADHD symptom improvements in both groups from pre to post (partial η^2=0.18; P<0.001). The results persisted at the 6-month follow-up. However, no statistically significant difference between mindfulness and psychoeducation groups were found. Regarding the secondary outcomes, there were improvements in depression, QoL and global distress from pre to post-treatment. Again, no statistically significant differences between the groups were found.

Table 3.8 Summary of outcomes on ADHD symptoms at end of treatment: MBIs

Study	Ctrl	n	ADHD Symptoms (ClinRO)	ADHD Symptoms (PRO)
Gu (2018)[125]	1	54		SMD –1.35 (–1.95, –0.75)
Hepark (2019)[126]	1	103	SMD –0.92 (–1.38, –0.47)	SMD –0.82 (–1.27, –0.37)
Janssen (2019)[127]	1	120	SMD –0.44 (–0.82, –0.05)	SMD –0.28 (–0.66, 0.10)
Schoenberg (2013)[128]	1	50*		SMD –1.22 (–1.87, –0.57)
Bachmann(2018)[129]	2	74	SMD 0.09 (–0.53, 0.71)	SMD 0.53 (–0.10, 1.16)
Hoxhaj (2018)[129]	2	81	SMD 0.01 (–0.45; 0.47)	SMD –0.02 (–0.47, 0.44)

*Source:*All SMD and Confidence intervals calculated by systematic review from Scholz et al[140]
Control: 1 non-active control group (waiting list, treatment as usual), 2 enhanced usual care or active control group
Abbreviations: CI, 95% confidence interval; Ctrl, control group stringency; IA, inattention subscale; HI, hyperactivity/impulsivity subscale; SMD, standardised mean difference; T, total score

3.2.3 Physical activity and exercise

Mehren et al (2019),[112] Mehren et al (2019).[111] These are two intervention studies with a very similar study design, conducted in the context of a larger research project. It is not explicitly stated how much the samples of participants of both reports overlap. Because of very similar participant demographics and recruitment reported, as well as the identical experimental sessions, it is assumed that the samples investigated were mostly identical. These two papers are therefore treated as a single study in this review.

The study compares an exercise intervention (30 minutes of stationary cycling) vs a control condition (watching a movie). Two groups were included: a group of adults with ADHD and a group of matched healthy controls. Each participant participated in three sessions, separated by at least two days. The first (pre-experimental) session included a maximal exercise test and a practise session of the experimental task

Table 3.9 Details on included studies on physical activity and exercise

Study	Intervention	Control group(s)	AT (Primary OC)	AT (Secondary OC)	Assessments
Mehren* (2019)[111,112]	Acute exercise	Control condition (MASC-Mck)	Flanker task (PerfO), Go/No-go task (PerfO) + fMRI (biomarker)		
Fritz and O'Connor (2021)[131]	6 week Yoga intervention, 2 sessions/week	Wait list	Flanker task (cog. Control): PerfO, DCCS (cog. Flexibility), LSWMT (working memory)		Pre, 3w, post
Kouhbanani (2023)[132]	24 week Pilates invervention, 3x/week for 45 min	TAU (continuation of pre-existing treatment)	WCST (attention switching), CPT (sustained attention): PerfO		Pre, post, 3m, 6m
Svedell (2025)[133]	12 week moderate-intensity mixed exercise; at least 2 weekly 50min sessions	TAU	ASRS (PRO)	CGI-S (ClinRO), CGI-I (PRO), many others	Pre, post
Dinu †(2023)[134]	10 min aerobic exercise (group 1); vs 10 min yoga (group 2)	Acute exercise (10 min, Yoga)	Test of Variables of Attention task, Delay Discounting Task, and Iowa Gambling Task to measure attention and impulsivity.		Pre, post
Mayer †(2024)[135]	Aerobic and muscle-strengthening activities 3 days/ week)	BLT; TAU	IDS-C30	IDS (other time points), BDI, ADHS-RS	Screening, pre, mid, post, 12-14w
Berger †(2014)[136]	No intervention	-	WURS-k (PRO), ADHD-SR (PRO), EDS-21		
Koch †(2012)[137]	No intervention	-	Accelerometer data (biomarker), e-diary ratings of positive/negative affect (PRO)		

*two separate study reports, summarised as one study
†broader inclusion criteria, included as additional evidence
Med (%): I/C; per cent of participants on ADHD medication in intervention group/control group
Abbreviations: ADHD-RS, ADHD Rating Scale; ADHD-SR, ADHD Self-Rating Behavior Questionnaire; AISRS, Adult ADHD Investigator Symptom Rating Scale; ASRS, Adult ADHD Self Report Scale; BDI, Beck Depression Inventory; BLT, Bright light therapy; CGI, Clinical Global Impression scale; CPT, Continuous Performance Task; DCCS, Dimensional Change Card Sort test; IDS, Inventory of Depressive Symptomatology; LSWMT, List Sorting Working Memory test; TAU, treatment-as-usual; WCST, Wisconsin Card Sorting Test; WURS-k, Wender-Utah-Rating-Scale-Kurzform

inside the fMRI scanner. One of two experimental sessions included the exercise intervention and the other the control condition, with each participant completing both conditions.

The outcomes investigated in both papers differed. In the first paper, published in Nature Scientific reports,[111] the assessment was a Go/No-go task (PerfO) during a fMRI scan, performed after the exercise or control condition.

The outcomes of the second paper, published in frontiers in Psychiatry,[112] were a flanker task (PerfO), performed before at the beginning of the experimental session inside of a fMRI scanner. This was followd by the exercise or control condition. After that, the flanker test and fMRI scan was repeated, and the Go/No-task, reported in the other paper, was performed.[112]

The primary outcome that was intended to be investigated by the Go/No-go task tests was response inhibition.

No effects of exercise on performance in the Go/No-Go task was found for either group. The flanker task was chosen to measure interference control (which is considered to be a component of the executive function category inhibition). The results of the flanker task showed significantly improved reaction times after exercise in the ADHD group, but not in healthy controls.

Fritz and O'Connor et al (2022).[131] This pilot RCT included 32 adult women screening positive for adult ADHD. They were randomised to a 6 week yoga group and a wait list control group. Regular use of medication (with the exception of birth control) was an exclusion criterion.

The outcome investigated where the three main executive functions (inhibitory control, measured using the Flanker Inhibitory Control and Attention Test, cognitive flexibility, measured using the Dimensional Change Card Sort Test, and working memory, measured using the List Sorting Working Memory Test).

The assessments were conducted at three time points: baseline, after three weeks and at post-treatment. Multilevel models were used to analyse the data, and investigate group x time interactions.

No significant group-by-time interactions were found for any of these variables in either group. A high dropout rate of 31% was reported for the yoga group. A major limitation reported by this study was its small sample size, also the female-only sample and the missing ADHD diagnosis of participants.

Kouhbanani et al (2023).[132] This RCT compared a 24-week Pilates training group with a TAU control group. The outcomes assessments used were the Wisconsin Card Sorting Test (PerfO) to test attention switching, and a Continuous Performance Task (PerfO) to test sustained attention. The assessments were conducted at pre-treatment, post-treatment and 6-month follow-up time points. The time point of primary interest was not specified. The data were analysed using multivariate ANCOVA, with age as covariate. Of the n=60 randomised, 52 participants were included in the analysis. No strategy for handling missing data (eg imputation) was described, therefore a per-protocol analysis seems likely.

Multiple hypotheses tested were reported, but no correction for multiple comparisons was discussed.

The results found were improvements in sustained attention (in CPT) at post-

treatment in the pilates vs the control group. The improvements were maintained at 6-month follow-up. Also, attention switching improved at post-treatment in the pilates vs the control group.

Svedell et al (2025).[133] This RCT compared a 12-week mixed-exercise intervention group with TAU. A subset (n=12) of the exercise group was additionally offered a cognitive skills training. The primary outcomes specified in the study protocol were ADHD symptoms (PRO), as well as severity of illness (ClinRO and PRO). However, the final study only reported ADHD symptoms (PRO) as the primary outcome and severity of illness (ClinRO and PRO) as secondary outcomes. Many different secondary outcomes were assessed. No main time point for the primary outcome was prespecified.

The results showed a significant improvement in self-rated ADHD symptoms at 12 weeks (post-treatment) in the intervention vs the TAU group, with a large effect size (d=0.93, 95% CI: -1.65 to -0.21).

The treatment protocol was published and referenced in the report.[141] There were several deviations from the published treatment protocol. Instead of the originally planned n of 120, the sample size of the final study was 63. In the study protocol, a 3-arm study design was prespecified (exercise vs exercise + cognitive skills training vs TAU), which was changed to a 2-arm design in the final study (exercise vs TAU). Cognitive skills training was offered to a subset of participants in the final study. However, all participants were considered to be part of the main intervention group. This was acknowledged as a limitation in the discussion: ”A further limitation of the study is that some participants received cognitive skills training in addition to the exercise intervention. Subgroup analyses was originally intended but, in the end, not feasible due to the small sample size. The cognitive skills training introduces a confounding factor, as it may have contributed to changes in the outcome measures that could not be isolated in the results.”[141] While limitations were discussed in detail, the points of deviation from the study protocol were not listed explicitly in the final study report.[133]

Dinu et al (2023).[134] In this RCT, two conditions of acute exercise were compared: 10 minutes of aerobic exercise (cycling) vs 10 minutes of mind-body exercise (yoga). Two groups were investigated: a group of 82 adults with ADHD, and one of 77 healthy controls. Included in the ADHD group were participants who self-reported having received a diagnosis from a clinician – this was not confirmed by the investigators. Participants of both ADHD- and non-ADHD groups were randomised to one of two interventions: 10 minutes of Hatha yoga or 10 minutes of cycling.

Assessments were carried out before and after the intervention. Three different neuropsychological tests (PerfO) were used for the assessments: the Test of Variables of Attention task (TOVA), the Delay Discounting Task, and the Iowa Gambling Task. These were intended to measure attention and impulsivity.

The results showed improved temporal impulsivity after exercise, with cycling having an effect in both groups, while the improvements of the yoga intervention were only significant in the ADHD group. Other outcomes (attention, cognitive and motor impulsivity) were not improved after exercise in the ADHD group; attention was found to be reduced post-exercise in the control group.

Mayer et al (2024).[135] This multicentre three-armed RCT compared three groups: a bright-light therapy (BLT) group, a physical exercise intervention (EI) group, and a TAU group. The study included individuals aged between 14 and 45 years with a diagnosis of ADHD. The 10-week interventions were carried out in a naturalistic setting; a mobile health system was used. It included a wrist-worn sensor to record physical activity and light exposure, and a smartphone app to deliver BLT and EI. The participants were assessed at screening (T1), before start of treatment (T2), mid-treatment (T3), post-treatment (T4), and at follow-up (T5, 12–14 weeks after T4).

The primary efficacy outcome was change in depression symptoms from pre to post-treatment. Multiple secondary efficacy outcomes were assessed, including changes in ADHD symptoms. Both the primary and secondary outcomes, including the exact time points of interest, were prespecified. Also, feasibility endpoints were prespecified.

The results showed small changes in depression symptoms from pre to post-treatment for all three groups, with no significant between-group differences detected.

The intervention adherence (defined as at least 80% completed sessions) was very low both for BLT (22%) and EI (7%).

Berger et al (2014).[136] In this observational study, a survey of a large sample (n=1615) representative of the German population was conducted. The goal was to investigate a possible association between excessive exercising and ADHD symptoms. The assessments conducted were self-report screenings of adult ADHD symptoms, (retrospectively rated) childhood ADHD symptoms, excessive exercising, eating behaviour, as well as of symptoms of depression and anxiety.

The findings reported included a 9% point prevalence of excessive exercising

in individuals with childhood-only ADHD. In comparison, the number was 2.7% in individuals without self-reported ADHD symptoms, and 4% in individuals with adult ADHD symptoms (4%) only.

The authors drew the conclusion that this association could possibly be explained by individuals with childhood-only ADHD successfully self-medicating their ADHD symptoms with high amounts of exercise. This would then lead to them no longer exhibiting self-reported ADHD symptoms.

Koch et al (2022).[137] This observational study investigated the possible association between mood and physical activity using wearables (with accelerometers) and e-diaries. Three groups of adults were compared: one with predominantly inattentive ADHD, one with ADHD with a combined presentation, and a control group of individuals without ADHD. The data collected to assess the outcome of the study was comprised of accelerometer data, measured 24 hours per day, and 12 random e-diary prompts per day, which participants received on their smartphones. These prompts assessed positive (six items) and negative affect (seven items) with ratings on a seven-point Likert scale. The data were processed using multi-level analysis in order to investigate within-subject effects of physical activity on positive and negative affect. The results indicated a positive association between physical activity and positive affect in all groups (cross-level interaction: ($F(2, 135.072)=5.733$; $P=0.004$)). The strongest association was found for the group individuals with a combined presentation, manifested as the steepest slope of all groups ($slope\_(inattentive)=0.005$, $P<0.001$; $slope\_(combined)=0.009$, $P<0.001$; $slope\_(controls)=0.004$, $P=0.008$.)[137] A statistically significant association between a decrease in negative affect and physical activity was only found in the group with a combined presentation of ADHD.

Chapter 4

Discussion

4.1 Synthesis and discussion of results

In addition to the synthesis of results of this literature review, conclusions of systematic reviews which investigated similar questions are summarised.

4.1.1 Evidence on CBT

Ten RCTs on CBT were included: five with preexisting treatment/WL controls and five with enhanced usual care or active controls.

Of the five RCTs with preexisting treatment or wait list control groups, three reported results favouring CBT compared to the control group at , with mostly medium effect sizes, and confidence intervals not including zero. One study reported a large effect size, but no confidence interval, while the fifth reported effects favouring CBT, but the confidence interval on one subscale included 0, indicating high uncertainty. Of the five studies with more stringent control groups, two found CBT to be superior to the alternative therapy (Solanto et al, with a support group as control; and Safren et al, with relaxation and educational support as control intervention). The other three studies found no significant difference to the control (with 95% CI of effect measures often including zero). The studies by Corbisiero et al (n=43) and Vidal et al (n=32) were especially limited by their small sample sizes.

Evidence from existing systematic reviews

The systematic review and network meta-analysis of Matsumoto et al (2024) investigated the efficacy of CBT for adults with ADHD at the level of individual therapeutic components, and at the level of the treatment (combination of components).[100] It

included 43 RCTs with a total of 3817 participants. The primary outcome investigated was treatment response on ADHD core symptoms. It was defined as a binary variable to indicate a clinically meaningful change, calculated using the Jacobson and Truax reliable change index – data used were from baseline and the assessment time point closest to 6 months after the intervention.

The results reported were superior response rates compared to placebo for Third-wave therapies (OR=4.80, 95% CI 2.50 to 9.19), behaviour therapy (OR=3.50, 95% CI 1.70 to 7.30), and CBT (OR=3.10, 95% CI 1.70 to 5.70). The results of the component-level analysis found that of the nine components (listed in Table 1.3), organisational strategies (incremental OR=2.03, 95% CI 1.27 to 3.24) and third-wave components (incremental OR=1.95, 95% CI 1.30 to 2.93) were associated with an increase in treatment response. Another finding was that problem-solving techniques showed an association with reduced inattention symptoms (incremental SMD=0.42, 95% CI 0.01 to 0.83).[100]

A large systematic review and component network meta-analysis by Ostinelli et al (2025) investigated a large number of RCTs on pharmacological and non-pharmacological interventions for adults with ADHD.[79] The main outcomes were efficacy (defined as change in ADHD core symptoms at the time point closest to 12 weeks, both on self-rated and clinician-rated scales) and acceptability (defined as all-cause discontinuation of treatment). Regarding the primary efficacy outcome, CBT was found to be more effective than placebo on clinician-rated scales (SMD=0.78, 95% CI 0.26 to 1.26), but not on self-rated scales (SMD=−0.55, 95% CI −1.24 to 0.14). On the timepoint closest to 52 weeks, the results were no evidence for a difference in efficacy on clinician-rated scales (based on two studies), but CBT was more efficacious than placebo on self-rated scales (based on five studies).

4.1.2 Evidence on mindfulness-based interventions

Six RCTs on mindfulness-based interventions were included: four with existing treatment/WL controls and two with active controls.

Of four studies with existing treatment/wait list controls, three found large effect sizes on ADHD symptoms compared to control (one one clinician-rated, three on self-rated scales), with the confidence intervals not including zero. The fourth study (Jansen et al)[127] found less clear effects, with the results favouring MBCT, but the CI including zero on clinician-rated outcomes. Of those, three studies reported medium-to large effect sizes for ADHD symptom improvements compared to the control group, while one didn't report effect sizes. The two RCTs which used an active control (psychoeducation group intervention) both found no statistically significant

between-group differences in outcomes (ADHD symptoms, and performance on the n-back task), while the outcomes improved for all groups over time.

The results on secondary outcomes were mixed across studies.

4.1.3 Evidence on exercise

The studies included on exercise and physical activity were very heterogeneous. A total of eight studies were included in the review. The study designs included two observational studies, five RCTs, and one experimental study of a different design.

The two included observational studies found associations that could be interpreted as supporting the hypothesis that physical activity is helpful for ADHD.

Of the six experimental studies, four were RCTs on chronic exercise, and two were studies (one RCT and one with a different design) on acute exercise.

The four RCTs on chronic exercise produced mixed results. One of them, conducted in a naturalistic setting, showed no efficacy for the primary outcome of depression symptoms, while being limited by extremely low adherence rates.

A second one – a small pilot RCT – found no significant between-group differences for the main outcome of performance in neuropsychological tests measuring executive functioning. A third RCT found improvements in the main outcome of performance in neuropsychological tests. A fourth RCT, which examined clinical outcomes, found larger improvements in ADHD symptoms after treatment compared to the control group. This was the only study for which ADHD symptoms were the primary outcome. While being limited by the confounding factor of a subgroup of the exercise group receiving an additional intervention, it found a large effect size for improvements in ADHD symptoms for the exercise group compared to the control group.

Two studies on acute exercise were included, which both examined effects on executive functions, and reported mixed results.

4.1.4 Conclusion

In conclusion, the strongest evidence for efficacy on the outcome of ADHD core symptoms was found for CBT and MBIs.

Both for CBT and MBIs, a strong association between choice of control group and treatment effects was found. Studies with wait list or existing treatment control conditions mostly found effects favouring CBT or the MBI (4 of 5 studies on CBT,

with one reporting mixed results; four out of four studies on MBIs). Studies that used more stringent controls (enhanced usual care or an active control group) found statistically significant between-group differences less often (only two of five studies on CBT, and none of two studies on MBIs).

However, drawing strong conclusions based on the available evidence is currently difficult due to several limitations of both the included studies and this review. These limitations are discussed in the following section.

4.2 Limitations of the evidence included in the review

There are several important limitations that complicate the interpretation of the available data. These are now discussed in more detail below.

4.2.1 Methodological challenges in researching behavioural interventions

There are several fundamental methodological and practical challenges in researching behavioural interventions. These also became evident in the included studies. In principle, behavioural intervention studies face additional challenges in their design and implementation when compared to pharmacological placebo studies, as there are additional confounding factors and methodological issues.[142]

A fundamental limitation in behavioural intervention studies is that it is very often not possible to blind participants to their group assignment.[142] Therefore, only single-blind designs are possible. This potentially increases the risk of bias of the study when compared to double-blind designs. Because of this limitation, behavioural studies are often downgraded in the ratings of quality of their evidence, for example in systematic reviews and meta-analyses.

As participants know to which group they have been assigned to, there is greater potential for positive expectancy (placebo) and negative expectancy effects (eg disappointment at being assigned to the control group).

This can have various consequences, leading to less valid results. For example, it has been shown that in exercise intervention studies, participants randomised to the control group tend to become more physically active.[143] As one of many hypothesised reasons, this could be explained by the disappointment of having been assigned to the control group. This could lead to the decision to become more physically active anyway, even if that behaviour does not correspond to the objectives of the study.

A high degree of heterogeneity was found among the studies assessed in this review. Major differences were found in study designs, for example with regard to inclusion and exclusion criteria, the type and length of intervention, the type of control group, the setting, the definition of the outcomes, and the length of follow-up. Another obstacle to comparability was the very large number of different assessment instruments used. Additionally, many of the questionnaires and diagnostic interviews are not freely and publicly accessible. Consequently, the comparability of the studies was drastically reduced.

Ideally, to meet high standards for quality of evidence, studies based on the same study protocol should be replicated by independent teams of researchers. However, this has yet not been achieved with regard to the studies that were included or considered for inclusion.

While no systematic analysis of statistical methods was carried out, some methodological limitations still became apparent during the review process. For instance, imprecise reporting was evident on multiple occasions, for example as when the number of participants randomised and analysed was mixed up. Another issue encountered was the reporting of an intention-to-treat analysis without imputation of missing data. In multiple cases, the primary and secondary outcomes were not precisely defined, and often the primary time point of interest was not specified. These are two occasions which increase the number of hypotheses tested, which increase the chance of finding a treatment effect where none exists (false positives; type I error). It is recommended that this multiple comparisons problem is transparently reported or that statistical corrections are carried out.

Another limitation was that follow-up was often brief or non-existent. Also, many of the studies had small sample sizes, and therefore lacked the statistical power to reliably detect effects.

Another limitation was the high dropout rates in some studies. In addition, the handling of missing data was not ideal in all studies. Some studies performed a per-protocol analysis, only including complete datasets. This is generally not recommended, as it can break randomisation, and increase the risk of bias.

There were also substantial differences in how missing data were handled in studies that reported performing an intention-to-treat analysis. Multiple imputation of missing data was used by some studies. Some studies used the LOCF (last observation carried forward) method for this imputation, which is often considered suboptimal.

The number of studies found on physical exercise interventions was very small.

In particular, few studies on chronic exercise were found.

It is not clearly established how well a change in certain measured outcomes, such as the neuropsychological tests assessing executive functioning, translates to a meaningful change in a person's daily life.

4.3 Limitations of the review process

This review was limited by several factors. Firstly, it is not a systematic review, which would analyse and document the available evidence much more rigorously, and follow guidelines like the Cochrane Handbook for the Systematic Review of Interventions or the PRISMA guidelines in full.

For example, the search process was not carried out in a structured manner; tere was no precise documentation of search terms or dates of searches. Two different inclusion criteria were defined for different types of interventions, which reduces the comparability of the included studies. Also, the time interval of the publication date of the included studies was extended (from 15 to 16 years, starting from 2010) after the review process had started. This was done to include an RCT on exercise interventions published in 2025.

No systematic assessment of risk of bias of the included studies was carried out. For this purpose, methods such as the Cochrane RoB 2 (risk of bias) tool have been developed, and are commonly used in systematic reviews. For example, in the RoB 2 tool, five different domains of bias are rated for each study, eg the risk of bias due to missing outcome data, or the risk of bias in selection of reported results.[106] Another limitation is that no systematic critical assessment of the statistical methods and reasoning of the included studies has been carried out. The statistical analysis methods chosen can present a major way of how study results can be influenced in a biased way. For example, there has been widespread discussion if there is a disproportionate number of false positive studies published. The phenomenon of p-hacking has been shown to be common.[144]

A further limitation is personal bias, such as the biased opinion that exercise and physical activity could be helpful for ADHD.

4.4 Efficacy of exercise interventions for other conditions

To provide additional context and to strengthen the argument for further research, this section gives on overview on the evidence on exercise for other psychiatric conditions. Evidence has been mounting to support the efficacy of physical exercise for improving symptoms and other outcomes in multiple psychiatric disorders.

A meta-review by Ashdown-Franks et al[105] examined 16 meta-analyses of exercise interventions for different mental disorders. It found evidence that exercise reduces depression in children, adults and older adults. It also found that exercise is effective in reducing symptoms of anxiety, as well as an adjunctive treatment for reducing positive and negative symptoms in schizophrenia. A global increase in cognition was found for children with ADHD and individuals with schizophrenia.

An umbrella review by Solmi et al[145] investigated exercise interventions as a transdiagnostic treatment for mental disorders, using empirical recommendations on reporting transdiagnostic research (TRANSD, by Fusar-Poli et al). It included 99 RCTs with more than 5,600 participants. It found moderate/vigorous aerobic exercise to be an effective transdiagnostic intervention to reduce primary symptoms in 11 disorders (including recurrent depressive disorder, panic disorder, generalised anxiety disorder, schizophrenia, ADHD, and PTSD) and to improve cognition in schizophrenia and ADHD. The effect size for symptom reduction was moderate (SMD=−0.67, 95% CI −0.84 to −0.50), the effect size for improvements in cognition was large (SMD=0.92, 95% CI 0.52 to 1.33).

4.4.1 Exercise and depression

A meta-analysis of prospective cohort studies by Schuch et al[146] investigated the relationship between physical activity (PA) and the incidence of depression. 49 studies comprising more than 260,000 participants were analysed. The data showed that compared to individuals with low levels of PA, those with high levels of PA had a reduced odds of developing depression (adjusted odds ratio=0.83, 95% CI 0.79 to 0.88; I2=0.00).

The causal relationship of physical activity and mental disorders was tested in a Mendelian randomisation study by Iob et al[147] – it found that the accelerometer-based average physical activity was associated with reduced risk for depression (b=−0.043, 95% CI −0.071 to −0.016; effect size (OR)=0.957)

A large systematic review and meta-analysis with meta-regression by Heissel

et al[96] examined the efficacy of exercise interventions on symptoms of depression compared with non-active control groups. Forty-one intervention studies, with more than 2000 participants were included – a moderate to large effect of exercise on depression symptoms was shown (SMD=−0.946, 95% CI −1.18 to −0.71). These effects remained when the analysis was limited to studies with low risk of bias.

A Cochrane Review (updated in 2026) investigated exercise as a treatment for depression, and provided a meta-analytic synthesis of results.[148] The results showed that exercise may be effective in reducing depression symptoms; also, no difference in efficacy was found between exercise and psychological therapy interventions, as well as to pharmacological treatments.

57 RCTs comparing exercise with either no treatment or control conditions were analysed in this review. The results favoured exercise for the outcome of depression symptoms at the end of treatment, with a pooled SMD of −0.67 (95% CI −0.82 to −0.52). The review also included ten RCTs which compared of exercise with psychological therapy interventions. Little to no difference between the groups (SMD=0.03, 95% CI −0.16 to 0.23) on the outcomes of depressive symptoms after treatment was found. A similar result was reported for studies comparing exercise with pharmacological treatments (based on five included RCTs), with a SMD of −0.11 (95% CI −0.33 to 0.10) for exercise.[148]

The growing body of evidence supporting its efficacy has resulted in the recommendation of exercise and physical activity as an adjunctive treatment for depression. This includes recommendations on physical activity by the WHO[98] and the NICE guidelines on depression (2022).[97]

4.4.2 Exercise in children and adolescents with ADHD

Dastamooz et al[149] conducted an umbrella review examining the effects of physical exercise interventions on ADHD symptoms, other mental health outcomes, and cognitive function in children and adolescents with ADHD. Ten meta-analyses and 12 additional individual studies were included. The review found evidence for the efficacy of exercise, with large-to-moderate effect sizes. The domains for which the effects were found included improving inattention (Hedges'g (G)=0.92, 95% CI 0.44 to 1.39), inhibitory control (G=0.82, 95% CI 0.52 to 1.13), and cognitive flexibility (G=0.52, 95% CI 0.32 to 0.72).

4.5 Implications for research and practice

Overall, the best evidence was found for CBT and MBIs – however there are still uncertainties that remain regarding the evidence. While many studies indicate clear a clinical benefit of CBT and MBIs, some reviews also highlight inconsistent results (for example the comprehensive meta-analysis of Ostinelli et al.[79]). More research is needed to shed light on the causes of these discrepancies, and to more clearly establish which components of CBT and MBIs are of greatest benefit for treating adult ADHD.

The drawing of strong conclusions regarding the efficacy of exercise interventions for adults with ADHD was limited by the high heterogeneity and the low number of available studies. While there some promising results, the evidence allows no definitive conclusion. A recommendation for exercise for adults with ADHD may still be possible based on many anecdotal reports in the literature on ADHD, the strong evidence for general broad health benefits, and the large evidence base on its efficacy for other psychiatric conditions. Regarding research, there is an urgent need for adequately powered, rigorous RCTs on physical exercise interventions.

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Appendix

Translation and language-editing tools (DeepL Translate and DeepL Write; DeepL SE) and ChatGPT (OpenAI) were used to assist with correction of spelling and grammar, and to provide rephrasing suggestions to improve clarity. All linguistic changes were selected and implemented manually on a case-by-case basis.