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NON-PHARMACOLOGICAL INTERVENTIONS FOR ADULT ADHD: SYSTEMATIC REVIEW

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JB, DH, RG, VP, LS, SL and DR contributed to the conception and design of this project, to interpretation and comments on revised drafts of this article and final approval of this article; LS, SL and VN-S conducted the literature searches and data extraction; AM and VN-S contributed to the analysis and interpretation of the results, the writing of the first draft and subsequent drafts of this article and final approval of this article.

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ABSTRACT

Background: Attention-deficit/hyperactivity disorder (ADHD) is a common developmental disorder, often persisting into adulthood. Whilst medication is first-line treatment for ADHD, there is a need for evidence-based non-pharmacological treatment options for adults with ADHD who are either still experiencing significant symptoms or for those who have made the informed choice not to start medication. Methods: We systematically searched PsycINFO, MEDLINE (Ovid), EMBASE, CINAHL and CENTRAL for randomised controlled trials of non-pharmacological treatments for ADHD in adults. After screening of titles and abstracts, full text articles were reviewed, data extracted, and bias assessed using a study proforma. Results: There were 32 eligible studies with the largest number of studies assessing cognitive behavioural therapy (CBT). CBT consisted of either group, internet or individual therapy. Conclusions: The majority found an improvement in ADHD symptoms with CBT treatment. Additionally, mindfulness and cognitive remediation have evidence as effective interventions for the core symptoms of ADHD and there is evidence for the use of group dialectical behavioural therapy and hypnotherapy. However, the evidence for these is weaker due to small numbers of participants and limitations due to lack of suitable control conditions, and a high risk of bias.

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Key words: ADHD, non-pharmacological therapy, systematic review, randomised controlled-trials; adults.

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD), is present in 2-4% of adults and is characterised by symptoms of inattention, over activity and impulsiveness (McCarthy et al., 2012). Features of ADHD emerge in childhood and symptoms persist into adulthood; 60% of adults have ongoing notable ADHD symptoms and 15-20% continue to meet the full diagnostic criteria (Agnew-Blais et al., 2016; Faraone, Biederman, & Mick, 2006). There are psychiatric and social comorbidities associated with ADHD; adults with ADHD are at increased risk of impairments in education and academic performance, serious traffic accidents, criminality and physical and mental health problems (Dalsgaard, Ostergaard, Leckman, Mortensen, & Pedersen, 2015; Ginsberg, Hirvikoski, & Lindefors, 2010; Ljung, Chen, Lichtenstein, & Larsson, 2014; Shaw-Zirt, Popali-Lehane, Chaplin, & Bergman, 2005; Spencer, Faraone, Tarko, McDermott, & Biederman, 2014). Pharmacological treatments are effective first-line treatments for ADHD (Cortese et al., 2018). However, up to half of patients discontinue medication within the first 3 years of treatment (Zetterqvist, Asherson, Halldner, Långström, & Larsson, 2013), with reported reasons being adverse effects and treatment ineffectiveness (Gajria et al., 2014). Recent guidelines produced by the UK National Institute for Health and Care Excellence (NICE) recommend that non-pharmacological treatment be used in combination with medication for adults who are still experiencing significant symptoms or for those who have made the informed choice not to start medication (NICE, 2018). Recent evidence notes that cognitive-behaviour-based treatments may be beneficial for adults with ADHD (Lopez et al., 2018). However, other modalities of non-pharmacological treatment require further review, particularly whether improvements occur beyond the core symptoms of ADHD

such as in social functioning (Davidson, 2008; Hodgson, Hutchinson, & Denson, 2014). This study aims to conduct a systematic review of the effectiveness of all non-pharmacological treatments for adult ADHD on improving the core behavioural ADHD symptoms, symptoms of functional impairment and comorbid conditions.

METHODS

Inclusion and exclusion criteria

Eligible studies included participants with ADHD or hyperkinetic disorder (HKD) diagnosed according to established diagnostic criteria (e.g., DSM-III-R, DSM-IV, DSM-5, or ICD-10); with participants *all* aged 18 years or over; and reported the results of a non-pharmacological intervention. Studies were excluded if the primary intervention was being used as a medicine, including dietary supplementation and homeopathy. All studies were required to use randomisation to allocate participants to either the intervention or a control condition. Control conditions included using a waiting list, treatment as usual, a pharmacological intervention, placebo, or an alternative non-pharmacological intervention. Outcomes of interest were improvement in the core behavioural symptoms of ADHD (i.e., those outlined in DSM-III-R, DSM-IV or DSM-5), improvement in comorbid symptoms (for example anxiety and depression) and in symptoms of functional impairment (defined as problems in life domains such as work/education, family, life skills, social skills and/or risk-related behaviours). Neuropsychological, neurophysiological and neurobiological outcome measures were not examined since this was considered beyond the scope of this review and because behavioural rating scales are chiefly relied upon for the diagnosis and assessment of

ADHD in routine clinical practice (NICE, 2018) Studies were also excluded if they were not available in English.

Search strategy

The following databases were searched in May 2018: PsycINFO, MEDLINE (Ovid), EMBASE, CINAHL and CENTRAL. Search strategies for all databases are available in Supplement Table 1. Titles and abstracts were screened for eligibility by independent reviewers LS, SL and VN-S. In cases of uncertainty, the full articles were obtained and independently inspected, and inclusion criteria applied by the reviewers. Where meta-analysis or systematic reviews of treatment were available, we referred to the primary studies and assessed these for eligibility and reviewed the references of all included studies to identify any additional studies.

Data extraction, assessment of bias and data analysis

Data from the studies were extracted using a purpose-designed proforma (Supplement Table 2). The quality of studies was appraised using the Cochrane Risk of Bias Tool (Higgins et al., 2011) and, where there was uncertainty, clarification was sought from a second reviewer. Where information was not known the corresponding author for the studies was contacted. It was decided *a-priori* to undertake a narrative synthesis of the data should an insufficient number of studies be identified, and/or the identified studies be at high risk of bias, and/or the identified studies appear highly heterogeneous in terms of methodology and study characteristics.

RESULTS

Search results

The results of the initial search, title and abstract screening, and selection of the final studies are presented in Figure 1. The search string identified 55,865 articles, the majority of which were excluded following review of titles and abstracts. Of the 75 full-text records screened for eligibility, 32 met inclusion criteria and were included in the systematic review. Two papers reported differing outcomes of the same trial, with the later paper presenting additional functional outcomes (S. Young et al., 2017; S. Young et al., 2015). Two papers reported the results of different comparison groups from within the same trial (Virta, Salakari, Antila, Chydenius, Partinen, Kaski, & Iivanainen, 2010; Virta, Salakari, Antila, Chydenius, Partinen, Kaski, Vataja, et al., 2010).

Risk of bias

Results of the risk of bias assessment are presented in Table 1. Only one of the included records was assessed as having a low risk of bias across all five domains and that was for only one of the interventions within the trial (Schonenberg et al., 2017), and nine records were assessed as having a low risk of bias in four out of five domains (Dittner, Hodsoll, Rimes, Russell, & Chalder, 2018; Gu, Xu, & Zhu, 2018; Janssen et al., 2018; Philipsen et al., 2015; Salomone et al., 2015; Stern, Malik, Pollak, Bonne, & Maeir, 2016; Vidal et al., 2013; S. Young et al., 2017; S. Young et al., 2015).

For a significant number of studies, it was not possible to assess the risk of bias in at least one of the five domains due to insufficient information.

Study characteristics

Study characteristics are presented in Table 2 (and results in supplement Table 3). The interventions fell into eight broad categories: 1. cognitive-behavioural therapy; 2. dialectical behavioural therapy; 3. mindfulness-based therapy; 4. hypnotherapy; 5. Psychoeducation; 6. neurofeedback; 7. cognitive remediation and other forms of "brain training", and; 8. a study skills intervention. Studies were highly heterogeneous in terms of sample size, age range, and gender of the participants and outcome measures. Due to this heterogeneity, and the aforementioned risk of bias, a narrative synthesis of results was used.

Narrative synthesis

Cognitive behavioural therapy (CBT)

There were fourteen randomised controlled trials of CBT and one additional study presenting outcomes of further results from an earlier study (S. Young et al., 2017). Details of CBT interventions are in Table 3 and supplement Table 4. None of the CBT studies were assessed as having a low risk of bias across all five domains and there was substantial variation in sample size across studies.

Five studies compared CBT with treatment as usual (TAU) (Dittner et al., 2018; Emilsson et al., 2011; Safren et al., 2005; S. Young et al., 2017; S. Young et al., 2015) CBT produced an improvement in independent and self-reported ADHD symptoms, both for group (Emilsson et al., 2011; S. Young et al., 2015) and individual (Dittner et al., 2018; Safren et al., 2005) therapy. Improvements included changes in inattentive and hyperactive-impulsive symptoms and were based on measures taken at pre and post-treatment and at follow-up. Three studies also reported lower Clinical Global Impression (CGI) scores following CBT (Dittner et al., 2018; Safren et al., 2005; S. Young et al., 2015). These results indicate a favourable effect of CBT compared to TAU. However, all studies had a high risk of bias associated with blinding as participants in the treatment arms received more attention than controls.

Three studies compared CBT to a form of generic counselling. The studies ranged in sample size from 32 (Vidal et al., 2013) to 433 (Philipsen et al., 2015). In two studies, both CBT and counselling were associated with improvements in ADHD symptoms; however there was no evidence that CBT led to greater improvements in either informant or self-reported ADHD (Philipsen et al., 2015; Vidal et al., 2013) and only one study found CBT improved CGI scores (Philipsen et al., 2015). The largest study was Philipsen *et al* (n= 433); however, it is limited by comparing group CBT with individual supportive clinical management and so arguably the control group received a more intensive treatment (Philipsen et al., 2015). In addition to this, the program manual followed in this study had more similarities with the DBT treatment described in a later study than other CBT studies (Table 3 and supplement Table 4) (Hesslinger, Philipsen, & Richter, 2004; Hirvikoski et al., 2011).

One study examined the impact of CBT on a “younger” (aged under 50) and “older” (aged 50 or older) group of patients with ADHD (Mary V Solanto, Surman, & Alvir, 2018). This found improvements in ADHD symptoms on both independent and self-reported measures in the “younger” group, but not the “older” group.

One study compared CBT to relaxation training (Safren et al., 2010). CBT was associated with greater improvements in independent ratings of ADHD symptoms and in clinician-rated CGI scores. CBT also led to quicker improvements in self-reported ADHD symptoms. Improvements were maintained at six and twelve-month follow-up. Two studies explored the use of internet-delivered CBT versus a waiting list control (Moëll, Kollberg, Nasri, Lindefors, & Kaldo, 2015; Pettersson, Sostrom, Edlund-Soderstrom, & Nilsson, 2017). Both studies found that, CBT was associated with significant improvements in self-reported ADHD symptoms.

Two studies examined meta-cognitive therapy, a form of CBT based on improving executive functioning skills. Group meta-cognitive therapy was associated with greater changes in clinician and informant ratings of inattentive ADHD symptoms and clinician ratings of time-management, organisation and planning skills when compared with group supportive therapy, although both CBT and supportive therapy were associated with changes in ADHD symptoms rated using the Brown Attention Deficit Disorder Scale (M. V. Solanto et al., 2010). One study compared individual meta-cognitive therapy with neurofeedback and sham neurofeedback, and found no significant difference between treatment groups for changes in self-reported ADHD symptoms (Schonenberg et al., 2017).

Two studies used the same sample to compare CBT with cognitive training, hypnotherapy and a control condition (Hiltunen et al., 2014; Virta, Salakari, Antila, Chydenius, Partinen, Kaski, Vataja, et al., 2010). CBT was associated with an improvement in one informant-rated measure of ADHD symptoms when compared to the control condition (Virta, Salakari, Antila, Chydenius, Partinen, Kaski, Vataja, et al., 2010). There were no differences between CBT and cognitive training based on informant or self-reported ADHD symptoms but CBT was associated with lower CGI scores. Compared with hypnotherapy, CBT produced no significantly different changes in informant or self-reported ADHD symptoms or CGI scores post-treatment. However, at follow-up, hypnotherapy but not CBT was associated with a change in informant ratings of ADHD (Hiltunen et al., 2014). These studies were particularly small with 10 or less individuals in each treatment group.

Dialectical behavioural therapy (DBT)

Two randomised controlled trials assessed group DBT. Details are presented in Table 3 and supplement Table 4. One (Hirvikoski et al., 2011) compared 14 sessions of DBT with a discussion group. DBT, but not the discussion group, was associated with a significant reduction in self-ratings of ADHD symptoms; however this difference was attenuated to a non-significant level when an intention-to-treat analysis was performed. This study was associated with a low risk of bias. The second study (Fleming, McMahon, Moran, Peterson, & Dreessen, 2015) compared DBT to self-help and was associated with a higher risk of bias. Those who received DBT performed

significantly better on measures of the clinical impact of executive functioning deficits after treatment and at three-month follow-up; however there was no significant effect of the intervention on self-rated symptoms of inattention.

Mindfulness-based interventions

Four studies examined mindfulness-based cognitive therapy (MBCT), an intervention that combines elements of mindfulness training with CBT, while two additional studies examined mindfulness interventions. These studies varied in terms of sample size and risk of bias, with none rated as low risk of bias for the blinding of participants. Details are presented in Table 4 and supplement Table 5.

Compared to TAU, group MCBT was associated with a significant improvement in post-treatment observer and self-reported ADHD symptoms and with improved behavioural ratings of executive functioning at three and six-month follow-up but not immediately after treatment (Janssen *et al.*, 2018). Two further studies, which compared group MBCT to a waiting list control, found significant improvements in ADHD symptoms post treatment for self-reported (Hepark et al., 2019; Schoenberg et al., 2014) and observer-reported (Hepark et al., 2019) ADHD symptoms immediately after the intervention but did not collect follow-up data. A fourth study compared individual MBCT to a waiting list control and found an improvement in self-reported ADHD symptoms at post-treatment and at follow-up (Gu et al., 2018).

Compared to an active control of group psychoeducation, group mindfulness did not produce a significant improvement in observer or self-reported ADHD symptoms either post-treatment or at six-month follow-up (Hoxhaj et al., 2018). However, it was noted that both interventions appeared to improve outcomes. A smaller study found that group mindfulness sessions produced a significant improvement in self- and observer-reported ADHD symptoms, however this was versus a waiting list control and had had high risk of bias (Mitchell et al., 2017).

Hypnotherapy

Hypnotherapy as a treatment for ADHD has been studied in two small RCTs, both of which were associated with a high risk of bias. Details are provided in Table 4 and supplement Table 5. One study compared hypnotherapy with CBT, the results of which are described above (Hiltunen et al., 2014). Another study (Virta, Salakari, Antila, Chydenius, Partinen, Kaski, & Iivanainen, 2010) compared the same participants to those receiving no intervention, finding that those in the ADHD group scored significantly lower for self-reported total ADHD scores and some subscales of the BADDS scale; however, there was no significant improvement in ADHD symptoms over time based on aggregate self and informant ratings of ADHD.

Psychoeducation

Group psychoeducation was measured as the primary intervention versus a TAU control in one study by Hirvikoski *et al* (n = 87) and in comparison to mindfulness-based cognitive therapy by Hoxhaj *et al* (n = 81). Both studies had a low risk of bias in three out of the five domains. Hirvikoski *et al* assessed the feasibility and effectiveness

of a group-based psychoeducation programme for people with ADHD and their significant others (Hirvikoski et al., 2017). ADHD behavioural symptoms were not measured and no significant differences were found in secondary outcomes of functional impairment (reported in supplement Table 3). Hoxhaj *et al* found no difference between the psychoeducation group and mindfulness group in observer or self-reported ADHD symptoms (see above)(Hoxhaj et al., 2018).

Neurofeedback

One randomised controlled trial compared neurofeedback with both sham neurofeedback and meta-cognitive therapy as control interventions (Schonenberg et al., 2017). This study was assessed as low risk of bias in all five domains, as the sham neurofeedback provided an effective control condition. There were no significant differences between neurofeedback, sham neurofeedback and metacognitive therapy for improvement in ADHD symptoms after treatment or at six-month follow-up.

Cognitive remediation and rehabilitation

Seven studies sought to improve both the behavioural symptoms and the neurocognitive functioning of people with ADHD using methods such as cognitive remediation, rehabilitation or another form of "brain training". Details of these interventions are given in Table 4 and supplement Table 5. Two studies examined therapist-delivered (C. S. Stevenson, Whitmont, Bornholt, Livesey, & Stevenson, 2002) and self-directed (Caroline S Stevenson, Stevenson, & Whitmont, 2003) cognitive remediation. Four studies examined computerised cognitive training

(Mawjee et al., 2017; Mawjee, Woltering, & Tannock, 2015; Stern et al., 2016; Virta, Salakari, Antila, Chydenius, Partinen, Kaski, Vataja, et al., 2010), with two focussing on working memory training (Mawjee et al., 2017; Mawjee et al., 2015). Finally, one study examined self-alert training (Salomone et al., 2015). Only two of the studies were assessed as having low risk of bias in only one of the five domains (Salomone et al., 2015; Stern et al., 2016), with the remainder having a high risk of bias or unknown risk of bias in at least two domains.

Therapist delivered cognitive remediation produced a significant improvement in ADHD symptoms and in organisation skills, which were maintained at two and 12-month follow-up. These findings remained after controlling for ADHD medication. (C. S. Stevenson et al., 2002). Self-directed cognitive remediation augmented with three therapist-led sessions also significantly improved ADHD symptoms and organisation post-intervention and at two-month follow-up (Caroline S Stevenson et al., 2003).

Two studies of working memory training consisting of standard (45 minutes of daily training), or a shortened (15 minute training), found no significant improvement in measures of ADHD symptoms or self-reported measures of deficits in executive function with either form of working memory training versus a waiting list control (Mawjee et al., 2017; Mawjee et al., 2015). However Mawjee *et al* 2017 found on post-hoc analysis that although self-reported symptoms of cognitive failures did not differ between shortened and standard length training and the control group, there was a significant difference when both forms of working memory training were compared together against the control. This study had limited power due to having a small sample size (n = 38).

The study comparing cognitive training versus a CBT and control group in a group of 32 individuals has been described above, noting that there was no significant difference in improvement in ADHD symptoms (Virta, Salakari, Antila, Chydenius, Partinen, Kaski, Vataja, et al., 2010). A larger study of 60 individuals comparing computerised cognitive training versus a control condition of generic exercises found no difference between the intervention and control on improvement in ADHD symptoms (Stern et al., 2016).

Self-alert training using biofeedback scored significantly lower post-intervention and at three-month follow-up for symptoms of inattention, impulsivity and emotional lability, for problems with self-concept, and for the ADHD index score compared with a control condition which used all aspects of the treatment except the use of biofeedback (Salomone et al., 2015). In contrast, there were no significant group differences for scores on the attention and memory problems scale, the hyperactivity and restlessness scale, the DSM-IV hyperactive symptoms scale, or the DSM-IV total symptoms scale. There was evidence of a treatment dose-response effect, whereby longer self-alert training practice was associated with greater reductions in inattentive symptoms of ADHD, but not to changes in other ADHD symptom domains. Participants in the training group reported significantly lower ratings for attentional slips than controls, but with no group differences for lapses in memory.

Study skills intervention and self-monitoring

There was one study which specifically explored a "study skills intervention" compared to a control condition (Scheithauer & Kelley, 2017). The details of this are

described in more detail in Table 4 and supplement Table 5. Significantly more individuals in the self-monitoring group versus the control group demonstrated clinical improvements in self-reported symptoms of ADHD. However, this study was noted to be of high-risk for bias.

Functional Impairment

Symptoms of psychiatric comorbidity and/or functional impairment were also examined in this review, with results summarised in supplement Table 3. In summary, of the 14 CBT studies (including one follow-up study) measuring comorbidity or functional outcomes, six found a positive result for CBT in at least one measure of these outcomes (Dittner et al., 2018; Emilsson et al., 2011; Moëll et al., 2015; Safren et al., 2005; S. Young et al., 2017; S. Young et al., 2015). One of the two DBT studies and one of the two hypnotherapy studies measuring comorbidity or functional outcomes found a significantly improved outcome in at least one measure favouring the intervention (Fleming et al., 2015; Hiltunen et al., 2014). None of the studies of psychoeducation or neurofeedback found a significant difference for measures of these outcomes. Seven of the cognitive remediation studies measured comorbidity and/or functional impairment, with four finding a statistically significant result in at least one measure (Mawjee et al., 2017; Salomone et al., 2015; Caroline S Stevenson et al., 2003; C. S. Stevenson et al., 2002). Self-monitoring was associated with significantly improved functional outcomes relating to academic studies (Scheithauer & Kelley, 2017). Four of the six mindfulness-based intervention studies found significant improvements in measures of comorbidity, favouring the intervention, but none of the studies found significant improvements in functional outcomes (Gu et al., 2018; Janssen et al., 2018; Mitchell et al., 2017; Schoenberg et al., 2014).

DISCUSSION

This systematic review examined the effectiveness of non-pharmacological interventions for adult ADHD. These studies used a wide range of outcome measures and most of the identified studies were small (<60 randomised participants)
and at a high risk of bias, with marked heterogeneity in terms of study design and delivery of the intervention. A meta-analysis was therefore considered inappropriate and these limitations impact on the extent to which firm conclusions can be drawn.

The results across studies suggest that non-pharmacological interventions perform significantly better than inactive control conditions when used to manage the core behavioural symptoms of ADHD. Studies with an active control condition gave more mixed results as often there was a significant within-group improvement in the control condition, which could be due to placebo effect or another aspect of the control condition providing an active treatment element, such as increasing patient knowledge, and motivation for engagement (Hoxhaj et al., 2018; Vidal et al., 2013), or through task demands such as practicing sustaining focus (Schonenberg et al., 2017), or through providing a therapeutic relationship (Philipsen et al., 2015). Nonetheless, these findings suggest that non-pharmacological interventions can play an important role in helping adults diagnosed with ADHD to manage their condition.

By far the greatest number of studies (n=14) examined cognitive behavioural therapy (CBT). The results of these studies broadly suggest that CBT is associated with a

reduction in the core behavioural symptoms of ADHD and can be delivered as either a group, individual or internet-based form of therapy. However, there was marked heterogeneity across studies, both in terms of sample size, study design and quality, and in terms of the kind of change in ADHD symptoms identified. For example, some studies found a reduction in informant but not self-reported ADHD symptoms and vice-versa; some identified lasting change in ADHD symptoms based on follow-up data but not immediately after the intervention and some studies failed to find any benefit of CBT over and above an active control condition. Further research into CBT interventions is therefore required, including studies that seek to replicate the promising results identified thus far.

Some other interventions also showed promise, in particular cognitive remediation and rehabilitation, mindfulness-based therapies and to some extent DBT and hypnotherapy. Both MBCT and DBT are similar to CBT in that they support people to change their behaviours, and indeed there are many parallels across all of the different classes of intervention identified in this study. However, MBCT and DBT are considered “third-wave” cognitive and behavioural therapies and differ from traditional CBT in that they help individuals to change the relationship with their thoughts as opposed to directly challenging the content of thoughts (Hayes & Hofmann, 2017). MCBT and DBT both also teach mindful awareness as a therapeutic technique, which involves gently redirecting attention to the present moment when it wanders. It is possible that this acts as a form of brain training, highlighting parallels between these interventions and cognitive remediation therapy, which also involves attention training and was associated with a reduction in the core symptoms of ADHD.

Symptoms of functional impairment and comorbidity were also examined in this review. There was a wide variation in results, with the most consistent effect of therapy being the impact of mindfulness-based therapies on psychiatric comorbidity, which is consistent with the use of mindfulness-based therapies on treating anxiety and depression (Hofmann, Sawyer, Witt, & Oh, 2010). Whilst studies reporting on comorbidity and functional outcomes were likely to be powered primarily to detect a change in behavioural symptoms of ADHD and not to detect changes in comorbidity, there is the potential for non-pharmacological interventions to improve quality of life for adults with ADHD in a much broader sense, and this is an area that should be explored further in future research.

There were a wide number of measures used for ADHD symptoms, comorbidity and functional impairment. This contributed to the heterogeneity of the results and difficulty in making comparisons between treatment approaches. Because of this, it seems important to recommend that future research takes a systematic approach. First, a set of core outcome measures could be established, including both observer and self-reported ratings of ADHD symptoms in accordance with diagnostic criteria. A set of core outcome measures could include measures of psychological distress, such as Beck's inventories for anxiety and depression (Beck & Steer, 1990; Beck, Steer, & Brown, 1996) and a scale of functional impairment such as the adult attention-deficit hyperactive disorder quality-of-life scale (AAQOL Scale) (Brod, Johnston, Able, & Swindle, 2006). Importantly, these should be developed in consultation with the adult ADHD community in order to ensure that 'real life' outcomes that matter to individuals are included in future trials.

Secondly, where there have been studies of non-pharmacological interventions that have shown promise, we need larger, better designed trials. Trials with a low risk of bias should ensure that allocation concealment occurs and that outcomes are assessed by independent, blinded assessors. Trials should aim to be powered to detect not only effects of treatment on the behavioural symptoms of ADHD, but also symptoms of comorbidity. Trials should also directly compare non-pharmacological interventions for ADHD with pharmacotherapy. This form of comparison was rarely undertaken, yet the right of adults with ADHD to make an informed choice about interventions sits at the heart of patient-centred care. One large study included in this review did compare non-pharmacological interventions to medication and in doing so found that methylphenidate had the greatest effect on ADHD regardless of the non-pharmacological intervention used (Philipsen et al., 2015).

Thirdly, and to help identify the 'active ingredients' of treatment, studies could begin to look at mediating variables to find out what leads to a change in symptoms following non-pharmacological treatment. In CBT, for example, it is not clear whether psycho-education, problem-solving, cognitive restructuring, behavioural change or a combination thereof, leads directly or indirectly to a change in ADHD or comorbid symptoms. Mediators may also include neurobiological, neurophysiological or neuropsychological performance, particularly as these variables are considered to be 'endophenotypes' of ADHD (Castellanos & Tannock, 2002) that may bridge the gap between genes and behaviours.

This review should be interpreted in the context of several limitations. First, the review was not pre-registered. Secondly, although much effort was made to retrieve

a maximum number of relevant studies, we cannot rule out the possibility that we have missed some relevant studies. For example, we only included published papers did not search the grey literature. We also focused on English-language publications due to resource limitations. This could have possibly introduced a cultural bias in terms of the kinds of interventions reported and may limit the extent to which findings generalise to different countries and cultures. Thirdly, due to heterogeneity and risk of bias across the identified studies, it was not possible to conduct a meta-analysis; therefore, the effect sizes across different studies were not examined. This makes it difficult to draw any direct comparisons between the different classes of intervention. Finally, many of the interventions described take similar approaches, meaning that the different classes of intervention have much in common.

Despite these limitations this review serves as a bellwether, identifying the state of research into non-pharmacological interventions for adult ADHD and highlighting their potential in clinical practice, and identifying gaps in the evidence with suggestions about the direction of future research.

Table 1: Risk of bias assessment for randomised controlled trials of non-pharmacological interventions for adult ADHD

Author (Year)	Number of participants.	Assessment of Bias				
		Selection Bias	Allocation concealment	Blinding of participants	Blinding of outcome assessment	Incomplete outcome data
Dittner *et al* (2018)	60	Low	Low	High	Low	Low
Emilsson *et al* (2011)	54	Unclear	Low	High	Low	High
Fleming *et al* (2015)	35	Unclear	Unclear	High	Low	Low
Gu et al (2018)	56	Low	Low	High	Low	Low
Hepark *et al* (2019)	103	Unclear	Low	High	Low	Low
Hiltunen *et al* (2014)	39	Unclear	Unclear	High	Low	Low
Hirvikoski *et al* (2017)	87	Low	Low	High	High	Low
Hirvikoski *et al* (2011)	51	Low	Low	High	High	Low
Hoxhaj *et al* (2018)	81	Low	Low	Unclear	Low	Unclear
Janssen *et al* (2018)	120	Low	Low	High	Low	Low
Mawjee *et al* (2017)	38	Low	Low	High	Low	High
Mawjee *et al* (2015)	97	Low	Low	High	High	Low[a]
Mitchell *et al* (2017)	22	Unclear	Unclear	High	High	Low
Moëll *et al* (2015)	57	Unclear	Unclear	High	Low	Low
Pettersson *et al* (2017)	45	Low	Low	High	Low	High
Philipsen *et al* (2015)	433	Low	Low	High	Low	Low
Safren *et al* (2010)	86	Low	Unclear	High	Low	Unclear
Safren *et al* (2005)	31	Unclear	Unclear	High	Low	Low
Salomone *et al* (2015)	51	Low	Low	Low	Low	High
Scheithauer and Kelley (2017)	52	Low	High	High	High	High
Schoenberg *et al* (2014)	61	Low	High	High	Low	Low
Schönenberg et al (2017)	118 Neurofeedback	Low	Low	Low	Low	Low
	Meta-cognitive therapy	Low	Low	High	High	Low
Solanto *et al* (2018)	88	Low	Unclear	Unclear	Low	Unclear
Solanto, *et al* (2010)	88	Unclear	Unclear	Unclear	Low	Low
Stern *et al* (2016)	60	Low	Low	Low	Low	High
Stevenson *et al* (2003)	35	Unclear	Unclear	High	Unclear	Low
Stevenson *et al* (2002)	44	Unclear	Unclear	High	Unclear	Low[a]
Vidal *et al* (2013)	32	Low	Low	High	Low	Low
Virta *et al.* (2010)	20	Unclear	Unclear	High	Low	Low
Virta *et al.* (2010)	32	Unclear	Unclear	High	Low	Low
Young *et al* (2017)	95	Low	Low	High	Low	Low
Young *et al* (2015)	95	Low	Low	High	Low	Low

[a]This refers to times T1 and T2 only as we cannot use time T3 as there is not a suitable control group.

Table 2: Overview of non-pharmacological intervention sample characteristics, outcome measures and results

Author (Year)	n	Intervention	Control	Sample characteristics	
				Mean age	% female
Individual CBT					
Dittner *et al* (2018)	60	Individual CBT	TAU	36 (CBT) 36 (TAU)	23 (CBT) 40 (TAU)
Safren *et al* (2010)	86	Individual CBT	Individual Relaxation	42 (CBT) 44 (Relaxation)	44 (CBT) 44 (Relaxation)
Safren *et al* (2005)	31	Individual CBT	TAU	46	55
Virta *et al.* (2010)	32	Individual CBT Cognitive training (CT)	Control group (not specified)	38 (CBT) 32 (CT) 34 (Control)	70 (CBT) 22 (CT) 60 (Control)
Hiltunen *et al* (2014) Study described below under "hypnotherapy"					
Group CBT and group meta-cognitive therapy					
Emilsson *et al* (2011)	54	Group CBT and medication	TAU and medication	34	63
Philipsen *et al* (2015)	433	Group CBT + methylphenidate (MPT) Group CBT + placebo	Clinical Management individual counselling (CM) + MPT CM + Placebo	35 (DBT+ MPT) 35 (DBT + placebo) 35 (CM + MPT) 35 (CM + placebo)	49 (DBT + MPT) 42 (DBT+ placebo) 46 (CM+ MPT) 55 (CM + placebo)
Schönenberg et al (2017) Study described below under "neurofeedback"					
Solanto *et al* (2018)	27 (older group) 61 (younger group)	Group CBT	Supportive therapy	56 35	63 67
Solanto *et al* (2010)	88	Group Meta-cognitive therapy (MCT)	Supportive therapy	41 (MCT) 42 (Control)	71 (MCT) 61 (Control)
Vidal *et al* (2013)	32	Group CBT	Psychoeducation group (PG)	39 (CBT) 40 (PG)	40 (CBT) 65 (PG)
Young *et al* (2017) **Young *et al* (2015)**	95	Group CBT and individual mentor meetings	TAU	34 (CBT) 36 (TAU)	63 (CBT) 68 (TAU)
Internet CBT					
Moëll *et al* (2015)	57	Internet CBT (CBTi)	WL	36 (CBTi) 37 (WL)	76 (CBTi) 61 (WL)
Pettersson *et al* (2017)	45	Internet CBT with group sessions (CBTi-Group) Internet CBT with self-help (CBTi-SELF)	WL	40 (CBTi- Group) 39 (CBTi- SELF) 34 (WL)	57 (CBTi- Group) 54 (CBTi- SELF) 78 (WL)
DBT					
Fleming *et al* (2015)	35	Group DBT	Self-help skills handouts	21 (DBT) 21 (Control)	41 (DBT) 44 (Control)
Hirvikoski *et al* (2011)	51	Group DBT	Discussion group	41 (DBT) 37 (Control)	73 (DBT) 52(Control)
Mindfulness-Based Cognitive Therapy (MBCT) and mindfulness					
Gu et al (2018)	56	Individual MBCT	WL	20 (MBCT) 20 (WL)	43 (MBCT) 46 (WL)

Hepark *et al* (2019)	103	Group MBCT	WL	37 (MBCT) 35 (WL)	62 (MBCT) 46 (WL)
Hoxhaj *et al* (2018)	81	Mindfulness Group (MG)	Psychoeducation Group (PG)	41 (MG) 39 (PG)	56 (MG) 48 (PG)
Janssen *et al* (2018)	120	Group MBCT	TAU	40(MBCT) 39 (TAU)	53 (MBCT) 53 (TAU)
Mitchell *et al* (2017)	22	Mindfulness Group (MG)	WL	41 (MG) 36 (WL)	55 (MG) 67 (WL)
Schoenberg *et al* (2014)	61	MBCT	WL	40 (MBCT) 34 (WL)	63 (MBCT) 40 (WL)
Hypnotherapy					
Hiltunen *et al* (2014) (a follow-up of Virta et al 2010)	19	Group Hypnotherapy (GH)	Individual CBT	39 (GH) 32 (CBT)	63 (GH) 67 (CBT)
Virta *et al.* (2010)	20	Hypnotherapy	Control group (not specified)	34 (Treatment) 34 (Control)	67 (Treatment) 60 (Control)
Psychoeducation					
Hirvikoski *et al* (2017)	87	Psychoeducation Group (PG)	TAU	39 (PG) 38 (TAU)	65 (PG) 54 (TAU)
Hoxhaj *et al* (2018) Study discussed under "Mindfulness-Based cognitive therapies" above.					
Neurofeedback					
Schönenberg et al (2017)	118	Neurofeedback (NEURO) Group CBT	Sham neurofeedback (SHAM)	40 (NEURO) 38 (CBT) 36 (SHAM)	49 (NEURO) 42 (CBT) 39 (SHAM)
Cognitive remediation and rehabilitation					
Mawjee *et al* (2017)	38	Standard Working Memory Training (STAN) Shortened Working Memory Training (SHORT)	WL	24 (STAN) 21 (SHORT) 23 (Control)	44 (STAN) 38 (SHORT) 58 (Control)
Mawjee *et al* (2015)	97	Standard Working Memory Training (STAN) Shortened Working Memory Training (SHORT)	WL	24 (STAN) 24 (SHORT) 24 (Control)	59 (STAN) 64 (SHORT) 56 (Control)
Salomone *et al* (2015)	51	Self-alert training group and practice (SAT)	Psychoeducation group and exercises (PG)	33 (SAT) 32 (PG)	33 (SAT) 26 (PG)
Stern *et al* (2016)	60	Computerised Cognitive Training, focussing on executive function	Generic computerised cognitive exercises which do not focus on executive function	38 (Treatment) 36 (Control)	56 (Treatment) 58 (Control)
Stevenson *et al* (2003)	35	"Self-help" strategy training	WL	39 (Self-help) 38 (WL)	41 (Self-help) 33 (WL)
Stevenson *et al* (2002)	44	Cognitive-remediation therapy	WL	36 (Treatment) 35 WL	27 (Treatment) 38 WL
Virta *et al.* (2010) Study described above under "CBT".					
Study skills intervention and self-monitoring					
Scheithauer and Kelley (2017)	52	Self-monitoring and study skills intervention	Study skills intervention	20	76

CBT= Cognitive behavioural therapy; DBT= Dialectical Behavioural Therapy; MBCT= Mindfulness Based Cognitive Therapy; TAU= Treatment as usual; WL= Waiting list

Table 3: Duration and details of cognitive behavioural- based interventions and dialectical behavioural therapy

Author (Year)	Intervention	Duration of Cognitive Intervention
Dittner *et al* (2018)	Individual CBT	15 CBT sessions over 30 weeks and a 16th follow-up session at 42 weeks
Emilsson *et al* (2011)	Group CBT	15 weekly sessions of 90 minutes group "R&R2ADHD" CBT (SJ Young & Ross, 2007) and 30 minutes of individual coaching
Fleming *et al* (2015)	Group DBT	8 weekly 90 minute group sessions and weekly one-to-one phone calls for coaching with one booster session during the first week of the follow-up quarter
Gu *et al* (2018)	Individual MBCT	6 weekly 1 hour individual MBCT sessions
Hepark *et al* (2019)	Group MBCT	12 weekly sessions
Hirvikoski *et al* (2011)	Group DBT	14 weekly 2 hour group sessions
Janssen *et al* (2018)	Group MBCT	8 weekly 2.5 hour sessions and a 6 hour silent day between the 6th and 7th sessions
Moëll *et al* (2015)	Internet CBT (CBTi)	7 modules over 6 weeks
Pettersson *et al* (2017)	Internet CBT with self-help	9 CBT treatment modules and a follow-up module
	Internet CBT with group sessions	9 CBT treatment modules and a follow-up module Group sessions met for 3hours once a week for 10 weeks
Philipsen *et al* (2015)	Group therapy, using aspects of a DBT based method (Hesslinger et al., 2004)	12 weekly 2 hour DBT sessions followed by 10 monthly 2 hour sessions over 52 weeks Each session was split into 2 with each half starting with a mindfulness exercise
Safren *et al* (2010)	Individual CBT	12 weekly 50 minute sessions of CBT
Safren *et al* (2005)	Individual CBT	15 weekly sessions of CBT
Schoenberg *et al* (2014)	MBCT	12 weekly 3 hour sessions of MBCT
Schönenberg et al (2017)	Group CBT, compared with Neurofeedback	12 weekly group CBT sessions
Solanto, *et al* (2018)	Group CBT	12 weekly 2 hour group CBT sessions
Solanto, *et al* (2010)	Group Meta-cognitive therapy (MCT)	12 weekly 2 hour group MCT sessions
Vidal *et al* (2013)	Group CBT	12 weekly 2 hour sessions of group CBT
Virta *et al.* (2010)	Individual CBT (compared with cognitive training)	10 weekly 1 hour individualised CBT sessions
Young *et al* (2017) and Young *et al* (2015)	Group CBT and individual mentor meetings	15 weekly sessions of 90 minutes group "R&R2ADHD" CBT and individual coaching in-between sessions

Table 4: Duration and details of all other interventions

Author (Year)	Duration of intervention
Hiltunen *et al* (2014) and Virta et al (2010)	10 weekly sessions of group hypnotherapy
Hirvikoski *et al* (2017)	8 session psychoeducation group
Hoxhaj *et al* (2018)	8 weekly 2.5 hour group mindfulness sessions and daily meditation homework
	8 weekly 2.5 hour psychoeducation group sessions
Mawjee *et al* (2017) and Mawjee *et al* (2015)	Standard Working Memory Training 25 training sessions (lasting 45 minutes) over 5-6 weeks
	Shortened Working Memory Training 25 training sessions (lasting 15 minutes) over 5 weeks
Mitchell *et al* (2017)	8 weekly 2.5 hour group mindfulness sessions and daily meditation homework
Salomone *et al* (2015)	Self-alert training groups and 5 weeks of home practice exercises, lasting 30 minutes a day
Scheithauer and Kelley (2017)	One Self-monitoring and study skills teaching intervention with self-monitoring lasting 4-6 weeks
Schönenberg *et al* (2017)	30 group neurofeedback training sessions over 15 weeks
Stern *et al* (2016)	12 weeks of 4-5 times a week 20-minute-long online cognitive training sessions
Stevenson *et al* (2003)	8 week intervention of "self-help" strategy training
Stevenson *et al* (2002)	8 weekly 2 hour group sessions
Virta *et al.* (2010)	20 twice weekly hourly computerised cognitive training sessions

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