Dismantling cognitive–behavioural therapy components for attention-deficit hyperactivity disorder in adolescents and adults: protocol for a network meta-analysis

Sayo Hamatani,1,2,3 Kazuki Matsumoto,4 Yoshihiko Kunisato,5 Sho Okawa,6,7 Masatoshi Yamashita,1,2 Yoshifumi Mizuno 1,2,3

ABSTRACT

Introduction Cognitive–behavioural therapy (CBT) consists of multiple treatment techniques for each treatment model and is tailored to the patient’s characteristics. Randomised controlled trials (RCTs) have reported that CBT is effective for attention-deficit/hyperactivity disorder (ADHD); however, which CBT components are effective is unknown. In order to provide the best treatment technique, it is important to know which therapeutic component or combination thereof is more effective and what the specific effect size is.

Methods and analysis We will perform component network meta-analysis (cNMA). The search will include studies published from database inception up to 31 March 2022, in English. The electronic databases of MEDLINE (via PubMed), EMBASE, PsycINFO, ClinicalTrials.gov and Cochrane Library will be searched. We will systematically identify all RCTs in the treatment of ADHD between the ages of 10 and 60 years, comparing interventions composed of various CBT components with controlled interventions. We will perform pairwise and network meta-analysis with random effects to estimate summary ORs and standardised mean differences. We will assess the risk of bias in selected studies using the Cochrane risk of bias tool.

Ethics and dissemination Since we will review published papers, ethical approval is not required. The results from this cNMA will provide a panorama of the CBT-based ADHD studies. The results of this study will be published in a peer-reviewed journal.

PROSPERO registration number CRD42022323898.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study aims to identify components of cognitive–behavioural therapy (CBT) that work effectively in the treatment of attention-deficit/hyperactivity disorder.
⇒ Component network meta-analysis can estimate a specific gradual effect size for each component.
⇒ Our design can estimate the additive and synergistic effects of combined CBT components.
⇒ Individual participant data analysis is not planned, so assessing the prognostic factors and effect modifiers of the components identified in the results obtained will not be possible.
⇒ This review is limited to literature published in English.

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is one of the neurodevelopmental disorders characterised by inattention, hyperactivity and impulsivity.1 Numerous studies have investigated the effectiveness of pharmacological and non-pharmacological therapies for ADHD.8,9,10 Currently, cognitive–behavioural therapy (CBT) is probably the most effective psychological treatment for ADHD, according to previous reviews.4,7 Not only for adults, CBT for the clinical manifestations of ADHD in adolescents is also effective with a large effect size.8 Notably, CBT is a complex psychotherapy that combines various techniques. The therapist adjusts to the patient’s background to provide the best treatment technique. It is important to know which therapeutic component or combination thereof is more effective and what is the specific effect size.

CBT components can be categorised for integrating evidence for complex interventions, and their relative effectiveness can be analysed in component network meta-analysis (cNMA).9,10 Although there is evidence of the effects of two CBT components in previous network meta-analyses, the scope of component examination is limited: cognitive and behavioural therapy only.11,12 In order to evaluate the efficacy of the CBT components for ADHD, analyses including organisation such as time management, cognitive therapy and third-wave CBT are required. In this study, we
will apply cNMA and leverage a randomised network of evidence to disassemble and compare the various components of CBT.

This study aims to gain insights into the best CBT components and the effects of those combinations. CBT is a complex combination of diverse treatment techniques, but we will discover techniques that will be more focused on this task, which will help us develop efficient treatment programmes.

**METHODS AND ANALYSIS**

This protocol is reported following the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols; the analyses will be performed in adherence to a protocol in PROSPERO (CRD42022323898).

**Eligibility criteria**

We will include all randomised controlled trials (RCTs) to investigate the effectiveness of CBT components against a control intervention in treating adolescents and adults with ADHD. We will include adolescents and adults of both sexes, aged 10–60 years, with ADHD. Assuming that around age 10 years the logical thinking that is essential for individual CBT is developed, we set this age 10 years as the lower limit. Table 1 shows the target CBT components and their definitions. All interventions will be included when these components are used alone or in combination. Concomitant pharmacotherapy will only be permitted if there is no systematic difference in drug administration between study groups. Table 2 summarises the CBT components and their combinations; the table also includes details of the psychotherapies and control conditions we plan to include in this cNMA. Studies can only be included if a fixed combination of the CBT components has been obligatory in each treatment group.

We are interested in the effects of interventions on the core symptoms of ADHD (inattention, hyperactivity/impulsivity). Therefore, behavioural techniques—such as social skills training, which focuses on solving interpersonal problems—will not be included in the CBT component of this study. In addition, CBT aims to identify three factors (symptoms, cognition and behaviours)

<table>
<thead>
<tr>
<th>Table 1 List of included CBT components</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>w</strong> Waiting component</td>
</tr>
<tr>
<td><strong>pl</strong> Placebo</td>
</tr>
<tr>
<td><strong>ps</strong> Psychological support</td>
</tr>
<tr>
<td><strong>pe</strong> Psychoeducation</td>
</tr>
<tr>
<td><strong>aba</strong> Applied behavioural analysis</td>
</tr>
<tr>
<td><strong>or</strong> Organisation</td>
</tr>
<tr>
<td><strong>cr</strong> Cognitive restructuring</td>
</tr>
<tr>
<td><strong>prob</strong> Problem-solving</td>
</tr>
<tr>
<td><strong>3w</strong> Third-wave CBT</td>
</tr>
<tr>
<td><strong>pr</strong> Progressive muscle relaxation</td>
</tr>
<tr>
<td><strong>pat</strong> Parent training</td>
</tr>
</tbody>
</table>

ADHD, attention-deficit/hyperactivity disorder; CBT, cognitive–behavioural therapy.
Table 2  Forms of CBT according to mixed components

<table>
<thead>
<tr>
<th>Combinations of included components</th>
<th>Corresponding intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>w (±pl±pe±ps±pat)</td>
<td>Waiting list</td>
</tr>
<tr>
<td>pl</td>
<td>Psychological/pill placebo</td>
</tr>
<tr>
<td>pl+pat</td>
<td>Parent-training psychological/pill placebo</td>
</tr>
<tr>
<td>pl+pe</td>
<td>Psychoeducation (PE)</td>
</tr>
<tr>
<td>pl±pe+pat</td>
<td>Parent-training PE</td>
</tr>
<tr>
<td>pl (±pe)+ps</td>
<td>Supportive psychotherapy</td>
</tr>
<tr>
<td>pl (±pe±ps)+pr</td>
<td>Physiological therapy</td>
</tr>
<tr>
<td>pl (±pe±ps)+pr+pat</td>
<td>Parent-training physiological therapy</td>
</tr>
<tr>
<td>pl (±pe±ps)+pr+cr+pat</td>
<td>Cognitive therapy (CT)</td>
</tr>
<tr>
<td>pl (±pe±ps)+pr+cr+pat</td>
<td>Parent-training CT</td>
</tr>
<tr>
<td>pl (±pe±ps)+pr+aba/or/prob</td>
<td>Behavioural therapy (BT)</td>
</tr>
<tr>
<td>pl (±pe±ps)+pr+aba/or/prob+pat</td>
<td>Parent-training BT</td>
</tr>
<tr>
<td>pl (±pe±ps)+pr+cr+aba/or/prob</td>
<td>CBT</td>
</tr>
<tr>
<td>pl (±pe±ps)+pr+cr+aba/or/prob+3w</td>
<td>Parent-training CBT</td>
</tr>
<tr>
<td>pl (±pe±ps)+pr+cr+aba/or/prob+3w+pat</td>
<td>Parent-training 3w</td>
</tr>
</tbody>
</table>

‘+’ means ‘and’; ‘±’ means ‘with or without’; ‘/’ means ‘and/or’.

aba, applied behavioural analysis; CBT, cognitive-behavioural therapy; cr, cognitive restructuring; or, organisation; pat, parent training; pe, psychoeducation; pl, placebo; pr, progressive muscle relaxation; prob, problem-solving; ps, psychological support; w, waiting component; 3w, third-wave CBT.

that maintain the problems of adolescents and adults with ADHD, and to help them learn more appropriate cognitive and behavioural patterns. Accordingly, we will also exclude cognitive training without identification and case conceptualisation for cognitive–behavioural patterns.

Information sources
We will search the following five databases: MEDLINE (via PubMed), EMBASE, PsycINFO, ClinicalTrials.gov and Cochrane Library. If there is a discrepancy in the selected studies, a consensus will be reached with all review team members, including a third researcher, if necessary. The search will cover studies published up to 31 March 2022 and will be limited to articles published in English. For studies that have no data available, we will contact the corresponding author. If we do not hear back, we will contact them again in a month. If the information is still not available, the study will be excluded.

Search strategy
We will search each database using the term “attention-deficit/hyperactivity disorder” and terms describing CBT components, such as “acceptance commitment therapy”, “applied behavior analysis”, “attention training”, “behavior therapy”, “cognitive restructuring”, “cognitive therapy”, “cognitive behavioral therapy”, “metacognitive therapy”, “mindfulness”, “organization”, “problem solving” and “relaxation”. The full search strategy is provided in the online supplemental appendix 1.

Study records
The first screening (checking the titles and abstracts) will be conducted by four authors (SH, KM, SO and MY) in electronic databases. For the second screening, three authors (SH, KM and SO) will review the full text of all studies selected at the first screening to make selection decisions based on the eligibility criteria. Reviewers will resolve disagreements by discussion. If no data are available for the studies included in this review, we will contact the corresponding authors monthly for 2 months.

Two independent reviewers (SH and KM) will determine the classification of all arm components according to the definitions in table 1. Any discrepancies will be decided at a meeting of all members of this research team, including a third researcher.

Outcomes and prioritisation
Our primary outcome is the remission of ADHD in the short term, defined as within 6 months. For studies with multiple evaluation time points within 6 months of treatment, we will prioritise the 3-month time point. In this study, remission will be defined as not meeting diagnostic classification criteria for ADHD in the International Classification of Diseases or Diagnostic and Statistical Manual of Mental Disorders at evaluation time after the treatment. Accepting the suggestions of Mattingly et al, we consider remission if the total ADHD Rating Scale scores are 18 or less (the 18 symptoms of ADHD are mild or
less on average). Other remission criteria are a mean score of 1 in Swanson, Nolan and Pelham, Version IV; a total score of 2 in Clinical Global Impressions-Severity scale; and a mean score of 5 in Conner’s Parent Rating Scale-Revised, Inattention/Overactivity subscale. As a secondary outcome, we will include treatment response and the ADHD core symptoms scales (see online supplemental tables 1 and 2 for scales). The response, as defined by the original investigators, is a dichotomous outcome expressing the number of patients who had a substantial improvement from baseline (eg, at least a 30% reduction in the Barkley Adult ADHD Rating Scale-IV score or in the Reliable Change Index as determined by another assessment method).

**Risk of bias in individual studies**

The risk of bias will be independently assessed by two authors (SH and KM) using the Cochrane tool.

**Data synthesis**

We will compare CBT components of interest with each other for remission and the change in core ADHD symptoms’ severity. The concepts of the components to be compared and their combinations are shown in tables 1 and 2. For the Bayesian analysis, we will perform a cNMA model presented by Welton et al. We will fit cNMA models using Stan according to the methods of Pompoli et al. We will estimate and compare the additive cNMA model and two-way interaction cNMA model. We will use uninformative prior distributions for the treatment effects and all coefficients in the meta-regression analyses, that is, $N(0,1000)$. A minimally informative prior will be used for the heterogeneity parameter, that is, $N(0,1)$ $I(0,.)$. For all analyses, we will run four chains of 40 000 samples and discard the first 20 000 samples. We will evaluate the convergence of the model using the Brooks-Gelman-Rubin diagnostic. We will conduct a sensitivity analysis with a different prior distribution for heterogeneity, $U(0,5)$. We will also report ORs, calculated standardised mean differences and Hedge’s $g$ with relative 95% CIs, for continuous and dichotomous outcomes. We will perform both frequentist and Bayesian analyses. In the sensitivity analysis, we will report combinations of the CBT components in a frequentist setting using the ‘discomby’ command in netmeta.

We will also conduct another sensitivity analysis using results from studies in which only an expert measured the outcome. If the participants in each RCT are limited to adolescents or adults, then their data will be used in subgroup analyses by a procedure similar to the main analysis.

To rank the components, we intend to use the surface under the cumulative ranking curve and the mean ranks. Depending on the pooled data, the model may not have enough power to draw useful conclusions. In that case, we will group the components in a clinically meaningful manner. In other words, we will examine whether the estimation can be improved by assuming general effects on applied behavioural analysis, organisation, third-wave CBT and progressive muscle relaxation.

We will measure the heterogeneity among the selected studies by estimating the common heterogeneity parameter $\tau$. For dropout outcomes, we will compare their empirical distributions. We will report changes in $\tau$ by including any differences observed between the studies in the model as covariates. We will also assess treatment-level inconsistency in the constructed network by using the design-by-treatment inconsistency model.

**Meta-bias(es)**

We will perform Egger’s test to test for small study effects, including publication bias.

**Patient and public involvement**

None.

**Ethics and dissemination**

Since we will review published papers, ethical approval is not required. The results from this cNMA will provide a panorama of CBT-based ADHD studies, and the findings will be published in a peer-reviewed journal.

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**Contributors**

All authors contributed to the design of this cNMA. SH contributed to the acquisition of research funding. KM and YK contributed to statistical analysis strategies. SH and KM contributed to the writing of the manuscript. YK, SO, MY and YM critically reviewed this manuscript and contributed to its quality improvement. YM contributed to the construction and management of the research team.

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**Competing interests**

None declared.

**Patient and public involvement**

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication**

Not required.

**Provenance and peer review**

Not commissioned; externally peer reviewed.

**Supplemental material**

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