DOI:
10.1002/erv.2522

Document Version
Peer reviewed version

Evidence for Cognitive Remediation Therapy in young people with anorexia nervosa: Systematic Review and Meta-analysis of the literature

Tchanturia K[1, 2,3*], Giombini L[1,4], Leppanen J[1], Kinnaird E[1]

[1] King's College London, Department of Psychological Medicine, Institute of Psychiatry, Psychology Neuroscience, London, UK

[2] South London and Maudsley NHS Foundation Trust, London, UK

[3] Illia State University, Tbilisi, Georgia

[4]Rhodes Wood Hospital, Elysium Healthcare, London (UK)

Address for correspondence: Dr Kate Tchanturia, PhD. PO59, King's College London, Institute of Psychiatry, Psychology and Neuroscience, Department of Psychological Medicine, De Crespigny Park, London SE5 8AF, UK. Tel: +44 (0)207 848 0134, Fax: +44 (0)207 848 0182, Email: kate.tchanturia@kcl.ac.uk, Website: www.katetchanturia.com

Running head: CRT young people meta-analysis

Abstract: 131; Word count: (without references and tables): 3519; Pages: 22;

Acknowledgments: We would like to thank Dr Amy Harrison and colleagues allowing us to include their data in the meta-analysis.

Abstract

Cognitive Remediation Therapy (CRT) for eating disorders has demonstrated promising findings in adult age groups, with randomised treatment trials and systematic reviews demonstrating medium to large effect sizes in improved cognitive performance. In recent years, several case series have been conducted for young people with anorexia nervosa (AN), but these findings have not been synthesized in the form of a systematic review. This systematic review aimed to evaluate the evidence for the efficacy of CRT in child and adolescent age groups. Nine studies were identified, with a subsequent meta-analysis suggesting improvements in cognitive performance with small effect sizes. Patient feedback was positive, with low dropout rates. These findings suggest that CRT has potential as a supplementary treatment for young people with AN, warranting further investigation using randomised treatment trials.

Keywords: cognitive remediation, systematic review, anorexia nervosa, adolescent, young adults, therapy

Introduction

Anorexia nervosa (AN) is a severe and chronic eating disorder (ED) with few effective treatments (NICE, 2004; Bulik, 2014). A key challenge in the treatment of AN is the neuropsychological profile of the illness: cognitive-interpersonal maintenance models suggest that difficulties in cognitive functioning contribute to the enduring nature of the disorder (Treasure & Schmidt, 2013; Southgate et al, 2005). Specifically, individuals with AN exhibit several inefficiencies in cognitive processing that may compromise the efficacy of conventional talking therapies that require the patient to engage in complex cognitive processes (Tchanturia & Lang, 2015).

Cognitive Remediation Therapy (CRT), an umbrella term for psychological interventions that use a range of cognitive training exercises to reflect on cognitive processes, develops new strategies and thinking skills and facilitates "thinking about thinking" to enable patients to make behavioural changes (Tchanturia et al, 2010). CRT was first introduced to ED treatment in 2005 as a new approach for adults with chronic and enduring AN (Davies & Tchanturia, 2005; Tchanturia et al, 2006). CRT has since been established as a manualised, brief intervention for AN (Tchanturia et al, 2010).

There are two key areas of executive functioning difficulty in adults with AN: set shifting, the ability to move flexibility across strategies, stimuli and different tasks; and central coherence, the ability to process information in a gestalt style that encourages the individual to look at a "bigger picture" context instead of focusing on details (Tchanturia et al, 2008; 2011; 2012; Lang et al, 2014, 2016a). This is reflected in the clinical presentation of AN, with symptoms including rule-focused behaviour, fixation with routines and resistance to change (Tchanturia et al, 2013). CRT for AN targets these domains using cognitive flexibility and gestalt processing exercises that encourage individuals to be aware of their cognitive styles, with the goal of developing alternative ways of thinking and applying these techniques in real life.

CRT is typically delivered on an individual basis over 10 sessions lasting 45 minutes, taking place once or twice weekly (depending on clinical resources and treatment programmes). In addition, CRT has been adapted into a briefer format for group interventions (Genders & Tchanturia, 2010) for adults and more recently for young people (YP) with AN (Pretorius et al, 2012). Case series, randomised treatment trials and systematic reviews for CRT in adults with AN have confirmed improved cognitive flexibility, quality of life and motivation to change, with medium to large effect sizes (for systematic review of adult studies: Tchanturia et al, 2014; for key single studies : Abbate-Daga et al, 2012; Brockmeyer et al 2013; Dingemans et al, 2014).

There have been fewer studies documenting the effects of CRT in YP with AN. Recent research has confirmed that this age group exhibits similar cognitive inefficiencies (Lang et al, 2015; Lang et al, 2016b; Westwood et al, 2016), and specific CRT protocols have been developed for use with adolescents in a variety of clinical settings (Maiden et al, 2014; Bakeret al, 2014; Fitzpatrick & Lock, 2015). These include the use of "stepped tasks" to accommodate a range of different cognitive abilities, and additional support to encourage metacognitive reflection. Games and exercises appropriate for a younger population have also been introduced into the group CRT manual for YP (Maiden et al, 2014). Nonetheless, the effect of CRT on AN in YP is not well documented: at present there are no randomised treatment trials, and the evidence consists of case studies and adaptations of CRT for adolescent group therapy.

Although two systematic reviews on CRT in adults with ED have been published in peer reviewed journals (Tchanturia et al 2014; Dahlgren & Rø, 2014), no review to date has examined this evidence in an adolescent population. Therefore, this systematic review aims to synthesise the existing evidence for the effects of CRT in YP with AN whilst comparing these findings to research in adult populations.

Method

The review was conducted according to the 'PRISMA' (Preferred Reporting Items For Systematic Reviews and Meta-Analysis) statement (Moher et al., 2009).

Eligibility Criteria

YP were defined in this study as individuals under the age of 18. Studies examining CRT or training interventions targeting AN either in an individual or a group context in adolescent clinical populations were included in the review. Only papers reporting data were considered; theoretical and opinion CRT papers were excluded. Self-help or web-based programmes were also excluded. Both quantitative and qualitative studies were considered.

Information Sources and Search

An electronic search was conducted between December 2016 and March 2017 using the PubMed, PsycInfo, Web of Science, SCOPUS databases. The search terms used were anore* and eating disorders combined with ((cognit*) and (remed* or train* neuropsychology)). These search terms allowed for multiple spellings, plurals and combinations. Only published, peer-reviewed literature available in English was considered. The titles, abstracts and full texts were screened by first and second authors. Articles were also found via hand searches of reference lists by first and second authors. First and second authors had consensus meetings to screen duplicates, inspect details of the manuscript and explore the possibility of conducting meta-analysis on reported outcomes. One unpublished study (Harrison et al, in progress) was identified by the first author and included in the review.

Summary Measures

As CRT targets cognitive styles, this systematic review focused on evaluating cognitive changes following the intervention. After the manual screen of the literature we decided to

conduct meta-analyses on outcomes where three or more studies had reported the same outcome measure. Consequently, meta-analysis was conducted on one set shifting task (TMT; Reitan, 1958), one central coherence task (ROCFT; Osterrieth, 1944), and the BRIEF (Guy, Isquith & Gioia, 2004). All above measures satisfied requirements to conduct meta-analysis on the data. TMT and ROCFT are experimental measures and the BRIEF is a self-report measure that assesses YP's views of their executive functions in everyday life. This generates scores on two key scales: the Behavioural Regulation Index (BRI), comprising of inhibit, shift, emotional control and monitor, and the Metacognitive Index (MI), comprising of working memory, plan/ organise, organisation of materials and task completion.

Statistical analysis

Statistical analyses were conducted using the Metafor package in R (Viechtbauer, 2010). Along with 95% confidence intervals, Standardised Mean Change (SMC) with change score standardisation was used to estimate the effect sizes, which were interpreted as small (≥0.20), medium (≥0.50), and large (≥0.80; Hedges, 1981). SMC adjusts the effect size estimates for the correlation in task performance and self-report assessments between the two assessments (pre-CRT, post-CRT). If correlation coefficients were not reported, they were estimated using the following formula: $r = \frac{SDpre^2 + SDpost^2 - SDchange^2}{2 * SDpre * SDpost}$ (Morris and DeShon, 2002).

In the ROCFT positive scores indicate better central coherence. Thus, positive effect size estimates in the present review indicate improved central coherence, as measured with the ROCFT following CRT, and negative effect size estimates indicate reduced central coherence. In the TMT and BRIEF questionnaire lower scores indicate less time spent on the task and better executive functioning, respectively. Thus, negative effect size estimates in the present review indicate improved performance on TMT or improved executive functioning as

measured by the BRIEF, and positive effect size estimates indicate reduced performance on the TMT or reduced executive functioning as measured by the BRIEF. A *p* value of <0.05 was considered significant.

We conducted random effects meta-analyses using the *rma* function to examine changes in participants' performance on the ROCFT and TMT from baseline to after CRT intervention. Because the BRIEF consisted of two subscales the data was entered into multivariate meta-analysis with an autoregressive structure using the *rma.mv* function to examine changes in participants' self-reported MI and BRI from baseline to after CRT intervention. Between-study heterogeneity was examined by calculating I^2 and Cochran's Q indexes. Significant between-study heterogeneity was further explored with meta-regressions to examine the extent to which the following variables moderated the heterogeneity: change in Body Mass Index (BMI) and number of sessions.

Risk of bias across studies

Publication bias was assessed using Begg's rank correlation test (Begg & Mazumdar, 1994). Robustness of significant findings was examined using Rosenthal's file drawer analysis, which provides a fail-safe number (N) of studies required to find non-significant results to reduce the observed effects to null. If the fail-safe N exceeds the Rosenthal's criterion, 5k+10, where k indicates number of studies in the meta-analysis, the observed effect can be considered robust (Rosenthal, 1979).

Results

Study Selection

After preliminary searches, a total of 217 studies were screened, 20 were followed up, and 9 studies were included in the review. This included one large dataset (Harrison et al, in progress) known to the first author as the clinical supervisor (Figure 1 and Table 1 for details). 11 articles were excluded due to not being written in English, not reporting data, or using a self-help intervention.

Figure 1. Study selection flow chart.

HERE

Study Characteristics

Case studies and series (Individual CRT)

The majority of studies identified in the review were either single or multiple case studies on individuals with AN. An inpatient case series (n=20) found significant improvements in a number of neuropsychological functions, including visuo-spatial memory, visuo-spatial processing and verbal fluency. However, they did not exhibit expected changes in executive functioning (Lindvall Dahlgren et al, 2013).

Whilst this study did not use control groups, a subsequent paper compared inpatients and outpatients receiving CRT to healthy controls (n=20; van Noort et al, 2016). Compellingly, this study found improvements in cognitive flexibility following the intervention (using different neuropsychological tests), whereas the healthy controls showed no improvement over the same time period. A subsequent follow up trial using this same sample, with some additional participants, (n=33) compared individuals with AN who received CRT to those who received no additional treatment (Herbich et al, 2017). Data was collected at the start of

treatment, at the end of treatment, and 6 months following the end of treatment. No significant differences in neuropsychological and clinical measures were identified between the groups, although BMI increases in the CRT sample showed a trend towards significance. However, the CRT sample exhibited higher levels of perfectionism and comorbidities at baseline, which may have negatively affected their response to treatment. The fact that improvements in cognitive flexibility immediately following CRT were not present at a 6 month follow up suggests that the short and long term effects of CRT needs further investigation.

Most recently, a larger uncontrolled trial (n=70) investigated the effects of CRT on inpatients with severe and complex ED (Harrison et al, in progress). Patients gave positive feedback, with low drop-out rates (1.43%), and demonstrated improvements in set shifting, central coherence and switching tasks with small to large effect sizes. There was also a large improvement in motivation to recover.

A single case study reported no change in neuropsychological profile, but the patient gave positive feedback and suggested that she was more conscious and reflective of her own thinking styles (van Noort et al, 2015). At 7 month follow up the patient exhibited a healthy, stable weight and a reduction in symptoms, with the patient and the treating psychiatrist reporting that the CRT intervention had helped her find a pathway to recovery. Self-report measures of cognitive flexibility were similarly positive: a patient and parent study (n=17; Lindvall Dahlgren et al, 2014) and an inpatient study (n=92; Giombini et al, 2016) both found that patients self-reported significant increases in cognitive flexibility and central coherence.

Group CRT

CRT for AN has been developed into a group format, delivered weekly over four sessions (Maiden et al, 2014). Similarly to individual interventions, Group CRT encourages flexible

and global thinking using psychoeducation, practical exercises and reflection, whilst additionally incorporating peer support, group facilitators, and the use of group discussion.

One study evaluated the effects of Group CRT for 30 adolescents being treated for AN as day patients (Pretorius et al, 2012). Patients received 10, twice weekly sessions for 30 minutes. Patients completed self-report measures and feedback forms at the first and last group sessions. There was a small effect size in self-reported cognitive flexibility and motivation to change following the group sessions, with cognitive flexibility changes approaching significance. Patients gave positive feedback, reporting that they enjoyed the practical tasks and found learning about thinking styles useful. The authors suggest that Group CRT could be a promising way to engage YP with AN in treatment.

In addition to individual CRT, Harrison et al (in progress) analysed outcomes for Group CRT. Intervention delivery was slightly different, with 55 patients receiving 10 sessions for 45 minutes once a week. Dropout rates were higher (9.0%) compared to individual CRT (1.4%), although overall patients gave positive feedback. Patients showed improvements in central coherence and self-reported cognitive flexibility, with small to medium effect sizes.

Qualitative studies

Whilst a number of the case studies incorporated qualitative elements in the form of patient feedback forms, a recent large study specifically analysed patient feedback letters (n=70) following individual CRT (Giombini et al, 2017). The majority of participants reported positive engagement in CRT, and reflected that they had learned about thinking styles and problem solving strategies. The exercises and homework used in CRT acted as a safe, unthreatening setting in which to practice cognitive skills which could then be applied in real life. Overall, the feedback suggests that CRT is an effective intervention for AN in YP.

Synthesis of results

Set Shifting

Four studies used the TMT to measure the effects of CRT on set shifting, as summarised in Figure 2. The random effects meta-analysis with a total sample size of 125 showed no significant effects of CRT intervention on TMT performance (SMC = -0.03, Z = -0.11, p = 0.911, 95% CI [-0.48, 0.43], k = 4).

Figure 2 Studies examining the effects of CRT intervention on set shifting.

HERE

SMCC = standardised mean change with change score standardisation; 95% CI = 95% confidence interval.

There was significant between-study heterogeneity (I^2 = 80.57%, Q = 14.34, p = 0.003), which was explored further with meta-regressions. Number of sessions significantly explained the between-study heterogeneity (R^2 = 93.65, Qm = 9.73, p = 0.002; Supplementary Figure 1), leaving no significant residual heterogeneity (I^2 = 22.91%, Qr = 2.31, p = 0.316). This finding suggests that studies that offered fewer sessions found greater improvement on the TMT. However, this meta-analysis only consisted of four studies. Therefore, this finding is likely due to the low number of studies examined and so should be interpreted with caution. Change in BMI following CRT intervention did not significantly explain the heterogeneity (R^2 < 0.01%, Qm = 1.03, p = 0.311; residual heterogeneity: I^2 = 75.09%, Qr = 7.82, p = 0.020; Supplementary Figure 2).

Begg's rank correlation test of funnel plot asymmetry did not reveal significant publication bias (T = -0.67, p = 0.333; Supplementary Figure 3).

Central Coherence

The forest plot of studies using the ROCFT to assess the effects of CRT on the central coherence of YP with AN is shown in Figure 3. The random effects meta-analysis with a total sample size of 272 showed a significant improvement in central coherence following CRT intervention with a small effect size (SMC = 0.41, Z = 6.49, p < 0.0001, 95% CI [0.29, 0.54], k = 6). There was no evidence of significant between-study heterogeneity (I^2 < 0.01%, Q = 5.39, p = 0.371).

Figure 3 Studies examining the effects of CRT intervention on central coherence.

HERE

SMCC = standardised mean change with change score standardisation; 95% CI = 95% confidence interval.

Begg's rank correlation test of funnel plot asymmetry did not reveal significant publication bias (T = 0.33, p = 0.469; Supplementary Figure 4). Rosenthal's file drawer analysis revealed a fail-safe N of 85, indicating that 85 studies finding no significant effect of CRT on the ROCFT would need to be added to the present meta-analysis to reduce the observed effects to null. This exceeds Rosenthal's criterion (5k+10=40) suggesting that the present finding was robust.

Executive Function Behaviours Inventory

The forest plot of studies using the BRIEF questionnaire to assess the effects of CRT on the executive functions of YP with AN is shown in Figure 4. The multivariate meta-analysis consisting of 148 participants showed an overall significant improvement in executive functioning following CRT intervention with a small effect size (SMC = 0.32, Z = 4.98, $p < 0.0001$, 95% CI [0.19, 0.44], k = 8, N of levels = 4). There was a significant improvement on both MI (SMC = 0.36, Z = 4.25, $p < 0.0001$, 95% CI [0.19, 0.53], k = 4, N of levels = 4) and BRI (SMC = 0.31, Z = 3.45, p = 0.001, 95% CI [0.13, 0.48], k = 4, N of levels = 4). There was no evidence of significant between-study heterogeneity (I^2 = 4.22e-08%, Q = 4.17, p = 0.760).

Figure 4. Studies examining the effects of CRT intervention on BRIF.

HERE

SMCC = standardised mean change with change score standardisation; 95% CI = 95% confidence interval.

Begg's rank correlation test of funnel plot asymmetry did not reveal significant publication bias (T = 0.00, p = 1.00; Supplementary Figure 5). Rosenthal's file drawer analysis revealed a fail-safe N of 67, indicating that 67 studies finding no significant effect of CRT on the BRIEF would need to be added to the present meta-analysis to reduce the observed effects to null.

This exceeds Rosenthal's criterion (5k+10=30) suggesting that the present finding was robust.

Discussion

The aim of this study was to systematically appraise the literature to explore the effects of CRT on young age groups with AN. Studies on CRT for AN for YP consisted of single case studies, case series, and qualitative assessments. The review used a number of outcomes to evaluate CRT, including cognitive changes measured with experimental methods, the executive function behavioural inventory BRIEF, and qualitative feedback. Studies identified were predominantly case studies and series with low numbers, which may have contributed towards the inconsistent findings on cognitive tasks across different papers. The number of sessions and quality of reported findings also varied between the studies.

Methodological differences across the case series made it difficult to compare findings, with studies frequently using different outcome measures. However, the meta-analysis of common outcome measures indicated small effect size improvements in central coherence following CRT for individuals, suggesting that YP exhibited a gestalt information processing style following CRT. Less consistency was observed on set shifting tasks across the different studies, with studies using fewer CRT sessions apparently showing greater improvement. This unusual finding is likely due to the small number of studies using this measure and small sample sizes in each study suggesting that whilst CRT could potentially be effective in

encouraging cognitive flexibility in YP, further research is needed to clarify these effects. This could include exploring the optimal number of sessions for YP in individual in group settings. Overall executive functioning, as measured by BRIEF, showed significant improvements after CRT. However, this analysis may have been compromised due to two studies from the same research group using overlapping samples (van Noort et al, 2016 and Herbrich et al, 2017).

All studies reported positive feedback from service users and clinicians, suggesting that CRT has good feasibility in YP. On the basis of these findings, CRT could be potentially helpful as a tool to aid therapeutic engagement in YP when the patient may not be able to participate in more intensive psychological therapies. This is particularly significant as early engagement in treatment is linked to better outcomes (Tchanturia, Lloyd, & Lang, 2013, Tchanturia et al, 2014). Although not all studies reported attrition rates, the majority of studies had less than 20% drop out rates. These findings suggest that CRT could have potential in YP; however, randomised control trials (RCT) are needed to clarify often inconsistent neuropsychological outcomes.

This study also examined findings from studies on Group CRT. Similarly to adult studies, patients in adolescent AN groups gave positive feedback (Zuchova et al, 2013). However, improvements in self-reported cognitive flexibility and motivation to change were non-significant, despite a small effect size. Group CRT needs further investigation in this age group using a consistent intervention format in order to investigate its effectiveness in cognitive outcomes, dropout rates and general functioning.

It is clear that the effects of CRT for YP with AN appear to be less constant than for adults, where improvements in set shifting and central coherence are more consistently documented (Lang et al, 2016, Tchanturia et al, 2012, Tchanturia, Lounes & Holttum, 2014). In particular,

the effect sizes found in this study are smaller than those compared to adult age groups (Tchanturia et al 2014, Dahlgren & Rø, 2014). However, these differences highlight the discrepancy in research output in these two age groups: CRT for adults with AN has been more widely investigated, with multiple RCTs with larger samples than the case series used to investigate YP. Further research into the efficacy of CRT in younger populations should investigate whether CRT is truly less effective in adolescents relative to adults, or whether effect sizes in YP studies improve with the use of larger sample sizes and study designs more comparable to studies using adult populations.

Research Implications

At present, the studies on CRT in adolescents with AN are predominantly case series with small sample sizes uncontrolled for potentially confounding variables. Nonetheless, taken together, these studies suggest that the benefits of CRT for adults with AN are potentially reproducible in YP. It is not clear from available studies whether CRT has any effect on factors such as functional outcomes, motivation, therapeutic uptake on further therapies or dropout rates. Therefore, CRT for YP with AN should now be evaluated using RCTs that include neuropsychological, self-report and clinical measures in order to draw firmer conclusions. The present findings will therefore aid future research studies in targeting these gaps in the existing evidence.

Conclusion

CRT is not a standalone treatment for eating disorder patients: in the course of 8-10 sessions it is unrealistic to change complex illness related behaviours and functioning. However, these studies indicate that it is possible over the course of this low-intensity treatment for YP with AN to develop awareness of their cognitive styles and information processing, using approaches that the patients respond to positively. Whilst these early studies indicate

promising results for CRT, RCTs are needed to fully explore the effects of the treatment on YP with AN.

References

Abbate-Daga, G., Buzzichelli, S., Marzola, E., Amianto, F., & Fassino, S. (2012). Effectiveness of cognitive remediation therapy (CRT) in anorexia nervosa: A case series. *Journal of Clinical and Experimental Neuropsychology*, 34(10), 1009-1015. doi:10.1080/13803395.2012.704900

Begg, C.B., Mazumdar, M., 1994. Operating characteristics of a rank correlation test for publication bias. Biometrics, 1088-1101.

Brockmeyer T, Ingenerf K, Walther S, Wild B, Hartmann M, Herzog W, Bents H, Friederich HC: Training cognitive flexibility in patients with anorexia nervosa: a pilot randomized controlled trial of cognitive remediation therapy. Int J Eat Disord. 2013, 47 (1): 24-31.

Bulik, C. (2014). The challenges of treating anorexia nervosa. *The Lancet*, 383(9912), 105-106. doi: 10.1016/S0140-6736(14)60007-6

Dahlgren, C., Rø, Ø. (2014) A systematic review of cognitive remediation therapy for anorexia nervosa: Development, current state and implications for future research and clinical practice. *Journal of Eating Disorder* 2:26

Dingemans, A. E., Danner, U. N., Donker, J. M., Aardoom, J. J., van Meer, F., Tobias, K., . . . van Furth, E. F. (2014). The effectiveness of cognitive remediation therapy in patients with a severe or enduring eating disorder: A randomized controlled trial. *Psychotherapy and Psychosomatics*, 83(1), 29-36. doi: 10.1159/000355240

Davies, H., & Tchanturia, K. (2005). Cognitive remediation therapy as an intervention for acute anorexia nervosa: A case report. *European Eating Disorders Review*, 13(5), 311-316. doi:10.1002/erv.655

Fitzpatrick, K. K., & Lock, J. D. (2015). CRT with children and adolescents in K. Tchanturia (Ed.), *Cognitive Remediation Therapy (CRT) for Eating and Weight Disorders* (pp 1-14). UK : Routledge.

Genders, R., & Tchanturia, K. (2010). Cognitive remediation therapy (CRT) for anorexia in group format: A pilot study. *Eating and Weight Disorders*, 15(4), e234-e239. doi : 10.1007/BF03325304

Giombini L., Moynihan, J., Turco, M., & Nesbitt, S. (2016). Evaluation of individual cognitive remediation therapy (CRT) for the treatment of young people with anorexia nervosa. *Eating and Weight Disorders*, 1-7. http://dx.doi.org/10.1007/s40519-016-0322-4

Giombini L., Nesbitt, S., Waples, L., Finazzi, E., Easter, A., Tchanturia, T. (2017). Young people's experience of individual Cognitive Remediation Therapy (CRT) in an inpatient eating disorder service: a qualitative study. *Eating and Weight Disorders* DOI: 10.1007/s40519-017-0369-x

Guy, S. C., Isquith P. K., & Gioia, G. A. (2004). *Behaviour Rating Inventory of Executive Function- Self Report version (BRIEF-SR).* USA : Psychological Assessment Resources Inc.

Harrison, A., Stavri, P., Ormond, L., McEneny, F., Akyol, D., Quershi, A., Al-Khairulla, H. (in progress). Cognitive Remediation Therapy for Children and Adolescents with Severe and Complex Eating Disorders in an Inpatient Setting : A Treatment Trial. Manuscript submitted for publication.

Hedges, L. V. (1981). Distribution theory for Glass's estimator of effect size and related estimators. Journal of Educational Statistics, 6(2), 107-128.

Herbrich., L., van Noort, B., Pfeiffer, E., Lehmkuhl, U., Winter, S., Kappel, V. (2017) Follow-Up Assessment of Cognitive Remediation Therapy in Adolescent Anorexia Nervosa: A pilot study. *European Eating Disorders Review* ;25(2):104-113. doi: 10.1002/erv.2501.

Lang K, Roberts M, Lopez C, Goddard E, Khondoker M, Treasure J, Tchanturia K; (2016) An investigation of central coherence in eating disorders: A synthesis of studies using the Rey Osterrieth Complex Figure Test; Plos one doi: 10.1371/journal.pone.0165467

Lang, K., Lopez, C., Stahl, D., Tchanturia, K., & Treasure, J. (2014). Central coherence in eating disorders: An updated systematic review and meta-analysis. *The World Journal of Biological Psychiatry*, 15(8):586-98. doi: 10.3109/15622975.2014.909606.

Lang, K., Lloyd, S., Khondoker, M., Simic, M., Treasure, J., Tchanturia, K. (2015) Do Children and Adolescents with Anorexia Nervosa Display an Inefficient Cognitive Processing Style? *PLoS ONE* 10(7): e0131724. doi:10.1371/journal.pone.0131724

Lang, K., Treasure, J., & Tchanturia, K. (2016b). Is inefficient cognitive processing in anorexia nervosa a familial trait? A neuropsychological pilot study of mothers of offspring with a diagnosis of anorexia nervosa. The World Journal of Biological Psychiatry, 17(4), 258-265.

Lindvall Dahlgren, C. L., Lask, B., Landrø, N. I., & Rø, Ø. (2013). Neuropsychological functioning in adolescents with anorexia nervosa before and after cognitive

remediation therapy: a feasibility trial. *International Journal of Eating Disorders*, 46(6), 576-81. doi: 10.1002/eat.22155.

Lindvall Dahlgren, C. L., Lask, B., Landrø, N. I., & Rø, Ø. (2014). Patient and parental self-reports of executive functioning in a sample of young female adolescents with anorexia nervosa before and after cognitive remediation therapy. *European Eating Disorders Review*, 22(1), 45-52. doi: 10.1002/erv.2265.

Maiden, L., Baker, L., Espie, J., Simic, M., Tchanturia, K. (2014) *Group Cognitive Remediation Therapy for Adolescents with Anorexia Nervosa. The Flexible Thinking Group*. Maudsley Hopsital, King's College London. http://media.wix.com/ugd/2e1018_bb804c6eeca3421d98e4fb29f20dea1e.pdf. Accessed 10 November 2016

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med*, 6(7), e1000097. doi:10.1371/journal.pmed.1000097

Morris, S.B., DeShon, R.P., 2002. Combining effect size estimates in meta-analysis with repeated measures and independent-groups designs. Psychological methods 7, 105-125.

National Institute for Health and Care Excellence (NICE) (2004). *Eating disorders: Core interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders*. Retrieved from http://guidance.nice.org.uk/CG9

Osterrieth, P. (1944). The test of copying a complex figure: A contribution to the study of perception and memory. *Archives de Psychologie*, 30, 206-356.

Pretorius, N., Dimmer, M., Power, E., Eisler, I., Simic, M., & Tchanturia, K. (2012). Evaluation of a cognitive remediation therapy group for adolescents with anorexia

nervosa: Pilot study. *European Eating Disorders Review*, 20(4), 321-325. doi:10.1002/erv.2176

Reitan, R.M. (1958). Validity of the Trail Making Test as indicator of organic brain damage. Perceptual and Motor Skills, 8, 271–276.

Rosenthal, R., 1979. The file drawer problem and tolerance for null results. Psychol Bull 86, 638-641.

Southgate, L., Tchanturia, K., & Treasure, J. (2005). Building a model of the aetiology of eating disorders by translating experimental neuroscience into clinical practice. *Journal of Mental Health*, 14(6), 553-566. doi: 10.1080/09638230500347541

Tchanturia, K., Davies, H., Lopez, C., Schmidt, U., Treasure, J., & Wykes, T. (2008). Letter to the editor: Neuropsychological task performance before and after cognitive remediation in anorexia nervosa: A pilot case-series. *Psychological Medicine*, 38(9), 1371-1373. doi: 10.1017/S0033291708003796

Tchanturia, K., Davies, H., Reeder, C., & Wykes, T. (2010). *Cognitive remediation therapy for anorexia nervosa*. London, UK: King's College London, University of London.

Tchanturia, T., Davies, H., Roberts, M., Harrison, A., Nakazato, M., Schmidt, U., . . . Morris, R. (2012). Poor cognitive flexibility in eating disorders: Examining the evidence using the wisconsin card sorting task. *PloS One*, 7(1), e28331. doi: 10.1371/journal.pone.0028331

Tchanturia, K., Harrison, A., Davies, H., Roberts, M., Oldershaw, A., Nakazato, M., … Treasure, J. (2011). Cognitive Flexibility and Clinical Severity in Eating Disorders. *PLoS ONE*, 6(6), e20462. http://doi.org/10.1371/journal.pone.0020462

Tchanturia, K. & Lang, K. (2015). Cognitive profiles in adults and children with anorexia nervosa and how they have informed us in developing CRT for anorexia nervosa. In

K. Tchanturia (Ed.), *Cognitive Remediation Therapy (CRT) for Eating and Weight Disorders* (pp 1-14). UK : Routledge.

Tchanturia, K., Lloyd, S., & Lang, K. (2013). Cognitive remediation therapy for anorexia nervosa: Current evidence and future research directions. *International Journal of Eating Disorders*, 46(5), 492-495. doi: 10.1002/eat.22106

Tchanturia, K., Lounes, N., & Holttum, S. (2014). Cognitive remediation in anorexia nervosa and related conditions : A systematic review. *European Eating Disorders Review*, 22(6), 454-462. doi : 10.1002/erv.2326.

Tchanturia, K., Whitney, J., & Treasure, J. (2006). Can cognitive exercises help treat anorexia nervosa? *Eating and Weight Disorders*, 11(4), e112-6. doi: 10.1007/BF03327574

Treasure, J., & Schmidt, U. (2013). The cognitive-interpersonal maintenance model of anorexia nervosa revisited: a summary of the evidence for cognitive, socio-emotional and interpersonal predisposing and perpetuating factors. *Journal of Eating Disorders*, 1, 13. http://doi.org/10.1186/2050-2974-1-13

van Noort, BM., Pfeiffer, E., Lehmkuhl, U., Kappel, V. (2015). Cognitive Remediation Therapy for Children with Anorexia Nervosa. Z Kinder Jugendpsychiatr Psychother. 2015 Sep;43(5):351-5. doi: 10.1024/1422-4917/a000372

van Noort, B. M., Kraus, M. K. A., Pfeiffer, E., Lehmkuhl, U., & Kappel, V. (2016). Neuropsychological and Behavioural Short-Term Effects of Cognitive Remediation Therapy in Adolescent Anorexia Nervosa: A Pilot Study. *European Eating Disorders Review*, 24(1), 69-74.

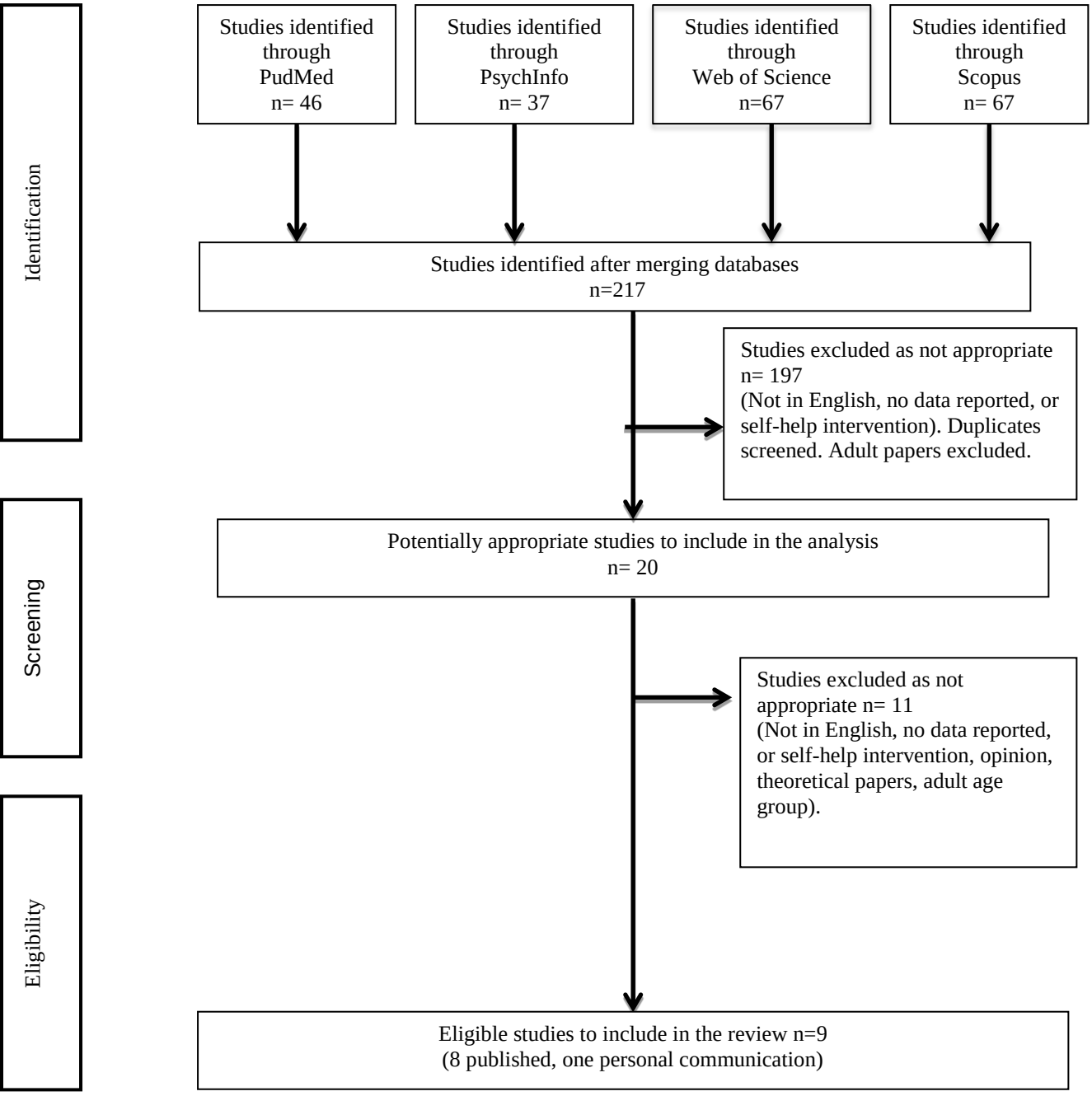
Viechtbauer, W. (2010). Conducting meta-analyses in R with the metafor package. Journal of Statistical Software, 36(3), 1–48.

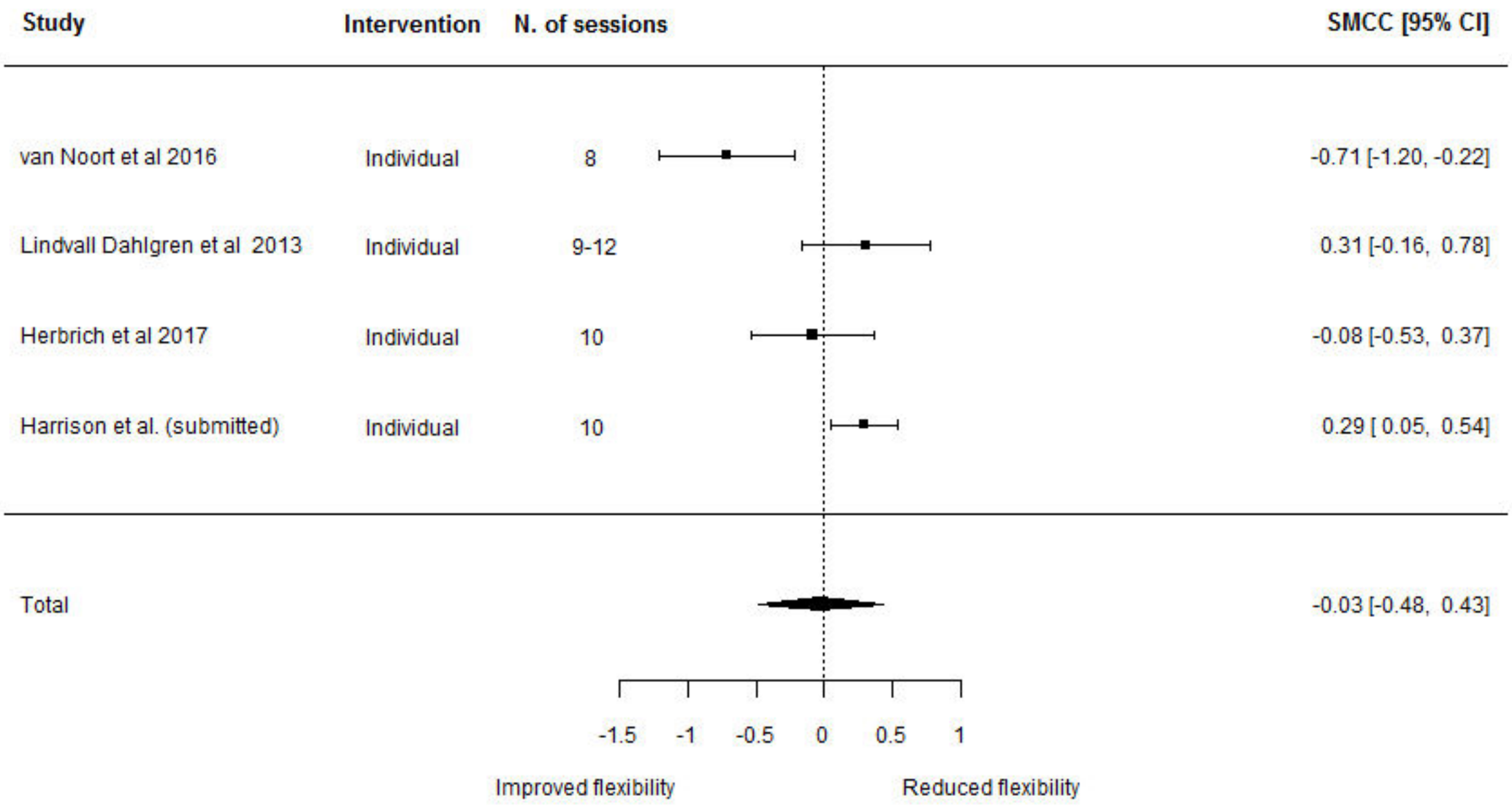
Westwood, H., Stahl, D., Mandy, W., & Tchanturia, K. (2016). The set-shifting profiles of anorexia nervosa and autism spectrum disorder using the Wisconsin Card Sorting Test: a systematic review and meta-analysis. *Psychological medicine*, 46(09), 1809-1827.

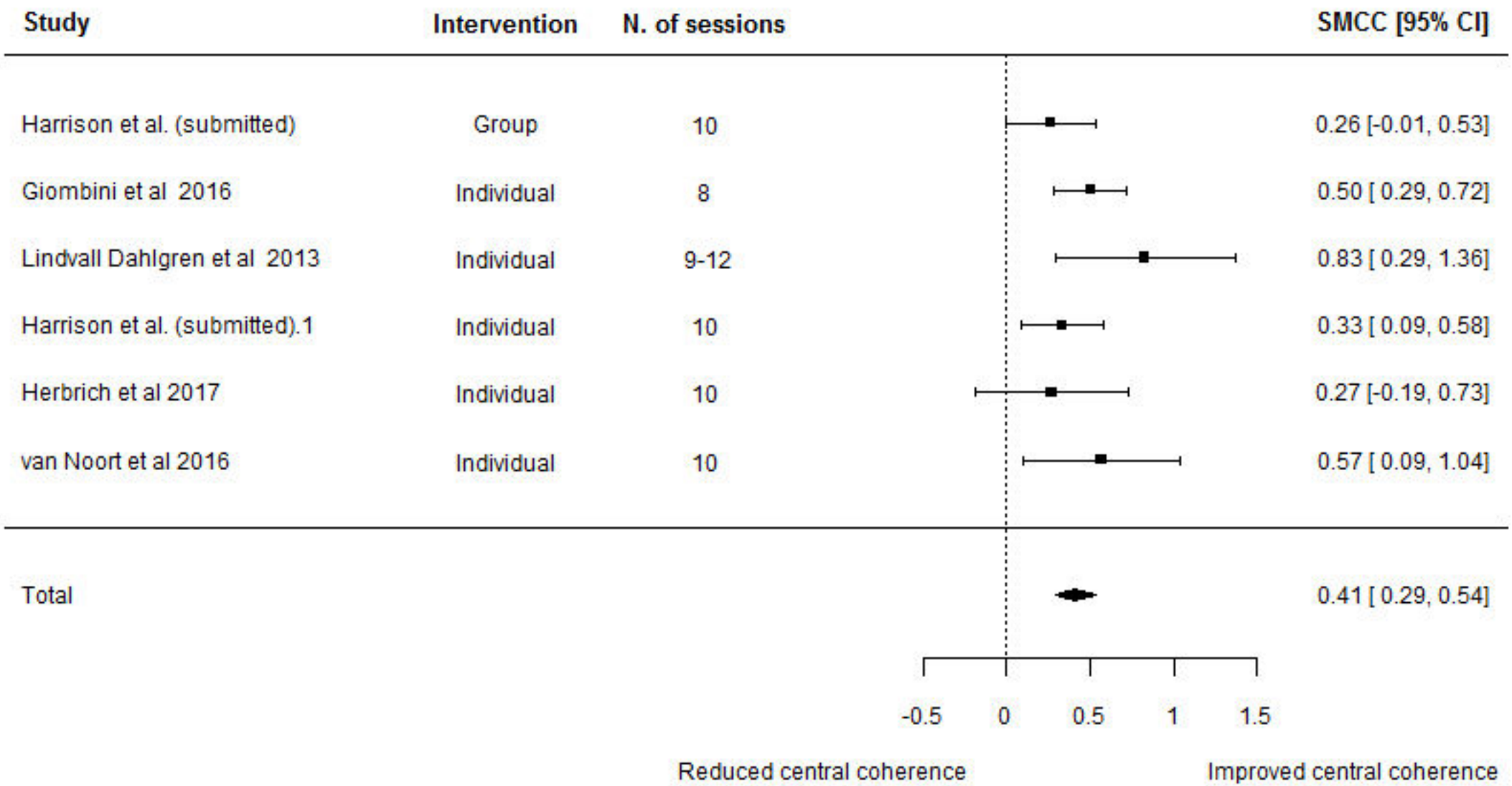
Wood, L., Al-Khairulla, H., & Lask, B. (2011). Group cognitive remediation therapy for adolescents with anorexia nervosa. *Clinical Child Psychology and Psychiatry*, 16(2), 225-231. doi:10.1177/1359104511404750

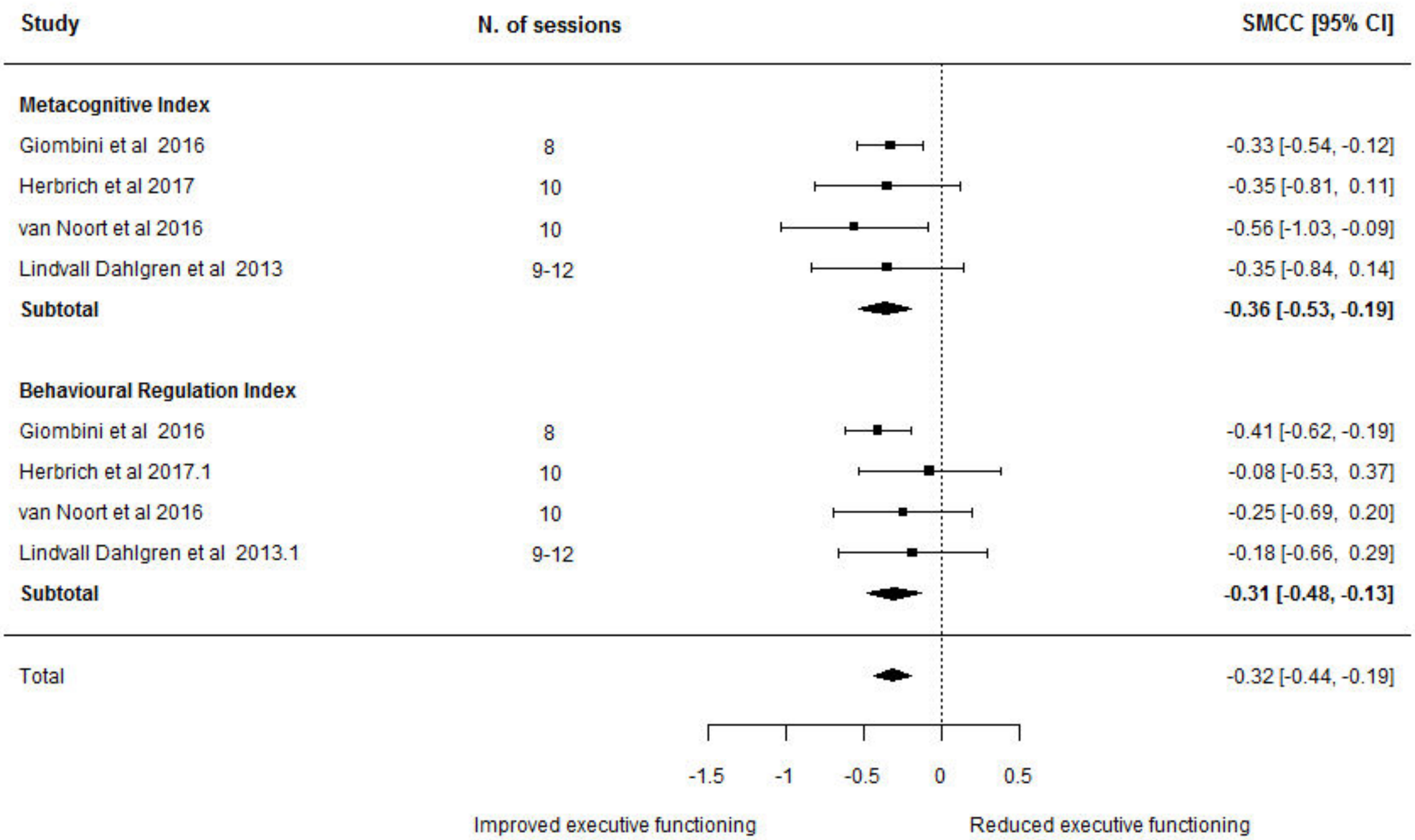
Zuchova, S., Erler, T., & Papezova, H. (2013). Group cognitive remediation therapy for adult anorexia nervosa inpatients: First experiences. Eating and Weight Disorders, 18, 269–273. doi: 10.1007/s40519-013-0041-z

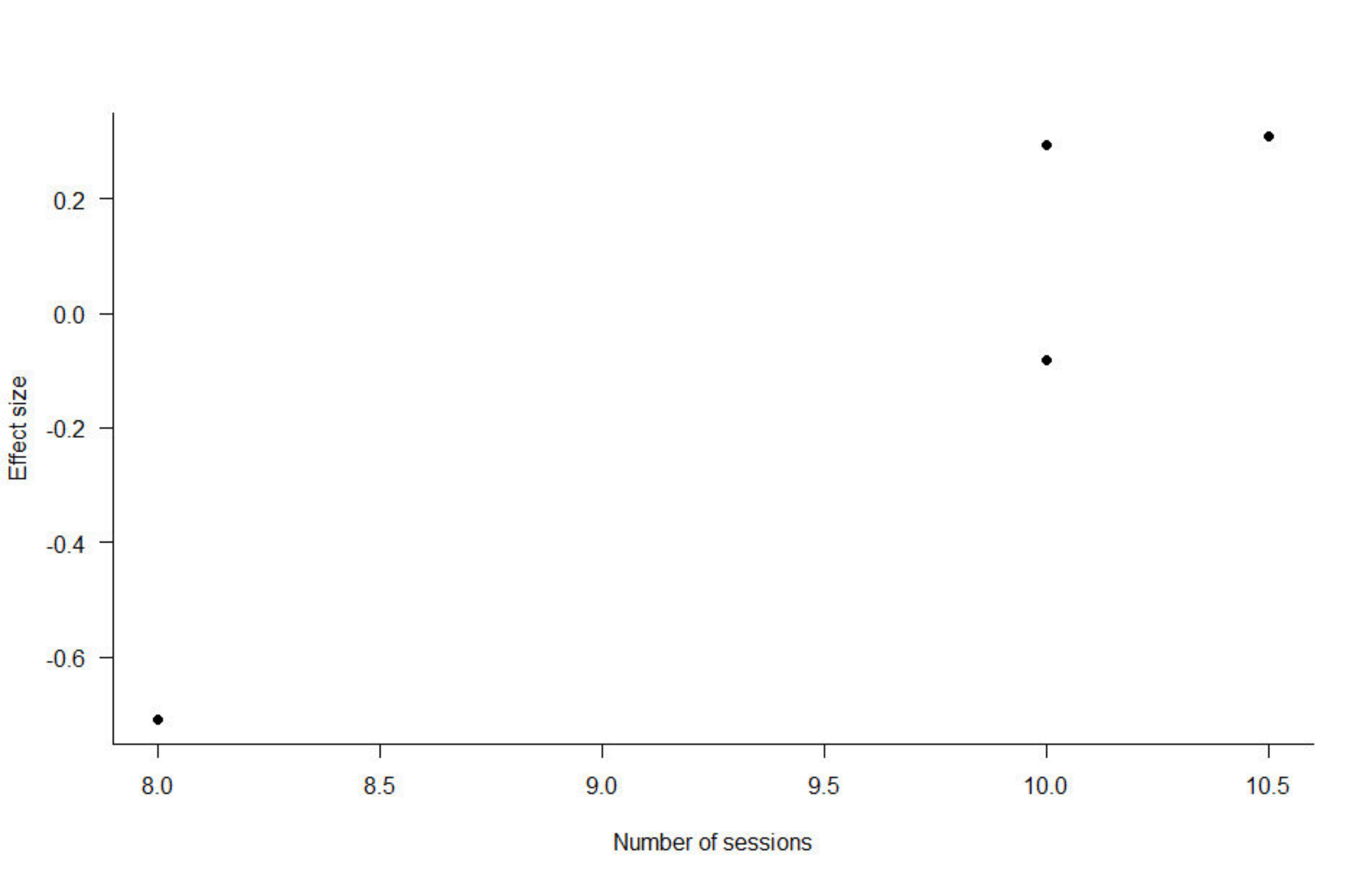
Figure 1: Flow diagram for the study




Study
Intervention
N. of sessions
SMCC [95% CI]
van Noort et al 2016
Individual
8
-0.71 [-1.20, -0.22]
Lindvall Dahlgren et al 2013
Individual
9-12
0.31 [-0.16, 0.78]
Herbrich et al 2017
Individual
10
-0.08 [-0.53, 0.37]
Harrison et al. (submitted)
Individual
10
0.29 [0.05, 0.54]
Total
-0.03 [-0.48, 0.43]
-1.5
-1
-0.5
0
0.5
1
Improved flexibility
Reduced flexibility


Study
Intervention
N. of sessions
SMCC [95% CI]
Harrison et al. (submitted)
Group
10
0.26 [-0.01, 0.53]
Giombini et al 2016
Individual
8
0.50 [0.29, 0.72]
Lindvall Dahlgren et al 2013
Individual
9-12
0.83 [0.29, 1.36]
Harrison et al. (submitted).1
Individual
10
0.33 [0.09, 0.58]
Herbrich et al 2017
Individual
10
0.27 [-0.19, 0.73]
van Noort et al 2016
Individual
10
0.57 [0.09, 1.04]
Total
0.41 [0.29, 0.54]
-0.5
0
0.5
1
1.5
Reduced central coherence
Improved central coherence


Study
N. of sessions
SMCC [95% CI]
Metacognitive Index
Giombini et al 2016
8
-0.33 [-0.54, -0.12]
Herbrich et al 2017
10
-0.35 [-0.81, 0.11]
van Noort et al 2016
10
-0.56 [-1.03, -0.09]
Lindvall Dahlgren et al 2013
9-12
-0.35 [-0.84, 0.14]
Subtotal
-0.36 [-0.53, -0.19]
Behavioural Regulation Index
Giombini et al 2016
8
-0.41 [-0.62, -0.19]
Herbrich et al 2017.1
10
-0.08 [-0.53, 0.37]
van Noort et al 2016
10
-0.25 [-0.69, 0.20]
Lindvall Dahlgren et al 2013.1
9-12
-0.18 [-0.66, 0.29]
Subtotal
-0.31 [-0.48, -0.13]
Total
-0.32 [-0.44, -0.19]
-1.5
-1
-0.5
0
0.5
Improved executive functioning
Reduced executive functioning


0.2
0.0
-0.2
-0.4
-0.6
Effect size
8.0
8.5
9.0
9.5
10.0
10.5
Number of sessions