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Review article

The Efficacy of Cognitive Remediation in Depression: A Systematic Literature Review and Meta-Analysis

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ABSTRACT

Background: Individuals with major depressive disorder often experience cognitive deficits. Cognitive remediation (CR) is an intervention aimed at improving cognition in psychiatric disorders. However, its efficacy on global and specific domains of cognition in adults with depression requires systematic investigation. Further, given individual differences in treatment outcome, moderators of CR effects in depression need to be identified.
Methods: We performed a systematic review and meta-analysis of published controlled trials of CR in adults with depression. We analyzed results from eight studies to estimate the efficacy of CR on global cognition and on six cognitive domains. We also examined three potential moderators, namely session format (individual vs. group), treatment duration, and participants' age.
Results: CR was found to improve global cognition ($g = 0.44$), verbal memory ($g = 0.60$), attention/processing speed ($g = 0.41$), working memory ($g = 0.35$), and executive functioning ($g = 0.30$). No significant improvements emerged for visuospatial memory and verbal fluency. Furthermore, no significant moderating effect of participant's age, session duration or session format were observed.
Limitations: Conclusions are limited by the small number of studies, the heterogeneity in cognitive measures, and the lack of indicators of everyday functioning.
Conclusion: Our meta-analysis supports the use of CR in improving global cognition in adults with major depressive disorder with a moderate effect size and this efficacy varies between cognitive domains.

Background

Major depressive disorder is characterized by depressed mood, decreased interest or pleasure in daily activities, weight changes, sleep and psychomotor disturbances, fatigue, feelings of worthlessness, difficulties concentrating, and suicidal ideation (American Psychiatric Association, 2013). Depression represents a major public health concern, with global estimates indicating that 10.8% of individuals are affected by this condition at some point in their lives (Lim et al., 2018). Depression is the leading cause of disability worldwide (World Health Organization, 2017) and accounts for 40.5% of the global burden of disease caused by psychiatric disorders, in terms of years of disability and years of life lost due to premature mortality (Whiteford et al., 2013). Hence, the development of successful treatment methods for depression is crucial.

Cognitive Deficits in Depression

Prior studies indicate that up to two-thirds of acutely depressed people are affected by cognitive deficits (Rock et al., 2014). These include difficulties in verbal, visuospatial, and working memory, as well as in attention and processing speed, executive functioning, and verbal fluency (Levin et al., 2007; Mattern et al., 2015; Snyder, 2013). Cognitive deficits negatively impact daily functioning and interfere with the

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ability to contribute actively to society by sustaining employment or schooling (Castaneda et al., 2008; Evans et al., 2013) and consequently aggravate the loss in productivity associated with depression (Murray & Lopez, 1996; Berto et al., 2000; Greenberg & Birnbaum, 2005). Despite the significance of cognitive deficits in depression, traditional psychiatric interventions have exclusively targeted mood and affective symptoms, leaving cognition untreated (Ahern & Semkovska, 2016). Several studies further indicate that cognitive difficulties tend to persist following remission of affective disturbances (e.g., Bora et al. 2013; Gorwood et al., 2008; Hasselbach et al., 2011; Vanderhasselt & De Raedt, 2009). Therefore, cognitive deficits in depression are an unmet treatment need.

Cognitive Remediation

Cognitive remediation (CR) aims to improve cognitive functioning with drill and practice exercises often supported by strategy coaching (Medalia & Lim, 2004). CR can be delivered in different formats (individually and in groups; Revell et al., 2015), and for different durations (one week to several months; Kim et al., 2018). A substantial body of evidence shows that CR can improve cognitive and functional outcomes in individuals with schizophrenia (Bowie et al., 2012; Cella et al., 2017; Guimond et al., 2018; Mothersill & Donohoe, 2019; Penadés et al., 2013; Wykes et al., 2011), and a growing number of studies have explored its effect in other psychiatric populations, such as affective disorders, attention-deficit/hyperactivity disorder, substance use disorders, and autism spectrum disorder (Kim et al., 2018).

To date, no meta-analysis has investigated the effect of CR in adults with depression on both global cognition and specific domains, with a focus on protocol characteristics that may moderate its effects. One meta-analysis has summarized aggregated cognitive outcomes across seven randomized and non-randomized studies in affective disorders at large, including participants with depression, bipolar, and schizoaffective disorders, thus precluding any conclusions specific to depression (Anaya et al., 2012). More recently, a second meta-analysis examined nine studies of CR in depression (Motter et al., 2016), focusing solely on computerized training and including a combination of CR with other treatments such as transcranial direct current stimulation (tDCS; Segrave et al., 2014). The authors examined the effect of CR on specific cognitive domains in a sample of participants with a depressive symptomatology rather than a formal diagnosis determined by a clinical professional. Results indicated that computer-based CR can improve attention and working memory with moderate-to-large effect sizes. However, this meta-analysis did not address CR effects across specific domains, an approach that has been frequently adopted in the context of other disorders (e.g., Revell et al., 2015; Wykes et al., 2011). Therefore, the effect of CR on global cognition in patients who have received a diagnosis of major depressive disorder should be specifically explored in a meta-analysis to determine the overall effect of CR in this population. This would help determine the overall effects of CR in depression and further facilitate comparisons between studies. Motter and colleagues (2016) also explored the moderating effect of participant characteristics (age, gender, and medication) on CR. However, illness variables like age of onset and disease duration, which have been shown to moderate CR effects in schizophrenia (Medalia, 2005), were not addressed. Additionally, the moderating effect of protocol characteristics like session format (individual or group) and duration, also associated with greater cognitive improvements in schizophrenia (McGurk et al., 2007), have never been systematically investigated on CR outcomes in depression (Medalia, 2005; Porter et al., 2013). Lastly, more recent CR studies have been conducted in this clinical population (i.e., Dong et al., 2017; Morimoto et al., 2020; Semkovska et al, 2015; Trapp et al., 2016). In light of the above, a novel meta-analysis is warranted in order to 1) estimate the specific effect of CR on global cognition in depression, 2) identify optimal protocol characteristics, and 3) summarize evidence from the most recently published controlled trials.

The Present Study

In the present study, we conducted a systematic literature review and meta-analysis of published controlled trials investigating the effect of CR on cognitive deficits in adults with depression.

First, we sought to evaluate the effect of CR on global cognition. Then, we investigated its specific effect on six specific cognitive domains, namely verbal memory, visuospatial memory, working memory, attention/processing speed, executive functioning, and verbal fluency. Finally, we aimed to explore potential moderators of the anticipated improvement in global cognition, including participant characteristics, namely age, gender, medication, age of onset and disease duration, and protocol characteristics, namely session format (individual or group) and duration.

Methods

Literature Search Procedure

Our systematic literature review and meta-analysis followed the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009). The literature search and study selection procedure are illustrated in the flowchart in Fig. 1.

Eligibility Criteria

Using PubMed and PsycINFO, we selected controlled trials published before September 3, 2020. We conducted a broad and systematic search of the literature using the terms “major depressive disorder” OR “depression” AND “cognitive remediation therapy” OR “cognitive

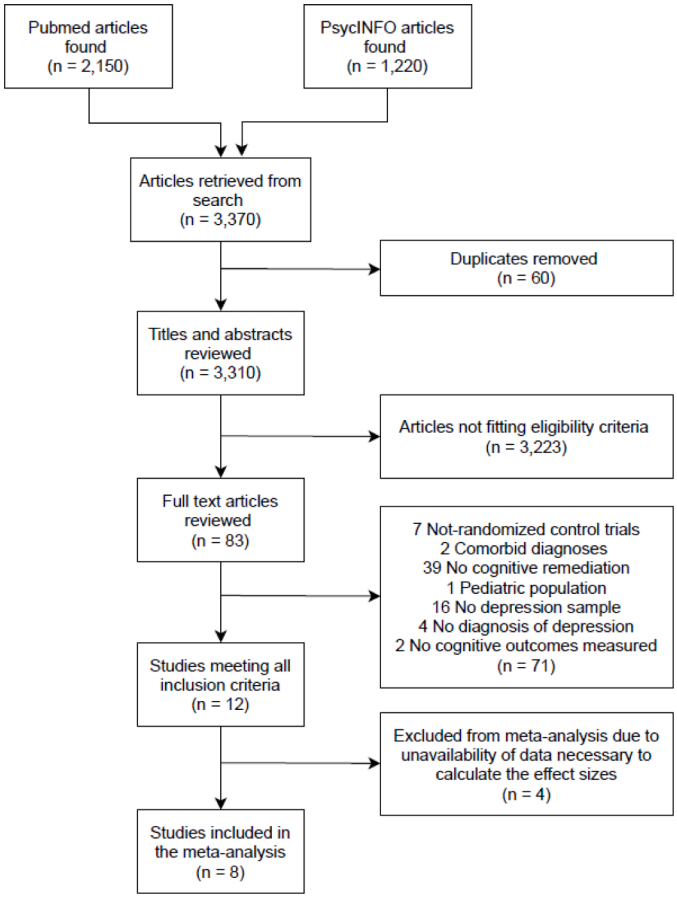

Fig. 1. Flow chart illustrating the literature search and study selection procedure.

rehabilitation" OR "cognitive training" with filters for randomized controlled trials.

We included studies involving participants 18 years old or older. Participants who received CR were acutely depressed and compared to a control group with the same symptomology. Major depressive disorder was assessed by a diagnostic interview established by either the DSM, the Research Diagnostic Criteria (Spitzer et al., 1978), or the International Classification of Diseases (World Health Organization, 1992). Publications had to be written in English.

We also excluded studies that did not include a control group with depression, and/or did not measure cognitive outcomes (see Fig. 1). To reduce sample heterogeneity, we further excluded studies involving participants with comorbid neurological illnesses, brain injuries, personality disorders, and substance use disorders.

Study Selection and Data Extraction

The initial search yielded 3,370 scientific articles (PubMed = 2,150 and PsycINFO = 1,220). Sixty duplicates were removed, thus resulting in 3,310 articles. Two authors (AT and MA) conducted a manual screening of all titles and abstracts to identify eligible studies. Disagreements during the selection process were solved with the input of a third author (SG). We excluded 3,223 articles after reading titles and abstracts, resulting in 83 publications. The totality of these articles was examined, and 71 were removed in compliance with exclusion criteria (see Fig. 1). Twelve articles met the inclusion criteria. However, four of those articles did not report means and standard deviations for the cognitive outcomes. We thus contacted the first and corresponding authors to obtain the missing information. While some authors positively replied to our inquiry, four either refused, did not reply to our emails, or reported no longer having the data (see Appendix 4 in Supplementary Material). Hence, we retained eight eligible articles for the current meta-analysis (i.e., Alvarez et al., 2008; Bowie et al., 2013; Dong et al., 2017; Elgamal et al., 2007; Morimoto et al., 2020; Naismith et al., 2011; Semkovska et al. 2015; Trapp et al., 2016).

Outcome Measures

Global cognition was computed by aggregating effect size scores across all measures for all cognitive domains within each study. Cognitive domain outcomes were grouped into six categories: (1) verbal memory, (2) visuospatial memory, (3) working memory, (4) attention/processing speed, (5) executive functioning and (6) verbal fluency. Please refer to Appendix 2 in the Supplementary Material for a list of cognitive assessments and corresponding cognitive domain categories.

Meta-Analysis Procedure

We used the metafor R package (Viechtbauer, 2010) to perform our meta-analysis (Morris, 2007). Analysis code used for the current meta-analysis is openly available (github.com/CRANIlab/MetaAnalysis_Depression_Cognitive_Remediation).

We generated a random effects model using the means and standard deviations reported in the selected studies. Relative to the fixed effects model, this approach assumes that differences between studies in CR effects are explained by real differences as well as by sampling variability (Schwarzer et al., 2015). We computed the standardized mean change from pre-test to post-test for both CR treatment and control groups to obtain a measure of effect size (Hedges' *g*; Hedges & Olkin, 1985). If a decreased mean score from pre-test to post-test implied a positive change, we reverse coded the means and ensured that, in both groups, a positive effect size reflected an improvement in the cognitive outcome at hand.

Specifically, for the treatment group, we computed the standardized mean change, Hedges' g_T, as:

$$g_T = c(n_T - 1)\ \frac{\overline{x}_{post,\ T} - \overline{x}_{pre,\ T}}{SD_{pre,\ T}} \quad (1)$$

where n_T represents the number of patients in the treatment group, $\overline{x}_{pre,\ T}$ and $\overline{x}_{post,\ T}$ are the pre- and post-test means for the treatment group respectively, and $SD_{pre,\ T}$ is the standard deviation of the pre-test results. The calculation also included a bias correction factor *c* (Becker, 1988) and a correlation factor, reflecting the correlation between pre-test and post-test measures. Since such correlations were not reported in the studies, we conducted a stability analysis to examine how the random effects estimates varied when the correlation factor ranged from 0.2 to 0.9. The estimates remained relatively consistent and statistically significant, with the most conservative correlation factor being 0.5. Thus, we selected a 0.5 correlation factor (see Appendix 3 in Supplementary Material).

For the control group, we computed the standardized mean change, Hedges' g_C, as:

$$g_C = c(n_C - 1)\ \frac{\overline{x}_{post,\ C} - \overline{x}_{pre,\ C}}{SD_{pre,\ C}} \quad (2)$$

where all terms are defined as in Equation 1, except that the *C* subscripts referring to the control group.

Next, we computed the effect size difference by calculating the difference in Hedges' *g* for the treatment and the control groups:

$$g = g_T - g_C. \quad (3)$$

The last calculated Hedges' *g* can be interpreted as the standardized difference between the change observed from pre-test to post-test in a cognitive outcome in the CR treatment group and the change observed in the control group. A 95% confidence interval was presented for all Hedges' *g* estimates.

Global cognition analysis

The Hedges' *g* estimates were aggregated within studies, resulting in one aggregated Hedges' *g* per study that reflected global cognition while controlling for the dependency between observations (Borenstein et al., 2009). A meta-analysis was then conducted on these Hedges' *g* values to determine whether CR had a significant effect on global cognition relative to the control conditions.

Sub-Group Analysis

We also conducted a sub-group analysis to assess the effect of CR on each cognitive domain (i.e., verbal memory, visuospatial memory, working memory, attention/processing speed, executive functioning, and verbal fluency). Since most studies used more than one outcome measure for each cognitive domain, Hedges' *g* estimates were aggregated by cognitive domain within each study (Borenstein et al., 2009). Please refer to Appendix 1 in the Supplementary Material for a list of cognitive assessments and corresponding cognitive domain categories.

Moderator Analysis

We used a mixed-effects model meta-regression to analyze the influence of the potential moderators on the effect of CR on global cognition compared to the control condition. We could not address the potential moderating role of participants' gender because raw data was collapsed across genders in all studies. Moreover, we could not address the potential moderating role of medication, as all participants included in the meta-analysis were medicated and the studies did not include information regarding the type of pharmacotherapy. In addition, the age of onset of depression and mean number of lifetime depressive episodes were reported in only two studies (Naismith et al., 2011; Elgamal et al., 2007), and average duration of the depressive episodes was also

reported in only two studies (Elgamal et al., 2007; Trapp, et al. 2016). Consequently, moderator analysis included one categorical variable, namely session format, which was coded as whether CR was delivered individually or in groups, and two continuous moderators, namely treatment duration (in hours) and participants' age (in years).

Study Heterogeneity

Since observations were sampled from different populations and used different measures, we also assessed study heterogeneity using the Cochran's *Q* test and the I^2 index (Borenstein, 2019). The Cochran's *Q* evaluates the null hypothesis that the treatment effect is the same across studies, with significant values indicating substantial variation between studies. The I^2 is computed based on the result of the Cochran's Q test and reflects the percentage of variation between studies that is due to heterogeneity rather than chance, with values between 40% and 60% being indicative of moderate heterogeneity (Higgins & Cochrane Collaboration, 2020).

Results

Our systematic literature review included eight controlled trials with a total of 268 adults with depression: 145 individuals who received CR and 123 individuals in control groups. The selected studies examined the effect of CR on six cognitive domains, namely verbal memory ($n = 7$), visuospatial memory ($n = 4$), working memory ($n = 5$), attention/processing speed ($n = 6$), executive functioning ($n = 6$), and verbal fluency ($n = 4$). CR duration ranged from 10 to 30 hours ($M = 16.88$; $SD = 6.44$). Participants were 21 to 82 years old ($M = 47.43$; $SD = 9.68$) and mostly females (71%). Study characteristics are summarized in Table 1.

The Effect of Cognitive Remediation in Depression

The results of our meta-analysis are reported in Table 2. We noted a significant moderate effect size of CR on improved global cognition from pre-test to post-test in adults with depression compared to control conditions ($g = 0.44$, $p = <.0001$, Fig. 2). Sub-group analysis further indicated significant improvements of CR compared to the control condition in verbal memory ($g = 0.60$, $p = <.0001$), attention/processing speed ($g = 0.41$, $p = .04$), working memory ($g = 0.32$, $p = .02$), and executive functioning ($g = 0.30$, $p = .02$) but no significant improvements in visuospatial memory ($g = 0.26$, $p = .12$) and verbal fluency ($g = 0.07$, $p = .72$, Fig. 3).

Moderators of Cognitive Remediation in Depression

The meta-regression estimates describing the effect of the potential moderators on the effect of CR on global cognition are reported in Table 3. We observed no significant moderating effect of CR session format ($p = .19$), meaning that the improvement in global cognition was not significantly different whether participants received CR individually or in groups. No significant moderating effect of participant's age nor session duration were observed ($p = .41$ and $p = .72$, respectively).

Study Heterogeneity

The model assessing the effect of CR on global cognition displayed low and non-significant levels of heterogeneity ($Q = 7.06$, $p = .42$, $I^2 = 0.00\%$). Heterogeneity was low for the sub-group models addressing the effect of CR on working memory ($Q = 0.71$, $p = .95$, $I^2 = 0.00\%$), executive functioning ($Q = 2.61$, $p = .76$, $I^2 = 0.00\%$), visuospatial memory ($Q = 1.13$, $p = .77$, $I^2 = 0.00\%$), verbal fluency ($Q = 1.38$, $p = .71$, $I^2 = 0.00\%$), and verbal memory ($Q = 1.96$, $p = .92$, $I^2 = 0.00\%$) but it was moderate for attention/processing speed ($Q = 9.62$, $p = .09$, $I^2 = 47.26\%$).

Heterogeneity was also low for the models testing the moderating effect of session format ($Q = 5.38$, $p = .50$, $I^2 = 0.01\%$), participants' age ($Q = 6.38$, $p = .38$, $I^2 = 0.00\%$), and CR duration ($Q = 6.96$, p = .32, $I^2 = 0.00\%$).

Discussion

Global and Domain-Specific Effects of Cognitive Remediation in Depression

The current study investigated the effect of CR on global cognition in people with depression. Our results provide evidence that CR can significantly improve global cognition in this population, with a moderate effect size ($g = 0.44$). The estimated effect size was comparable to the first meta-analysis of studies involving people with various affective disorders (i.e., $g = 0.44$; Anaya et al., 2012) and in line with prior reviews and meta-analysis supporting the overall efficacy of CR in schizophrenia and schizoaffective disorders (Kim et al., 2018; Keshavan et al., 2014; Wykes et al., 2011).

When analyzing cognitive domains separately, we found that CR had a high significant effect on verbal memory ($g = 0.60$) and a moderate significant effect on attention/processing speed ($g = 0.41$), working memory ($g = 0.32$), and executive functioning ($g = 0.30$). No significant effect was observed on visuospatial memory and verbal fluency. Thus, the overall improvement observed in global cognition was likely influenced by domain-specific changes in verbal memory, attention/processing speed, working memory, and executive functioning. The extant literature on cognitive impairments in depression offers possible explanations for these results. Evidence suggests that certain domains, particularly executive functioning and attention/processing speed, can be more extensively impaired than others in both medicated and unmedicated individuals with depression relative to healthy controls (Pu et al., 2017; Liu et al., 2019). This is also consistent with findings from neuroimaging studies indicating abnormal connectivity in regions involved in executive control and information processing in individuals with depression displaying cognitive deficits (Gong et al., 2017). On the other hand, domains like visuospatial memory and verbal fluency, which pose relatively limited executive demands and are more dependent on hippocampal activity (Hinkelmann et al., 2009), can be modestly impaired in depression (Henry & Crawford, 2005). Deficits in these domains might be secondary impairments and, therefore, less amenable to change with CR alone.

Significant effects of CR on attention/processing speed and working memory that we observed are consistent with the findings of Motter and colleagues (2016). However, we observed significant improvements in verbal memory and executive functioning which were not reported in this previous meta-analysis. Since three of the four studies measuring verbal memory in Motter et al. (2016) did find significant CR effects, it is possible that the nonsignificant result reported in their meta-analysis was driven by the fourth study (Lohman et al., 2013). Specifically, Lohman and colleagues (2013) tested a treatment inspired by CR (participants taught mnemonic strategies and practiced tests) in a large elderly sample (N = 1,401; no formal depression diagnosis) and found no significant improvements. Regarding executive functioning, it seems plausible that our significant result was explained by increased power due to the inclusion of four additional studies investigating these outcomes, all of which reported significant improvements in that specific domain (Dong et al., 2017, Morimoto et al., 2020, Semkovska et al., 2015 and Trapp et al., 2016).

Toward Best Practices for Cognitive Remediation in Depression

The current meta-analysis examined the effect of only three potential moderators, namely session format, duration, and participants' age, because information on other potential moderators was not available for analysis. Regarding session format, we observed no significant difference in cognitive improvements following individual and group CR. It has been suggested that individually delivered CR creates a better

Table 1
Characteristics of the eight studies included in the meta-analysis

Study	Country	Diagnostic measure (assessor)	Measured cognitive outcome	CR Group			Control Group		Participants					
				Format	Description	Duration (h)	Condition	Description	*N* CR group	Control group	Age *M* (*SD*) CR group	Control group	Gender (% female) CR group	Control group
Alvarez et al., 2008	Mexico	DSM–IV (psychiatrist)	Attention/Processing Speed	Individual	Alcor	16	TAU	Stable dose of antidepressants	20	11	23.0 (3.3)	23.8 (2.7)	55	63.6
Bowie et al., 2013	Canada	DSM–IV (psychiatrist)	Verbal Memory, Working Memory, Attention/Processing Speed, Executive Functioning, Verbal Fluency	Group	Scientific Brain Training Pro (sbtpro.com)	15	Waitlist	N/A	17	16	49.2 (11.8)	42.2 (13.4)	75	65
Dong et al., 2017	U.S.A.	DSM–IV-TR (psychologist)	Verbal Memory	Individual	CBT (Beck, 1979) with mnemonic strategies	12	TAU	CBT without mnemonic strategies	25	23	43.9 (9.9)	44.65 (12.2)	48	73.9
Elgamal et al., 2007	Canada	DSM–IV (psychiatrist)	Verbal Memory, Working Memory, Attention/Processing Speed, Executive Functioning, Verbal Fluency	Individual	PSSCogReHab (Bracy, 1994)	20	TAU	Stable dose of antidepressants	12	12	50.3 (6.4)	47.4 (6.8)	58.3	58.3
Morimoto et al., 2020	U.S.A.	DSM-IV (psychiatrist)	Executive Functioning Working Memory Verbal Memory Verbal Fluency Visuospatial Memory	Individual	Brain HQ	30	Active	Psychoeducation	18	12	74.7 (7.6)	72.2 (9.9)	63.6	63.6
Naismith et al., 2011	Australia	DSM-IV-TR (psychiatrist)	Verbal Memory, Attention/Processing Speed, Executive Functioning, Visuospatial Memory	Individual	Neuropsychological Educational Approach to Remediation (NEAR; Medalia & Mambrino, 2010)	10	Active	Psychoeducation	22	19	64.8 (8.5)	64.8 (8.5)	41.5	41.5
Semkovska et al., 2015	Ireland	DSM–IV (not reported)	Verbal Memory, Working Memory, Attention/Processing Speed, Executive Functioning, Verbal Fluency, Visuospatial Memory	Individual	RehaCom (Semkovska et al. 2015)	20	Active	Online games	8	7	42.4 (14.9)	44.4 (13.0)	50	41.6
Trapp et al., 2016	Germany	DSM-IV (psychiatrist)	Verbal Memory, Working Memory, Attention /Processing Speed, Executive Functioning, Verbal Fluency, Visuospatial Memory	Individual	X-Cog (Trapp, 2003)	12	TAU	CBT, Relaxation, Physical Training, Occupational Therapy	23	23	34.3 (11.6)	36.9 (12.1)	60.9	73.9

Note. Results were combined and averaged for both CR groups in Alvarez et al., 2008; *N* = Sample size; *M* = Mean; SD = Standard Deviation; DSM = Diagnostic and Statistical Manual of Mental Disorder; SCID = Structured Clinical Interview for DSM; CBT = Cognitive Behavioral Therapy; TAU = Treatment as usual.

Table 2
Effect of cognitive remediation on cognition in depression.

Cognitive Domain	*N*	Hedges' *g*	95% *CI*	*Z* score	*p*-value
Verbal Memory	7	0.60	0.37, 0.84	5.08	<.0001*
Visuospatial Memory	4	0.26	-0.07, 0.58	1.55	0.12
Working Memory	5	0.35	0.06, 0.65	2.33	.02*
Attention/Processing Speed	6	0.41	0.03, 0.80	2.10	0.04*
Executive Functioning	6	0.30	0.05, 0.55	2.33	0.02*
Verbal Fluency	4	0.07	-0.30, 0.43	0.35	0.72

Note. N = number of studies addressing the cognitive domain; Hedges' g = effect size difference between CR and control conditions; *CI* = Confidence Intervals; Z value = Hedge's g / Standard error. * = Statistically significant at $p < .05$

setting for the development of a therapeutic alliance, for patient-tailored goal setting, and for adapting exercise pace to the individual progress (Dong et al., 2017; Morimoto et al., 2020, Semkovska et al., 2015). Nonetheless, our results show that significantly improved cognition can also be observed in group CR. Hence, group CR appears as a cost-effective option in depression (Medalia & Choi, 2009; Revell et al., 2015). It is also important to note that outcomes unavailable in this study, such as everyday functioning and mood symptoms, might be influenced by different session formats and should be further investigated.

We also found that participant's age did not significantly moderate the effect of CR, in contrast with the previous meta-analysis by Motter et al. (2016). We believe the difference in those results is explained by the fact that we excluded Lohman and coleagues (2013) from our analysis. Interestingly, there is evidence that shows that addressing cognitive deficits early in the course of depression is beneficial regardless of the person's age (Listunova et al., 2020). It is also possible that different age groups will benefit from different protocol characteristics, given that cognitive deficits associated to depression can be further aggravated by age-related cognitive decline (Wilson et al., 2014). In addition to illness duration and number of lifetime episodes, prolonged avoidance of cognitively challenging activities in daily life might also affect response to CR in depression (Tran et al., 2020). Future studies are therefore needed to clarify the interplay between longitudinal changes in cognitive ability relating to age and lifestyle factors, CR protocol characteristics, and CR effects.

Interestingly, longer CR treatment was not associated with greater improvements in global cognition. This might imply, as in other disorders such as schizophrenia, schizoaffective disorder, bipolar disorder with psychotic features, or major depressive disorder with psychotic features, that cognitive treatment response in depression can occur early on after CR onset (Best et al., 2019). Nonetheless, CR research in individuals with schizophrenia has indicated that other desired outcomes, such as improved quality of life and everyday functioning, are likely to lag behind cognitive responses (Bowie et al., 2012). Therefore, more work is needed to clarify the optimal duration for producing and sustaining cognitive improvement and transfer of those improvements to indicators of daily functioning in depression.

Limitations of The Present Study and Areas of Improvement in the Literature

To date, the number of controlled trials investigating the effect of CR on cognition in adults with depression is limited. Our literature search and study selection identified twelve studies that could be included in the meta-analysis. However, we were unable to directly extract the means and standard deviations for the pre-test and post-test cognitive assessments from numerous articles that initially met our inclusion criteria. Even after contacting the authors, four studies had to be excluded due to a lack of available cognitive outcome data (see Appendix 4 in Supplementary Material). Thus, there is a critical need for greater transparency and accessibility in the field. Additional efforts in that sense should be made not only to facilitate future meta-analyses, but also to improve the rigor and quality of the evidence that is published (Dwan et al., 2013)

The eight studies included in our meta-analysis differed considerably in terms of assessment methods. Specifically, we noted the limited use of standard comprehensive cognitive assessments. The large variation in

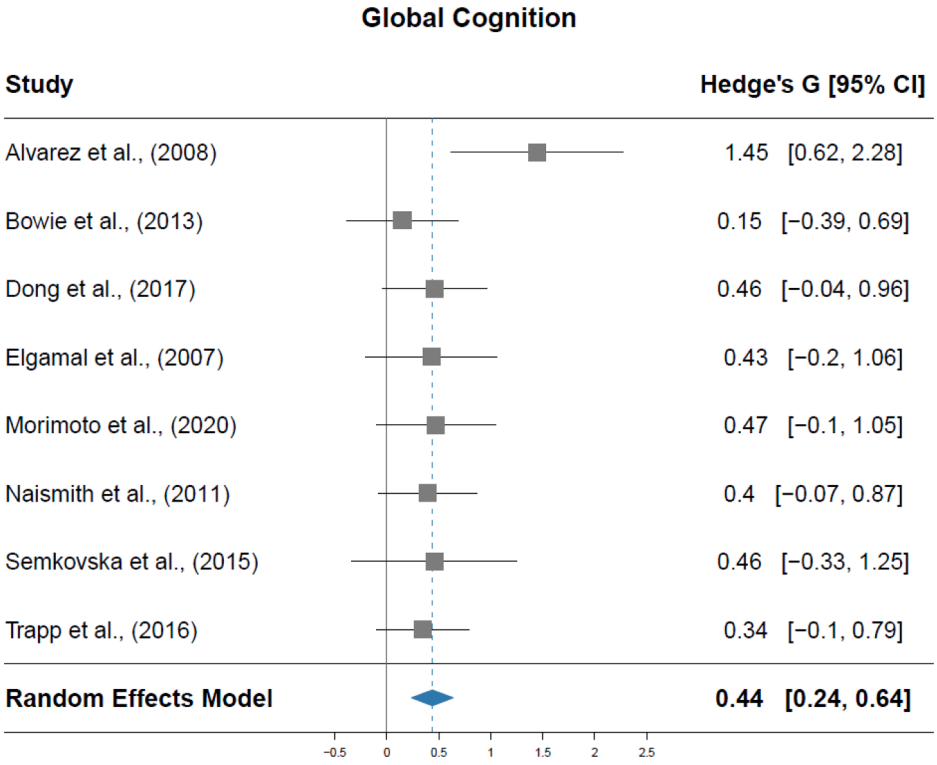

Fig. 2. Forest plot displaying the estimated effect size for each study, which describe the effect of cognitive remediation therapy on general cognition in depression

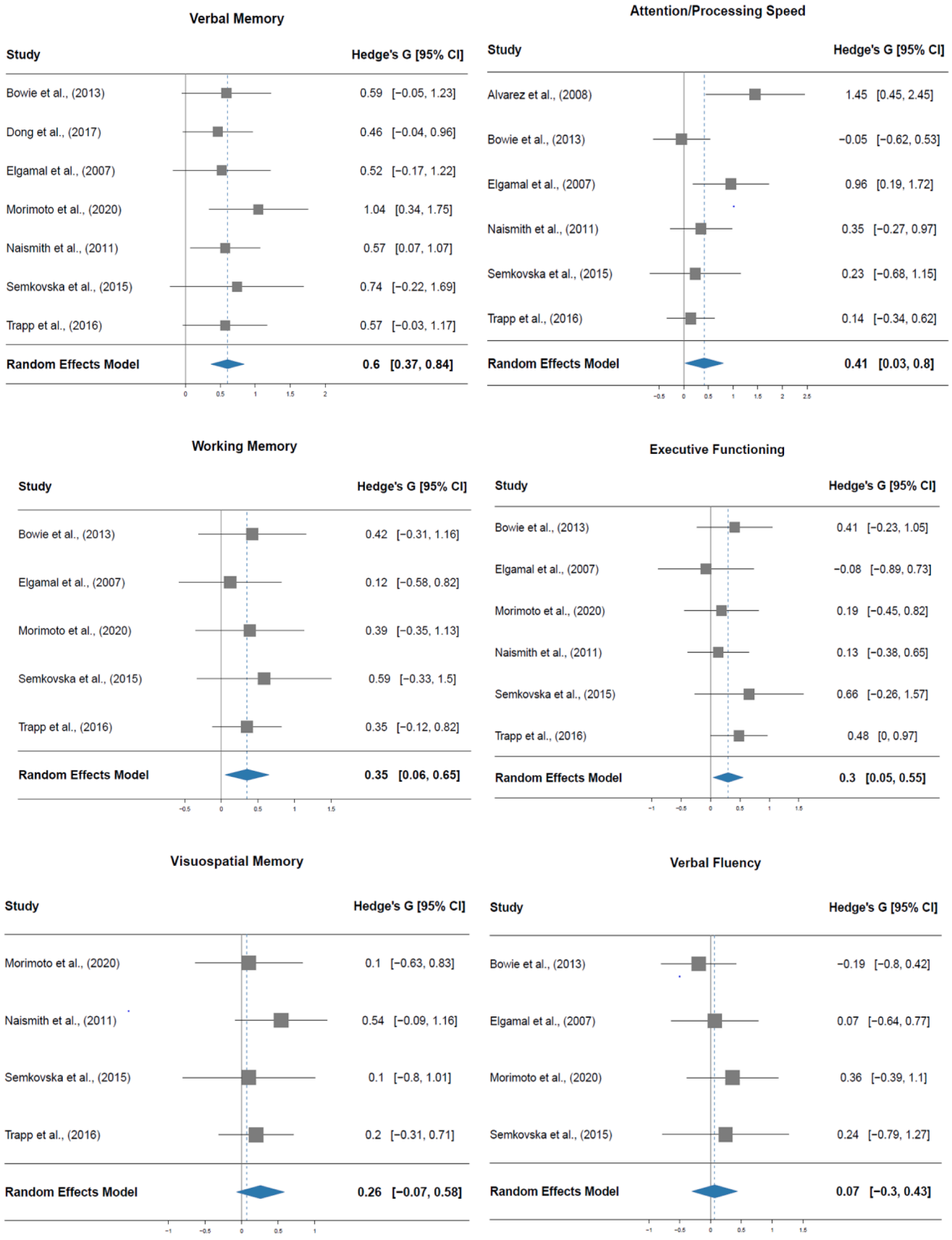

Fig. 3. Forest plots displaying the estimated effect size for each study, which describe the effect of cognitive remediation on specific cognitive domains in depression.

Table 3
Mixed effect model meta-regression estimates for four potential moderators of the effect of CR on global cognition.

	n	*b*	95% CI	Z Score	*p*-value	Post-hoc sub-groups	n	*b*	95% CI	Z Score	*p*-value
Session format	8	0.26	-0.13, 0.66	1.30	.19	Group	3	0.31	0.03, 0.60	2.20	.03*
						Individual	5	0.57	0.29, 0.85	3.98	<.0001*
Duration	8	0.005	-0.03, 0.04	0.33	.74	N/A					
Age	8	-0.006	-0.02, 0.008	-0.83	.41	N/A					

Note. *N*= number of studies; *b* = Meta-regression coefficient; *CI* = Confidence Intervals, NA= not applicable. * = Statistically significant difference at $p < .05$

assessment measures between studies might have contributed to the moderate significant study heterogeneity we observed when testing the effect of CR on global cognition, verbal memory, and attention/processing speed. In light of this, achieving a consensus on a comprehensive yet concise and practical battery of cognitive tests for depression could facilitate comparisons between studies (Russo et al., 2014).

Furthermore, limited information was available on participants' characteristics like medication, age of onset of depression, as well as mean number of lifetime depressive episodes and their duration. Reporting such information should be encourged as it could allow for more extensive moderation analyses and could help in developing CR protocols tailored to specific patient characteristics.

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Contributors

Authors AT, SG and MA have designed the search strategy, search databases, completed the title and abstract screening, full-text screening and data extraction.

Author AH was part of the analysis team and provided comments on the initial drafts of this manuscript. AT performed all analysis and wrote the first draft of the manuscript.

Authors CB, PP and SG helped with analysis and data interpretation, and revised the manuscript critically for substantial contributions. All authors have contributed to and have approved the final manuscript.

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Conflict of Interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2021.02.009.

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