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Review

Computerized cognitive training and functional recovery in major depressive disorder: A meta-analysis

Jeffrey N. Motter[a,b], Monique A. Pimontel[a,b], David Rindskopf[a], Davangere P. Devanand[c], P. Murali Doraiswamy[d], Joel R. Sneed[b,c,*]

[a] The Graduate Center, City University of New York, USA
[b] Queens College, City University of New York, USA
[c] Columbia University and the New York State Psychiatric Institute, USA
[d] Duke Medicine and Duke Institute for Brain Sciences, USA

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ABSTRACT

Objective: Depression is common, frequently resistant to antidepressant treatment, and associated with impairments in cognition and everyday functioning. Computerized cognitive training (CCT) paradigms offer potential to improve cognition, mood and everyday functioning, but their effectiveness is not well established. The goal of this article was to conduct a systematic review and meta-analysis to determine the efficacy of CCT in depressive disorders.

Method: A search was conducted to identify high quality randomized controlled CCT trials per PRISMA guidelines using PsycINFO and MEDLINE with the keywords "Cognitive training" or "Cognitive remediation" or "Cognitive rehabilitation" and "Depression". 9 randomized trials for depressed adults met inclusion criteria. Effect sizes (Hedge's g) were calculated for key outcome measures of mood symptom severity, daily functioning, and cognition. A 3-level Bayesian hierarchical linear model was used to estimate effect sizes for each domain and study. Publication bias was assessed using Classic Fail Safe N's and homogeneity was evaluated using Q and I^2 indexes.

Results: Significant small-moderate effects for Symptom Severity (0.43) and Daily Functioning (0.72), and moderate-large effects for Attention (0.67), Working Memory (0.72), and Global Functioning (1.05) were found. No significant effects were found for Executive Functioning or Verbal Memory. Moderator variable analysis revealed decreased effect of CCT with age. Gender and concurrent medication treatment did not affect the results.

Limitations: Small sample size, short duration, pseudo-specificity, and high heterogeneity for Verbal Memory measures.

Conclusions: CCT is associated with improvement in depressive symptoms and everyday functioning, though produces inconsistent effects on cognition.

Contents

* Correspondence to: Department of Psychology, Queens College of the City University of New York, 65-30 Kissena Blvd, Queens, NY 11367, USA.
E-mail address: joel.sneed@qc.cuny.edu (J.R. Sneed).

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1. Introduction

Major depressive disorder (MDD) is a common disorder among adults with a lifetime prevalence of 16.6% in the United States (Kessler et al., 2005). Depression is associated with greater psychosocial disability (Judd et al., 2000), higher functional impairment (Rapaport et al., 2005), and higher rates of mortality (Cuijpers and Smit, 2002). Depressed adults are at greater risk of developing anxiety disorders (Kessler et al., 2008) and cardiovascular diseases, such as ischemic heart disease and cerebrovascular disease (Holt et al., 2013). In terms of everyday functioning, lack of energy, loss of interest, apathy, and insomnia make it difficult to complete daily tasks. An estimated 7% of depressed adults commit suicide, largely in part due to lack of treatment or low treatment efficacy (Bostwick and Pankratz, 2000). It is estimated that only 37.5% of adults receive minimally adequate treatment (Wang et al., 2005). Beyond the impairment to health, depression is responsible for low productivity, missed work days, and an estimated $83 billion dollars in economic loss annually (Greenberg et al., 2003).

In addition to physical health problems, depression often manifests with cognitive impairment. Specifically, depressed individuals have deficits in working memory, verbal fluency, processing speed, attention, and executive function (Austin et al., 2001). Impairment in cognitive functions in depressed adults predicts low functional outcome as well as treatment nonresponse (Alexopoulos et al., 2005; Dunkin et al., 2000; Gorlyn et al., 2008; Kampf-Sherf et al., 2004). Further, these deficits are linked with reduced quality of life (Jaeger et al., 2006). While treatments such as psychotherapy and antidepressants have proven efficacy for improving mood, cognitive deficits often remain following remission (Baune et al., 2010; Paelecke-Habermann et al., 2005). It is essential that treatments address cognitive impairments, as they are a risk factor for suicide attempts and development of dementia (Keilp et al., 2001). Development of novel interventions to improve antidepressant response can have an enormous public health benefit.

One approach beginning to receive attention is computerized cognitive training (CCT) (Morimoto et al., 2012; Porter et al., 2013), in which cognitive exercises or games are used to target specific neural networks in order to improve cognitive functioning through neuroplasticity. CCT has been used in healthy adult populations (Mahncke et al., 2006; Stern et al., 2011; Willis et al., 2006) as well as in a variety of diagnostic conditions including attention-deficit hyperactivity disorder (Rapport et al., 2013), schizophrenia (Wykes et al., 2011), bipolar disorder (Preiss et al., 2013), traumatic brain injury (Salazar et al., 2000), mild cognitive impairment (Li et al., 2011), and Alzheimer's disease (Sitzer et al., 2006). It is administered through an automated computer program, oftentimes accessible over the internet. Advantages CCT hold over existing treatments for depression are that it is relatively inexpensive, noninvasive, and can be tailored to meet the specific cognitive needs of the individual. Further, there is no concern for medicinal side effects and training can be completed in the patient's own home. Because CCT necessitates computer access and sometimes an internet connection, it may be difficult to implement for populations that traditionally have low computer access, such as those with low household income and older adults.

The growth of CCT as an intervention is met with contention in regards to its effectiveness. Proponents highlight systematic reviews claiming CCT improves cognitive abilities in various patient populations, with some evidence of these benefits transferring to everyday functioning (Mahncke, 2014). Skeptics criticize the manufacturer's claims that CCT leads to increased mental fitness as being overstated and potentially misleading to patients and consumers (Max Planck Institute for Human Development and Stanford Center on Longevity, 2014). There is little evidence that the cognitive benefits are broad, and performance gains may reflect similarity between training paradigms and neuropsychological measures. Even when positive results are found, studies often lack methodological rigor to account for participant motivation and expectancy. The current debate demonstrates the urgent need for answers to questions about the value of CCT.

The purpose of this meta-analysis is to evaluate the efficacy of CCT for depressed individuals. In doing so, we attempt to answer several important questions. First, does CCT improve cognition, and in what domains? Depression is associated with numerous cognitive impairments, making it critical to understand which, if any, can be improved by CCT. Secondly, does it improve mood? Alleviation of cognitive impairments may enhance ongoing treatments, as might completion of rewarding tasks distract from ruminative thoughts. Finally, does the improvement transfer to everyday life functioning? While enhancing cognitive abilities is the immediate objective of CCT, it is done with the expectation that this facilitates improved quality of life. The absence of transfer would make it difficult to conclude CCT is not merely teaching to the test.

2. Method

PRISMA guidelines for conducting and reporting systematic reviews were followed during this analysis (Moher et al., 2009). Studies for the meta-analysis were selected using PsycINFO and MEDLINE. The following keywords were used: "Cognitive training" or "Cognitive remediation" or "Cognitive rehabilitation" and "Depression." Results were further limited to (1) English language articles, (2) participants aged 18 years or greater, and (3) study design of clinical trial, controlled clinical trial, multicenter study, randomized trial, or randomized control trial. The initial search returned 2938 results. From these articles, 613 exact duplicates were dropped. The titles and abstracts of the remaining 2325 articles were examined against previous exclusion criteria, in addition to excluding articles that were review papers, did not utilize a CCT paradigm, or did not contain depressed participants (defined by a minimum score on a depression rating scale or confirmation via a structured clinical interview). The full text of the remaining 75 articles were examined against previous exclusion criteria, in addition to excluding articles that did not report sufficient outcome data for meta-analytic review, contained comorbid diagnoses, did not stratify results by diagnosis when multiple disorders were present, or did not contain adequate control groups. One article not found using our search parameters was provided by the author (Siegle et al., 2014), supplanting a previously found article. Using these methods, 9 articles were selected for inclusion in the meta-analysis (Alvarez et al., 2008; Bowie et al., 2013; Calkins et al., 2014; Elgamal et al., 2007; Lohman et al., 2013; Naismith et al., 2011; Owens et al., 2013; Segrave et al., 2014; Siegle et al., 2014). Fig. 1 details the selection process. One study contained patients with a diagnosis of dysthymia (Owens et al., 2013). This article was retained in an effort to remain inclusive of studies involving CCT in depressed individuals.

Outcome measures were categorized to functional and cognitive domains of Symptom Severity, Daily Functioning, Attention, Working Memory, Verbal memory, Executive functioning, and Global Functioning according to guidelines outlined by Lezak et al. (2012) and Strauss et al. (2006). The 'Symptom severity' category included measures of mood and anxiety, such as the Beck Depression Inventory. 'Daily functioning' was comprised of outcome measures that assess transfer of training to everyday activities. These measures assess functions such as social skills, work ability, and mobility. 'Attention' contained measures of one's ability to maintain focus, such as Digit Span Backwards and Trails Making

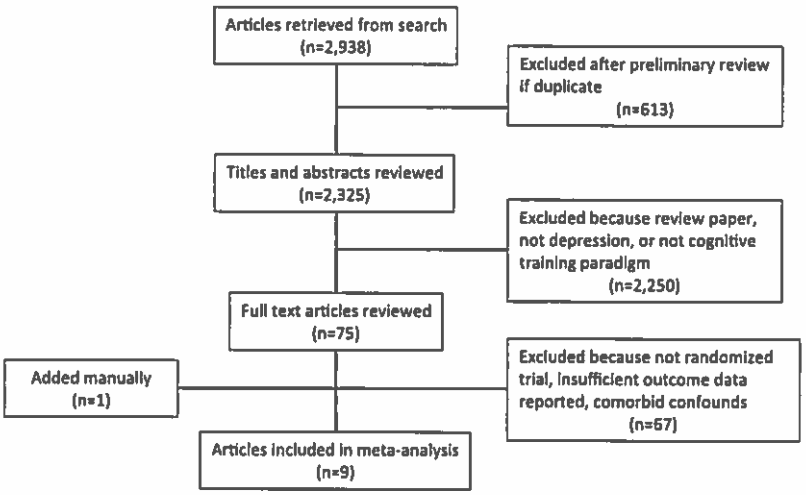


Fig. 1. Flowchart of systematic review.

Test Part A. Measures that utilize inhibition, such as the Stroop test, or verbal fluency, such as the Controlled Oral Word Association Test, or task switching, such as Trails Making Test Part B, were assigned to 'Executive Functioning.' 'Verbal Memory' contained measures of and verbal memory such as the Hopkins Verbal Learning Test. 'Working Memory' was comprised of n-back tasks, Digit Span Forwards, and the Paced Auditory Serial Addition Task. Finally, 'Global Functioning' consisted of measures that assess comprehensive abilities across a wide range of cognitions (McLennan and Mathias, 2010). This included the WAIS Verbal and Performance IQs.

Effect sizes were calculated from pre and post means and standard deviations using Comprehensive Meta-Analysis (CMA) Version 2. CCT groups were compared to the most comparable control group. Hedges' g was calculated for each domain and study to correct for biases resulting from small sample size. When multiple outcomes under a single domain were reported within a study, the mean effect size of these measures was used. For instances in which data required for effect size calculations were not reported in the original articles, we attempted to contact study authors. When unavailable, pre-post correlations were estimated to be 0.600. This value was chosen by calculating correlations on previously obtained neuropsychological testing data. Effects of 0.2, 0.5 and 0.8 were interpreted as small, medium, and large respectively (Cohen, 1988). Standard errors, the Q-index, I^2 tests, and N_{fs} were also computed. I^2 values of 25%, 50% and 75% were interpreted as low, moderate and high, respectively. The diversity of participant populations and CCT paradigms necessitated the usage of a random effects model. Mixed-effects model meta-regression based on the Q-index was utilized to evaluate the potential impact of several moderator variables: age, gender, control type (active (Calkins et al., 2014; Owens et al., 2013; Segrave et al., 2014) or non-active (Alvarez et al., 2008; Bowie et al., 2013; Elgamal et al., 2007; Lohman et al., 2013; Naismith et al., 2011; Siegle et al., 2014)), and concurrent treatment (whether the participants were taking antidepressants and or undergoing therapy as part of the study (Alvarez et al., 2008; Bowie et al., 2013; Elgamal et al., 2007; Naismith et al., 2011; Segrave et al., 2014; Siegle et al., 2014) or not (Calkins et al., 2014; Lohman et al., 2013; Owens et al., 2013)).

A total of 57 individual measures extracted from nine different studies were included in this analysis as indicators of domains for cognition, mood, and everyday functioning. We used the open variant of the Bayesian Inference Using Gibbs Sampling software package (OpenBUGS) (Lunn et al., 2000; Spiegelhalter et al., 2000) to estimate a 3-level meta-analytic model (DuMouchel, 1994; Sutton and Abrams, 2001) in which observations are nested within domain (cognition, mood, and everyday function), which in turn are nested within study. Table 2 reports the domain, effect sizes, and standard errors of each individual measure and shows the key elements of the structure of the data analytic model:

I. The design is a 9 (studies) × 7 (domains) factorial. One dimension (studies) is random, while the other (domain) is fixed. Thus, the model is a combination of a fixed and a random effects model, and is therefore sometimes called a mixed effects model in meta-analysis.
II. Because some studies report multiple neuropsychological measures, these data are not independent, which needs to be taken into account in the analysis.
III. Many cells in the design are empty, because not all studies measured all domains in the analysis.
IV. A large number of missing cells make it difficult to accurately estimate any potential interactions between studies and domains. The only cells contributing to such an estimate would be cells that occur in a pattern of four cells, such that two studies measure the same two domains. We decided not to try to estimate this because of the sparseness of the data.

Issues (i) through (iii) can be dealt with by using a hierarchical linear model, with effect sizes of different domains nested within studies to take into account the dependence of the outcome data. As such, the statistical model for estimating domain effect sizes represented each observed effect size as a sum of three types of components: (i) an effect due to the specific study (where studies were considered random effects), (ii) an effect due to the specific measure used, and (iii) measurement error. Because some domains were measured in more studies than other domains, and studies had different sample sizes, the accuracy with which we can estimate each effect (i.e. the standard errors) will be different.

The model can be written as

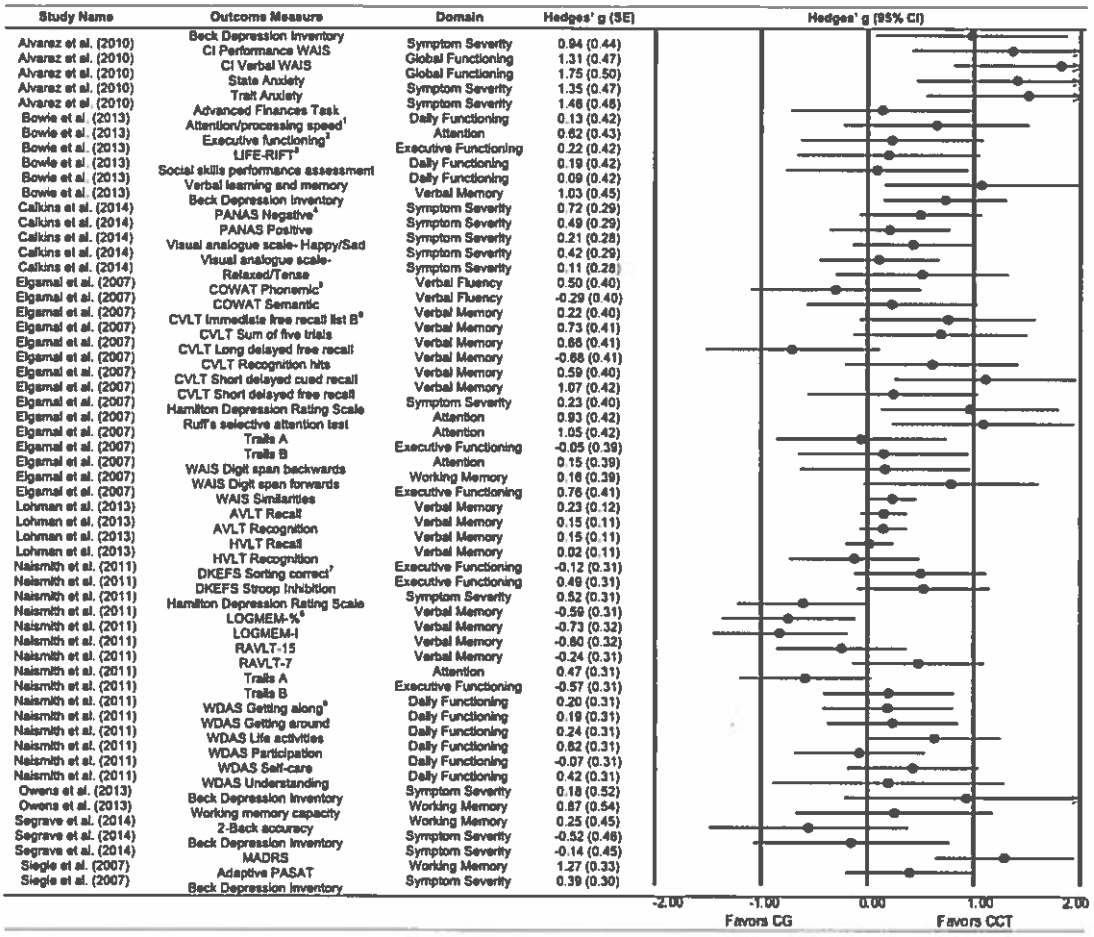
```
g[i]~↓normal(m[i], s[i])m[i]
    = ↓b0[study[i]] + b1*e. symptom[i]
      + b2*e. dailyfuntioning[i] ↓+ b3*e. attention[i]
      + b4*e. executivefunction[i] + b5*e. verbal memory[i] ↓
      + b6*e. working memory[i] + u0[study[i]]
```

where i indexes the 57 observed effect sizes, g[i] is the

Table 1
Study characteristics.

	Computerized Cognitive Training (CCT)				Control Group (CG)				
Study	***N***	**Age (SD)**	**Gender (% female)**	**CCT task**	***N***	**Age (SD)**	**Gender (% female)**	**CG task**	**Duration of training**
Alvarez et al. (2008)	10	23.3 (3.7)	50.0	(i) 'Alcor' cognitive training program. Participants complete mental arithmetical operations or series completion tasks with difficulty modulated by performance. (ii) Received fluoxetine, paroxetine, or imipramine antidepressant treatment	11	23.8 (2.7)	63.6	Received fluoxetine, paroxetine, or imipramine antidepressant treatment	16 weeks with a total of 64 sessions
Bowie et al. (2013)	11	49.2 (11.8)	65.0	(i) 'Scientific Brain Training Pro' cognitive training program. Modules involve processing speed, attention, working memory, delayed memory, and executive functions. Difficulty increased by participant and experimenter. (ii) Strategic self-monitoring training (iii) 'Bridging' discussions to facilitate transfer to everyday behavior (iv) Two homework sessions per day	10	42.2 (13.4)	75.0	Waitlist	One 90 min session per week for 10 weeks Two 20 min homework sessions per day
Calkins et al. (2014)	24	35.7 (13.5)	54.2	'Cognitive Control Training' program. Modules involve modified Wells Attention Training and Paced Serial Attention Task	24	35.8 (15.9)	54.2	'Peripheral Vision Training' used as a non-active control paradigm. Participants viewed a circular array of discs with their peripheral vision and identify a target color.	Three 30-min sessions over 2 weeks
Elgamal et al. (2007)	12	50.3 (6.4)	58.3	'PSSCogRehab' cognitive training program. Modules involve attention, verbal memory, psychomotor speed, and executive function. Difficulty increases over the course of each module	12	47.4 (6.8)	58.3	Waitlist	Two 45–60 min sessions per week for 10 weeks
Lohman et al. (2013)	146	75.3 (6.5)	78.8	'ACTIVE' memory training program	164	75.0 (6.5)	85.4	Waitlist	Ten 60–75 min sessions over 6 weeks
Naismith et al. (2011)	22	64.8 (8.5)	41.5	(i) 'NEAR' cognitive training program. (ii) Psychoeducation training on health and cognitive functioning	19	64.8 (8.5)	41.5	Waitlist	One 60 min CCT session once per week for 10 weeks One 60 min Psychoeducation session once per week for 10 weeks
Owens et al. (2013)	7	27.7 (5.3)	54.5	Cognitive training using dual n-back task.	6	22.6 (3.4)	72.7	Non-adaptive dual 1-back task	Eight sessions over a 4 week period.
Segrave et al. (2014)	9	42.6 (18.3)	22.2	(i) 'Cognitive Control Training' program. Modules involve modified Wells Attention Training and Paced Serial Attention Task (ii) Transcranial Direct Current Stimulation delivered for 24 min	9	33.8 (13.0)	44.4	(i) 'Peripheral Vision Training' used as a non-active control paradigm. Participants viewed a circular array of discs with their peripheral vision and identify a target color. (ii) Transcranial Direct Current Stimulation delivered for 24 min	~30 min training sessions each day for 5 days 24 min tDCS each day for 5 days
Siegle et al. (2014)	23	39.0 (9.2)	70.0	(i) Cognitive training using Weil's Attention Training and adaptive Paced Auditory Serial Attention Task (ii) Outpatient treatment as usual; medication management, supportive group psychotherapy, and milieu therapy	20	40.1 (11.9)	67.0	Outpatient treatment as usual; medication management, supportive group psychotherapy, and milieu therapy	Six 35 min sessions over 2 weeks

Table 2
Effect sizes for individual measures by study and domain categorization.



[1]Composite of Symbol Coding Task, Continuous Performance Test-Identical Pairs Version, Controlled Oral Word Association Test and Animal Naming tests, and Trails Making Test Part A
[2]Composite of the Letter Number Sequencing Test, Trails Making Test Part B, and the Stroop Color-Word test.
[3]Longitudinal Interval Follow-up Evaluation Range of Impaired Functioning Tool
[4]Controlled Oral Word Association Test
[5]California Verbal Learning Test
[6]Delis Kaplan Executive Functioning System
[7]LOGMEM-I: total score for stories A and B on WMS-III Logical Memory learning trials; LOGMEM%: percentage of story material retained at 25–35 delayed recall
[8]World Health Organization Disability Assessment Schedule

observed Hedges' g for effect i, s[i] is the standard error of g[i], m[i] is the true effect size, study[i] is the study in which the effect g[i] is found, and e.symptom, e.daily functioning, e.attention, e. executive function, e.verbal memory, and e.working memory are effects codes indicating the difference between the referenced domain and the overall average. The u0 term represents the difference between the estimated individual study effect size and the actual study effect size. The parameter values in the vector b0 were specified to have a normal distribution with mean mu0 and variance var0. All the parameters were given vague prior distributions.

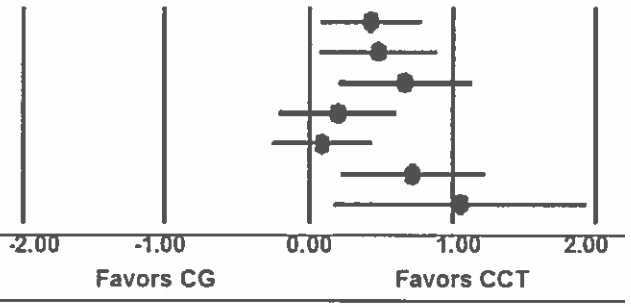
We used OpenBUGS, a Bayesian program, to estimate the parameters of this model, both because it can handle the complexities of the design and because Bayesian interpretation is conceptually (though not computationally) simple. A classical (frequentist) interpretation of the results is also possible for those who do not prefer Bayesian results; with vague prior distributions for the parameters, these results are nearly identical. Our interpretation will be made in classical terms, because we presume readers will be more familiar with these interpretations. The OpenBUGS code, data, and results for this procedure are reproduced in Appendix A.

3. Results

Nine studies met criteria for inclusion in our study (Alvarez et al., 2008; Bowie et al., 2013; Calkins et al., 2014; Elgamal et al., 2007; Lohman et al., 2013; Naismith et al., 2011; Owens et al., 2013; Segrave et al., 2014; Siegle et al., 2014). Across all studies, the average participant age was 44.1% and 55.0% were female. There were no significant differences between the CCT groups and control groups on the basis of demographics such as age, gender, or education. Table 1 summarizes demographic information and

Table 3
Bayesian hierarchical linear model estimates of domain effect sizes, standard error (SE) and 95% confidence intervals (CI).

Domain	Hedges' g	SE	95% CI	Z-Value
Symptom Severity	0.43	0.18	0.07 – 0.79	2.39*
Daily Functioning	0.48	0.21	0.09 – 0.91	2.29*
Attention	0.67	0.24	0.21 – 1.15	2.79*
Executive Functioning	0.20	0.21	-0.19 – 0.63	0.95
Verbal Memory	0.09	0.18	-0.26 – 0.47	0.50
Working Memory	0.72	0.26	0.22 – 1.24	1.23*
Global Functioning	1.05	0.45	0.14 – 1.89	2.33*



*$p < .05$

characteristics of the CCT interventions.

A total of 57 outcome measures were extracted. Mean effect size estimates, standard errors, 95% confidence intervals, and z-values for each domain are presented in Table 3. As can be seen from this table, the mean effect sizes of Symptom Severity (0.43), Daily Functioning (0.48), Attention (0.67), Working Memory (0.72), and Global Functioning (1.05) were accurately different from zero; these effect sizes ranged from small to large. The effect size estimates for Executive Functioning (0.20) and Verbal Memory (0.08) were small and statistically non-significant. No study effect size was accurately different from the average study effect size (see Table 4).

We used traditional meta-analytic methods to assess heterogeneity and moderators of the relationship between CCT and outcome. There was no evidence of heterogeneity in the effects of individual measures ($Q=11.935$, $p=0.154$, $I^2=32.968$). At the domain level, moderate to high heterogeneity was found for Verbal Memory measures ($Q=38.962$, $p<0.000$, $I^2=64.068$). Heterogeneity was not detected in any other domain. A moderator variable analysis revealed a significant Q-index for age ($Q_{Model}=5.728$, $p=0.017$, $Q_{Residual}=6.206$, $p=0.516$), with a slope of −0.012 and an intercept of 0.970 indicating the effect of CCT decreases with age. Other moderators of interest were not significant [type of control condition ($Q=3.828$, $p=0.050$), concurrent treatment ($Q=2.850$, $p=0.091$), gender ($Q=0.117$, $p=0.732$)]. The N_{fs} analysis found that 618 measures would be necessary to achieve a non-significant p-value.

Table 4
Individual study ES versus average study ES.

Study	b_X-b_0[a]	Standard error	95% CI	z-value
Alvarez et al. (2008)	0.48	0.29	−0.01–1.10	1.66
Bowie et al. (2013)	−0.04	0.21	−0.47–0.37	−0.19
Calkins et al. (2014)	−0.04	0.20	−0.44–0.36	−0.2
Elgamal et al. (2007)	0.08	0.18	−0.30–0.43	0.44
Lohman et al. (2013)	0.04	0.19	−0.34–0.40	0.21
Naismith et al. (2011)	−0.30	0.18	−0.70–0.03	−1.67
Owens et al. (2013)	−0.03	0.27	−0.60–0.51	−0.11
Segrave et al. (2014)	−0.40	0.27	−0.99–0.06	−1.48
Siegle et al. (2014)	0.15	0.23	−0.29–0.63	0.65
Average study ES	0.52	0.16	0.21–0.83	3.25*

* $p < 0.05$
[a] b_X-b_0 = difference between individual study ES (average outcome) and average study ES (average outcome).

4. Discussion

The purpose of this meta-analysis was to assess the impact of CCT on depression; in particular, whether CCT improves depressed mood, daily functioning, and five domains of cognitive functioning (attention, executive functioning, verbal memory, working memory, global functioning). The results of our meta-analysis reveal small to large effects for CCT on depressed mood, daily functioning, and three of five cognitive domains assessed (attention, working memory, and global functioning), suggesting that CCT may be an effective treatment option for adult depression. Although there was a large effect for Global Functioning, it must be interpreted with caution as it was based on only two outcome measures from the same study (Alvarez et al., 2008). In sum, CCT improved cognition inconsistently.

CCT significantly improved depressed mood; however, the mechanism by which this occurs is unclear due in part to treatments administered alongside CCT in several studies (Alvarez et al., 2008; Bowie et al., 2013; Elgamal et al., 2007; Naismith et al., 2011; Segrave et al., 2014; Siegle et al., 2014). Participants in these trials were treated with antidepressants, psychotherapy, or transcranial direct current stimulation either as part of the trial or were allowed to be on these treatments concurrently from outside sources. Concurrent treatment, however, did not account for a significant amount of variance in the results. It is possible that positive changes in cognitive functioning directly improves mood, or indirectly by enhancing the effects of ongoing treatments. We have recently discussed a model by which cognitive training may enhance antidepressant response (Motter et al., inpress). Late life depression often manifests with executive dysfunction and processing speed deficits which are associated with poor treatment response (Manning et al., 2015; Sneed et al., 2010). These impairments are due in part to reduced functioning of the cognitive control network, a neural pathway that regulates higher-order cognitive processes (Alexopoulos et al., 2012; Braver and Barch, 2002). CCT targeting processing speed may enhance executive functioning, strengthen functional connectivity in the cognitive control network, and in turn, produce improvements in antidepressant response.

Executive Functioning and Verbal Memory did not improve with CCT. Although Verbal Memory was a target in half the studies, Executive Functioning was targeting in one study during the last two weeks of the training (Bowie et al., 2013), and for only one session of psychoeducation in another (Naismith et al., 2011). As part of their CCT program, participants in Owens et al. (2013) completed a dual *n*-back task, which requires selective attention

and task switching. While executive function ability was trained, the dual *n*-back task itself and the four-item outcome measure are most accurately described as tests of working memory (Salminen et al., 2012). Similarly, studies that utilized Well's Attention Training and the Paced Auditory Serial Addition Task (Calkins et al., 2014; Segrave et al., 2014) tapped into executive control processes, but did not use outcome measures that directly evaluated executive functioning ability (Strauss et al., 2006). Although we did not find a significant effect for Executive Functioning, it is premature to conclude that CCT does not improve Executive functioning, because it was not targeted in most studies and insufficiently assessed.

Our analyses revealed that the effect of CCT declines slightly with age. This does not imply that the aging brain does not improve with CCT, but only that the effects of CCT diminish slightly with age. There is considerable evidence for neuroplasticity and cognitive improvement in the aging brain. In a trial of 42 elderly subjects randomized to 8-week verbal memory training versus passive control, memory training improved source memory performance and increased regional cortical thickness. Thickness change in the right fusiform and lateral orbitofrontal cortex correlated positively with improvement in memory, suggesting possible functional significance of the structural changes (Engvig et al., 2010). Another study tested the effect of 4-week training on a car racing video game on cognition in 46 elderly subjects. The game increased in difficulty as subjects got better. After training, trained subjects had scores that were higher than that of untrained 20-year-olds, and the skill remained six months later without practice. Certain cognitive abilities that were not specifically targeted by the game improved and remained improved, e.g., working memory and sustained attention (Anguera et al., 2013). Taken together, CCT appears to be a promising intervention for older adults despite smaller gains.

4.1. Limitations

The analyses performed in this meta-analysis were limited by the small number of studies for CCT in depression. Analyses were also limited by the fact that not all studies measured all outcome domains; this is a characteristic of many meta-analyses, which our 3-level Bayesian methods take into account. The problem, if traditional methods are used, is that studies in which more domains are measured are weighted more than those studies with fewer domains measured. Our methods, therefore, improves upon previous meta-analyses. Another limitation is the use of different diagnostic criteria to define depression. Although heterogeneous diagnostic samples increase the generalizability of the findings, it also decreases the specificity with which we can conclude that a specific treatment or training protocol is beneficial for a specific group.

4.2. Future directions

There are three critical issues facing CCT: (1) transfer, (2) teaching to the test, and (3) controlling for motivation and expectancy. An important question of CCT is whether improvements in cognitive ability transfer to everyday functioning. There was a moderate effect for Daily Functioning, indicating transfer to everyday life activities with CCT. Only two studies, however, collected outcome measures that were able to assess this transfer (Bowie et al., 2013; Naismith et al., 2011) so this finding needs to be interpreted with caution. Another related concern involves the similarity between CCT training protocols and outcome measures leading to the criticism that CCT "teaches to the test." The problems surrounding teaching to the test can be mitigated by administering a non-adaptive version of the CCT protocol to the control group. The procedure for both groups is virtually identical except for the scaling of task difficulty in the CCT group. A final critical issue facing CCT is controlling for expectancy and motivation (Rutherford and Roose, 2013). When not accounted for in the experimental design, expectancy and motivation can contribute to differential performance between the training and control group. One way to mitigate this is by incorporating active control protocols into the study design, in which participants take part in a task that is equally engaging and comparable with respect to duration and frequency.

Future analyses should attempt to determine if the effects of CCT are influenced by depressive severity. It is not understood if CCT has the same effects for currently symptomatic individuals compared to those in remission. Additionally, determining optimal dose and frequency of administration is important before CCT can be considered a viable intervention for depressed adults. Finally, understanding whether concurrent psychosocial interventions are necessary for functional gains must be established in order to best use CCT as a standalone or adjunctive treatment.

Appendix A. Supplementary Information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jad.2015.09.022.

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