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Review Article

Cognition-Specific Computerized Cognitive Training in Older Adults with Mild Cognitive Impairment: A Systematic Review and Meta-Analysis

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SUMMARY

To date, previous meta-analyses reported that computerized cognitive training (CCT) was a clinically beneficial intervention for cognitive function in older adults with mild cognitive impairment (MCI). However, little is known about the efficacy of narrowly defined cognition-specific CCT excluding commercial video games on cognitive function in patients with MCI. Randomized controlled trials (RCTs) of CCT in older adults with MCI were searched through CINAHL, Embase, Medline, PubMed, and PsychINFO. The overall cognitive domains, global cognitive function, attention, memory, working memory, and executive function were pooled separately for MCI. The overall effect on cognitive function in MCI across 8 trials was moderate (Hedges' g = 0.48, 95% confidence interval (CI) = 0.003–0.974). There was no significant publication bias. Moderate to large effects were found for global cognitive function, memory, and working memory, with the exception of attention, and executive function. Cognition-specific CCT was beneficial in improving global cognitive function, memory, and working memory in older adults with MCI. Therefore, this intervention warrants long-term trials with a larger number of subjects to investigate the effect on conversion from MCI to dementia.

1. Introduction

People with mild cognitive impairment (MCI) have been actively studied since a higher proportion of people with MCI develop Alzheimer's disease (AD) compared to healthy controls.[1] People with MCI show deficits in cognitive function.[2] Thus, previous studies have mainly focused on treatments effective for maintaining or improving cognitive function.[3,4]

Previous studies have revealed that people with MCI show cognitive plasticity, suggesting that they could benefit from cognitive training (CT).[5–9] CT has been used for people with MCI and as it has been found to be clinically effective.[10,11] Among different types of CT, computerized cognitive training (CCT) uses computers to deliver CT. It differs from conventional CT based on table-top activities.[12,13] CCT has been implemented for individuals with a cognitive impairment since the early 1980s. It has the advantage of customizing training difficulty levels according to an individual's function.[13] Generally, CCT can focus on one or several cognitive domains and offers a variety of cognitive tasks with a personalized level of difficulty to maximize clinical effects.[13] Recent meta-analyses have shown that CCT has moderate effect sizes on cognitive function in people with MCI.[10,13]

Unfortunately, previous meta-analyses have reported no significant effect of CCT on specific cognitive domains except for global cognitive function since CCT includes commercial video games and game apps defined as non-specific CCT in previous studies.[8,13–16] In contrast, the effect of cognition-specific CCT designed to improve specific cognitive domains remains unclear.[8,13–16]

Thus, more detailed and advanced research on MCI is needed beyond prior studies on CCT. In addition, CCT should consist of scientific programs designed to clinically improve cognitive function. Accordingly, it is necessary to synthesize CCT studies on MCI, not just on focusing commercial products, but also include cognition-specific CCT, to reaffirm whether cognition-specific CCT is meaningful in therapeutic areas. We assume that cognition-specific CCT would have positive effects on patients with MCI. Therefore, the aim of this study was to conduct systematic reviews and meta-analyses of narrowly defined CCT in MCI patients to confirm potential its beneficial effects on cognitive function.

2. Methods

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) using a PICO approach (Participants, Interventions, Control Outcomes, and Study Design),[17] and was prospectively registered with PROSPERO (CRD42020177874).

2.1. Literature search and study selection

A literature search was completed in March 2020. We searched randomized controlled trials (RCTs) examining the effects of CCT on cognitive function or depressive symptoms in people with MCI. This review focused on trials published from January 2010 to December

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2019 using the CINAHL, Embase, Medline, PubMed, and PsychINFO databases. The search terms were "computerized" OR "computer-assisted" OR "cognitive stimulation" OR "cognitive training" OR "cognitive rehabilitation" OR "cognitive intervention" OR "non-pharmacological training" with different combinations of "mild cognitive impairment" OR "mild cognitive disorder" OR "cognitive disorder" OR "cognitive dysfunction" OR "age-associated memory impairment" OR "cognitive decline".

Two reviewers (J-H. and S. Y.) independently conducted the initial eligibility screening based on the titles and abstracts and selected the studies. The reviewers agreed upon the selected studies after resolving disagreements by consultation with an additional reviewer.

2.2. Eligibility criteria

2.2.1. Types of subjects

The mean age of the subjects was more than 60 years old. The participants had a diagnosis of MCI using criteria in accordance with Petersen (2004) and no other psychiatric or neurological disorders.[1] Studies with healthy older people or those with AD were excluded if we could not separate the data for the subjects with MCI.

2.2.2. Types of interventions

Studies conducting cognition-specific CCT using a computer program developed to train one or more specific cognitive domains were included. To be included, cognition-specific CCT had to be the specific primary intervention. Thus, studies combining CCT with other interventions or using videogames with non-specific cognitive domains were excluded.

CCT with the following sub-factors was included:

1) Training was conducted on a computer or hardware console body.
2) The monitor application type was included.
3) Screen touching or panel button pressing actions was included.
4) The program was developed for the purpose of cognitive improvement, and otherwise only adopted the judgment of clinicians or their agreement using cognitive therapy.
5) The results were numerically quantified so that raw data could be clearly acquired.

2.2.3. Types of controls

Active controls (e.g. sham CCT, psychoeducation, and videogames) or usual treatment (e.g. pencil-and-paper cognitive training) were required. Wait-list control conditions or physical exercise as a sole intervention were excluded.

2.2.4. Types of outcomes

The outcomes were pre- and post-test measures of cognitive function (global cognitionor specified cognitive domains).

2.3. Data collection and coding

The coding of the outcomes into cognitive domains and depressive symptoms was conducted independently by two reviewers (J-H. and S. Y.). All outcomes were recorded as means, standard deviations, p-values, *t*-values or *F*-values for each group at pre-test and post-test or follow-uptesting.

2.4. Risk of bias and quality appraisal

To examine the risk of bias in the selected studies, Cochrane Collaboration's risk of bias tool was used.[18] If the studies were identified as having a high or unclear risk of bias for the assessors' blinding or incomplete outcome data sections, they were considered to have a high risk of bias.[13,18] The methodological quality of the included studies was assessed using the Physiotherapy Evidence Database Rating (PEDro) Scale.[19] All assessments were independently implemented by two reviewers (J-H. and S. Y.). Both reviewers established consensus scores after a discussion of any disparate assessments.

2.5. Data analysis

The statistical heterogeneity, effect size and publication bias of the included studies were analyzed using Comprehensive Meta-Analysis version 2.0 (Biostat, Englewood, NJ, USA). We calculated Hedges' *g* to derive the standardized mean differences. Pooled of the standardized mean Hedges' g estimates of < 0.30, ≥ 0.30 and < 0.60, and ≥ 0.60 represented small, moderate, and large effect sizes, respectively. Meta-analyses were conducted using a random-effects model where three or more studies examined comparable outcomes using a random-effects model. Analyses were carried out for cognitive and depression domains separately. When the selected studies included multiple measurements of a certain domain for the analysis, the measurements for each domain were averaged to one pooled effect size. To investigate statistical heterogeneity, the I^2 statistic was used and considered as low, moderate, or large at 25%, 50%, or 75%, respectively.[20] Publication bias was visually analyzed using funnel plots and Egger's regression intercept test.[21] Asymmetrical points on the funnel plot indicated publication bias and an Egger's regression intercept test with a p-value above 0.05 meant there was no publication bias.

3. Results

3.1. Study selection

In the initial literature review, a total of 10,236 studies were identified. After removing the duplicates, the titles and abstracts of 8,642 were screened. Of these, eight articles that met the inclusion criteria were finally selected (Figure 1).

3.2. Participant characteristics in the included studies

The total number of subjects included was 328 (CCT: n = 169, mean group size: n = 21.1, control: n = 159 mean group size: n = 19.8). The age range of all subjects was between 55.0 and 78.2 years old. The subjects' education levels were precluded due to disparity and a lack of reporting. The mean PEDro score was 8.0/10, and 3/8 studies had a high or unclear risk of bias (Table 1 and Supplementary Figures 1 and 2).

3.3. Cognition-specific computerized cognitive training

Cognition-specific CCT was mainly delivered as a PC program designed to improve various aspects of cognitive function. The most common intervention type in the included studies was multi-domain (62.5%). In the three single-domain intervention studies, two used memory training whereas one conducted processing speed training. The training dose of the cognition-specific CCT varied, with a total length ranging from 4 to 80 hours (Table 1).

3.4. Meta-analysis of outcome measures

3.4.1. Overall effect on cognitive outcome measures

The overall effect size was moderate and statistically significant

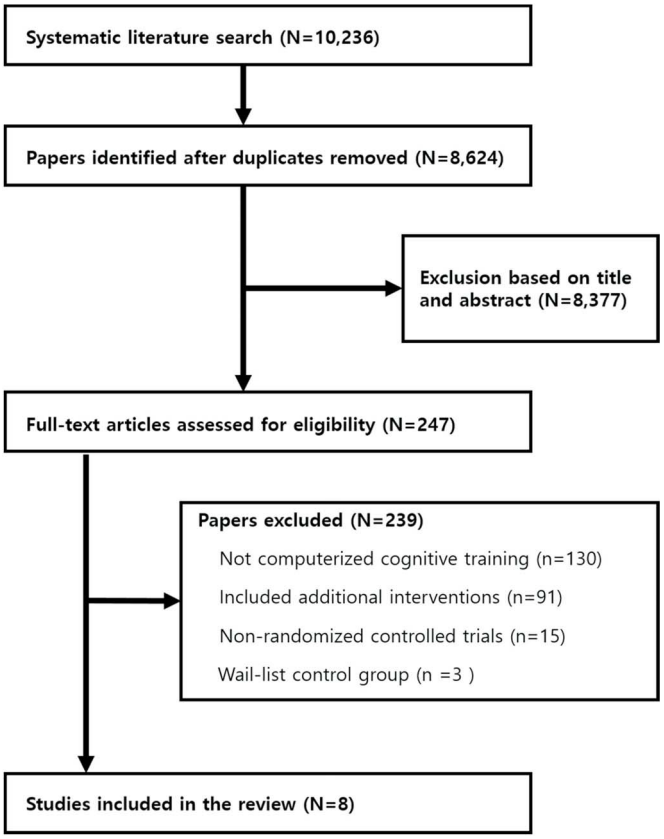

Figure 1. Flow chart of the study selection process.

(k = 7, g = 0.48, 95% confidence interval (CI) = 0.003 to 0.974, I^2 = 78.69%) with high heterogeneity (Figure 2). The effect size was a positive value, meaning the cognition-specific CCT groups had a significantly higher value than the active control groups. The funnel plot did not show significant asymmetry (Egger's intercept = 3.02, p = 0.05), suggesting no significant publication bias (Figure 3).

3.4.2. Global cognitive function

The pooled effect size of cognition-specific CCT on global cognitive function was large and statistically significant (k = 5, g = 0.60, 95% CI = 0.146 to 1.064, p = 0.001, I^2 = 69.94%) compared to the active control groups (Supplementary Figure 3). The funnel plot did not reveal significant asymmetry (Egger's intercept = 3.39, p = 0.06) (Supplementary Figure 4A).

3.4.3. Attention

The meta-analysis showed no significant effect in cognition-specific CCT compared to the controls (k = 3, g = 0.86, 95% CI = -0.851 to 2.590, p = 0.322, I^2 = 96.20%) (Supplementary Figure 3). The funnel plot did not indicate asymmetry (Egger's intercept = 6.22, p = 0.39) (Supplementary Figure 4B).

3.4.4. Memory

The effect of cognition-specific CCT on memory was moderate and significant compared to the active control conditions. The meta-analysis revealed a pooled effect size of 0.57 (k = 5, g = 0.45, 95% CI = 0.087 to 1.071, p = 0.021) with high heterogeneity between the studies (I^2 = 76.85%) (Supplementary Figure 5). The funnel plot showed significant asymmetry (Egger's intercept = 5.10, p = 0.02)

Table 1
Characteristics of the studies included in the systematic review and meta-analysis.

Author and year	Participants	Intervention	Control condition	Dose (hour)	Outcomes	Results	PEDro-scale
Djabelkjr et al., 2017[42]	N = 20 (CCT = 10; control = 10) Mean age (CCT = 78.2, control = 75.2)	Computer program Multi-domain	Computerized cognitive engagement	18	Executive function, global cognitive function, working memory	Both groups did not differ significantly in cognitive and psychosocial changes	8
Singh et al., 2014[43]	N = 51 (CCT = 24; control = 27) Mean age (CCT ≥ 55, control ≥ 55)	Computer program Multi-domain	Cognitive stimulation using videos	80	Attention, executive function, global cognitive function	CCT had no significant effects on cognitive functions compared to the control condition	10
Gooding et al., 2016[44]	N = 51 (CCT = 31; control = 20) Mean age (CCT = 75.6, control = 75.6)	Computer program Multi-domain	Computer games and puzzles	30	Global cognitive function, memory	Significant differences were seen in cognitive functions. However, there was no significant difference in depression between both groups	8
Han et al., 2017[45]	N = 43 (CCT = 23; control = 20) Mean age (CCT = 73.7, control = 74.5)	Computer program Memory	Paper-pencil based cognitive training	4	Global cognitive function, memory	The CCT group had larger improvement in memory than the control group but not in global cognitive function and depression	8
Herrera et al., 2012[46]	N = 22 (CCT = 11; control = 11) Mean age (CCT = 75.1, control = 78.2)	Computer program Multi-domain	Paper-pencil based cognitive training	24	Attention, executive function, global cognitive function, memory	The CCT group showed greater improvements in all outcomes than the control group	6
Lin et al., 2016[47]	N = 21 (CCT = 10; control = 11) Mean age (CCT = 72.9, control = 73.1)	Online program Processing speed	Mental leisure using a computer	24	Attention, executive function, working memory	CCT led to significantly larger improvements in all cognitive domains than the control condition	8
Park & Park, 2018[29]	N = 78 (CCT = 39; control = 39) Mean age (CCT = 66.9, control = 67.6)	Computer program Multi-domain	Commercial video games	15	Attention, executive function, memory	A greater improvement in attention were seen in the control group than the CCT group	10
Savulich et al., 2017[48]	N = 42 (CCT = 21 control = 21) Mean age (CCT = 75.2, control = 76.9)	Computer program Memory	Paper-pencil based cognitive training	8	Global cognitive function, memory	Significant differences were found for global cognitive function and memory between both groups	6

CCT: computerized cognitive training.

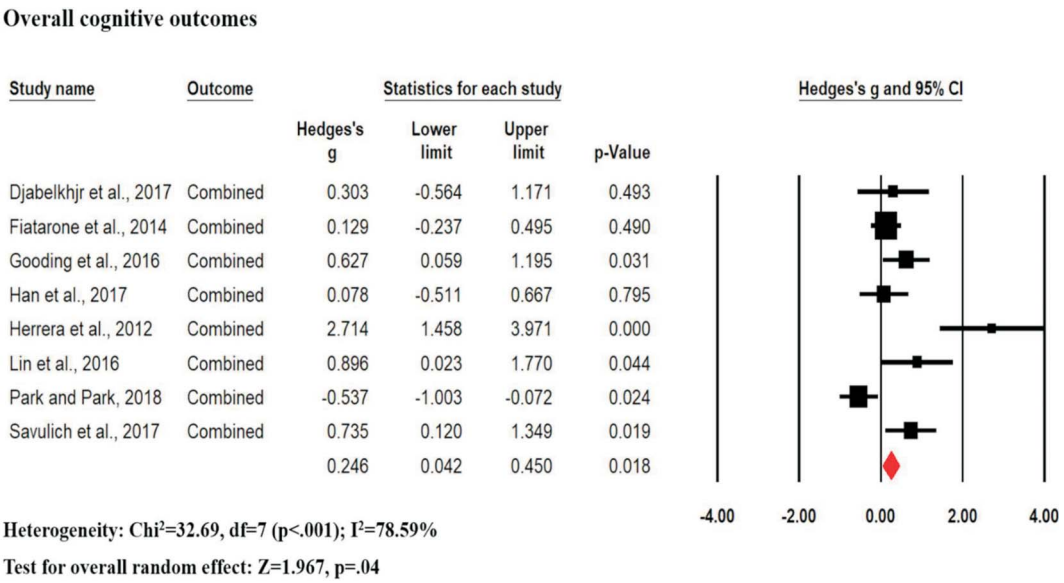

Figure 2. Forest plot demonstrating the efficacy of CCT on the overall cognitive outcomes.

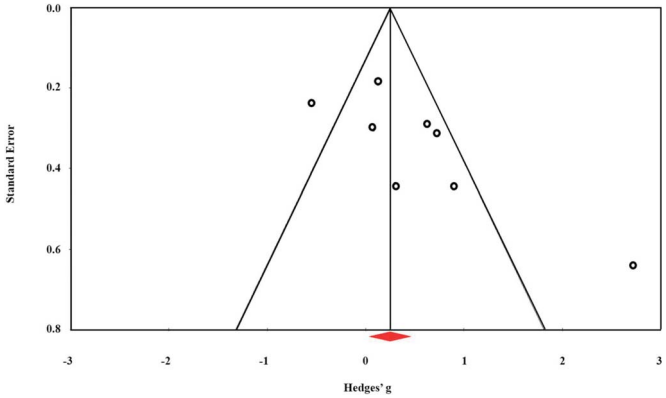

Figure 3. Funnel plot demonstrating the bias of CCT on the overall cognitive outcomes.

(Supplementary Figure 6A). A trim and fill analysis did not impute additional studies.

3.4.5. Working memory

The pooled effect size of cognition-specific CCT on working memory was large and statistically significant (k = 2, g = 0.68, 95% CI = 0.009 to 1.350, p = .04, I^2 = 39.93%) compared to the active control groups (Supplementary Figure 5). The funnel plot did not indicate significant asymmetry (Egger's intercept = 4.97, p = 0.94) (Supplementary Figure 6B).

3.4.6. Executive function

The meta-analysis showed no significant effect of cognition-specific CCT on executive function compared to the active controls (k = 3, g = 0.05, 95% CI = -0.214 to 0.366, p = 0.714, I2 = 0.0%) (Supplementary Figure 7). The funnel plot revealed asymmetry (Egger's intercept = 1.67, p = 0.02) (Supplementary Figure 8). A trim and fill analysis imputed one study; the adjusted effect size was small and not statistically significant (g = 0.01, 95% CI = -0.23 to 0.26).

4. Discussion

Based on the results from the eight studies, cognition-specific CCT was found to be a promising intervention for improving cognitive function in elderly people with MCI. There were moderate to large positive effect sizes identified in the cognitive outcomes, with statistical significance reached for global cognitive function (g = 0.60, 95% CI = 0.146 to 1.064), memory (g = 0.45, 95% CI = 0.087 to 1.071), and working memory (g = 0.68, 95% CI = 0.009 to 1.350) but not for attention (g = 0.86, 95% CI = -0.851 to 2.590) or executive function (g = 0.05, 95% CI = -0.214 to 0.366), which is largely consistent with a previous meta-analysis study (Zhang et al., 2019). The overall effect size on cognitive function (g = 0.48, CI = 0.003 to 0.974) in this study was larger than that in a recent meta-analysis study (g = 0.35), indicating the clinical benefit of cognition-specific CCT for MCI.[13]

Based on previous studies, the intervention domain that cant enhance cognitive functions includes memory domain or multi-domain, which is consistent with studies included in the present analysis.[5] In addition, findings of this study were consistent with results of Zhang et al. showing positive effects of CCT.[10] However, the difference between our study and the study of Zhang et al. was that they included console games that could be classified as non-specific cognitive training[22] and compared treatment groups with control groups involving non-active controls such as wait-list groups, whereas the present study included only CCT designed to provide cognition-specific training without other interventions and compared the intervention only to active control groups. Although we analyzed the effectiveness of narrowly defined cognition-specific CCT, results of our study were similar to those of the previous study. This clearly indicates that cognition-specific CCT is more effective than conventional cognitive intervention. These methodological issues are crucial as they could contribute to effects of CCT.[15,23] Indeed, contrasted with our findings, results of a previous meta-analysis have revealed no clear effects of CCT on cognitive function for individuals with MCI contrasted with our findings.[24] The previous meta-analysis only included studies with a minimum 12-week intervention period. Even people at risk of cognitive decline were included as MCI subjects in the previous meta-analysis.[24] Additionally, previous studies have indicated methodological issues such as non-active control groups and CCT combined with other interventions, resulting in no clear evidence on effects of cognition-specific CCT.[15,23] Given these issues, the current meta-analysis makes a clear and useful contribution to the evidence on the effectiveness of cognition-specific CCT for improving cognitive function in patients with MCI.

Specifically, moderate effect sizes on global cognitive function and memory are encouraging given that people with MCI are at risk

of progression to AD.[25] Considering that most previous studies lack evidence for effects of CT on individuals with AD,[26] our results suggest that cognition-specific CCT is useful at a stage of MCI to obtain its optimal benefit before patients progress to AD. In particular, large effect sizes on working memory were found in this study, which is consistent with a previous study.[5] Given that working memory is considered a central focus in most cognitive interventions, this result is unsurprising, but promising in terms of primary complaint in MCI cases. In contrast, we reported a lack of effectiveness of CCT for attention and executive function, which is consistent with results of previous meta-analyses of CCT.[13,14,27] Attention could be enhanced by learning new cognitive tasks.[28] Indeed, Park and Park (2018) have reported that active control conditions such as video games might improve attention as they could facilitate their learning in a fun manner with a fancy avatar and environment that can motivate subjects to participate more actively.[23] In the studies included the present meta-analysis, video games were used as an active-control condition, which might have positive effects on attention. In contrast, a lack of evidence on executive function could be attributed to the fact that cognitive training benefits generally reflect training contents.[29,30] This result suggests that cognition-specific CCT has insufficient training contents for executive function such as inhibitory control, abstract thinking, and reasoning in the included studies.[13]

This meta-analysis was mainly focused on RCTs of cognition-specific CCT in people with MCI. However, since most RCTs investigated short-term cognitive outcomes using neuropsychological assessments, our study had insufficient data to confirm long-term outcomes. Considering that the main goal of cognitive intervention for people with MCI is to slow the progression to AD or prevent AD, our results were far from meeting the goal. To determine whether small to moderate effects seen in this study could transfer to meaningful benefits in everyday function, studies on the long-term transfer to untrained functional ability need to be conducted in the future. In addition, included studies were barely double-blinded given the nature of CCT. Nevertheless, this could induce the risk of expectation bias that might exaggerate the results. Finally, this study did not differentiate subtypes of MCI such as amnestic MCI and non-amnestic MCI, which might lead to different intervention effects among participants and make it difficult to confirm the effectiveness of cognition-specific CCT in the present study. Therefore, long-term transfer effects of cognition-specific CCT by sub-types of MCI should be investigated in the future to determine the potential of using CCT to reduce the social burden induced by AD.

Clinical advantages of cognition-specific CCT are that it provides personalized treatment based on neuropsychological patterns of individuals with cognitive impairment by stimulating damaged area[10,31] and that it can reduce the time and cost of treatment.[13,32] Since the introduction of cognition-specific CCT, patients have some chance to objectively evaluate their ability to perform tasks and obtain systematic treatments. It not only can standardize and provide structural training tasks by cognitive domains but also can control training difficulty in accordance with individual cognitive levels.[32] Performances on cognition-specific CCT can be accurately and continuously recorded and compared, thus increasing its usefulness in clinics.[32]

In conclusion, although we narrowly defined CCT, this meta-analysis demonstrated that cognition-specific CCT was effective for global cognitive function, memory, and working memory. However, the effects on attention and executive function were negligible. Furthermore, long-term transfer of the effectiveness of cognition-specific CCT and its potential to reduce AD prevalence remain unknown. Future clinical trials are needed with larger sample sizes to determine whether its effects can last over long periods and slow or prevent the progression of MCI to AD.

Acknowledgement

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Conflict of interest

The authors have no potential conflicts of interest to disclose.

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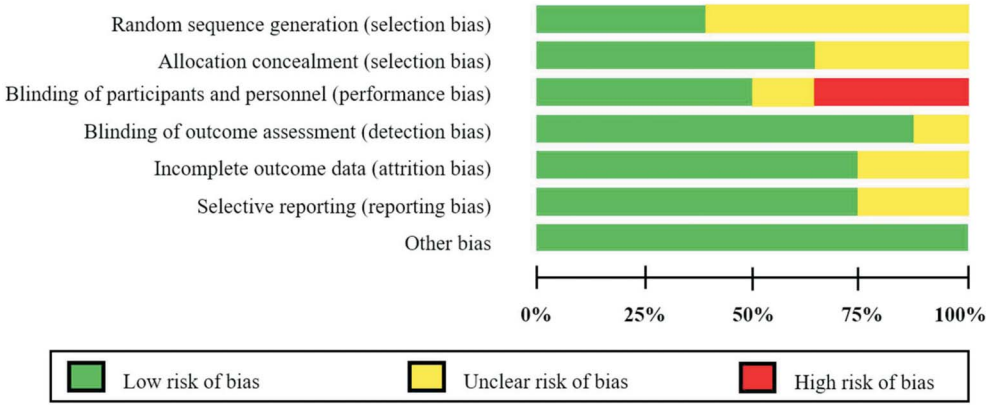
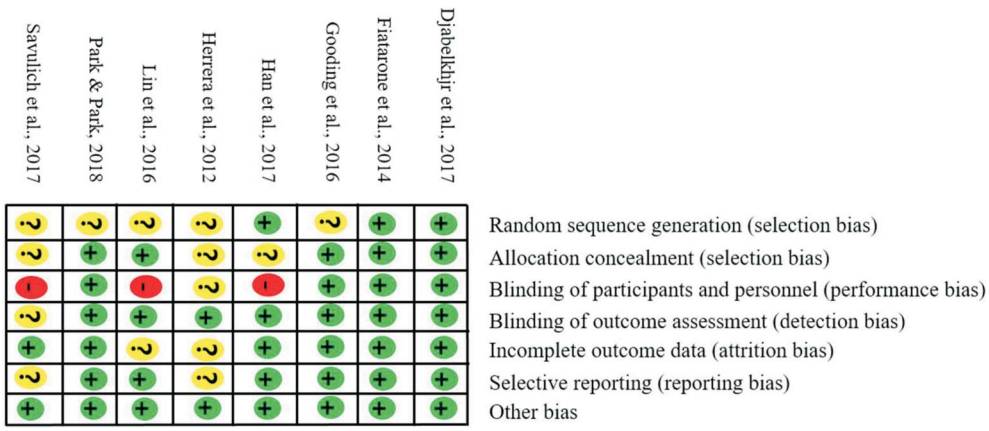
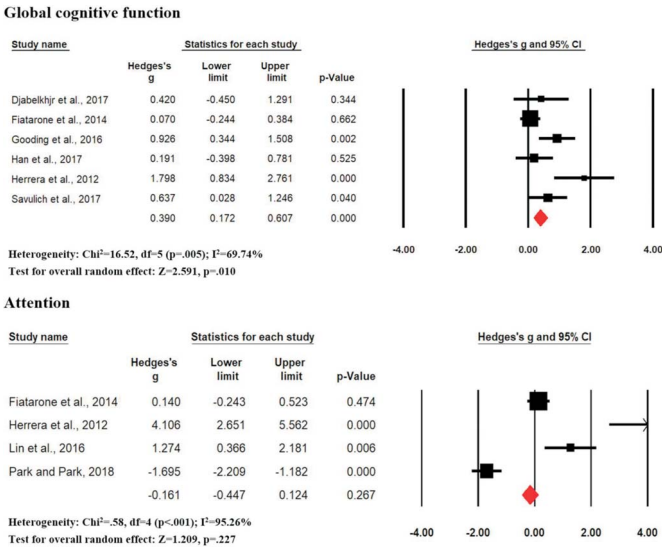
Supplement



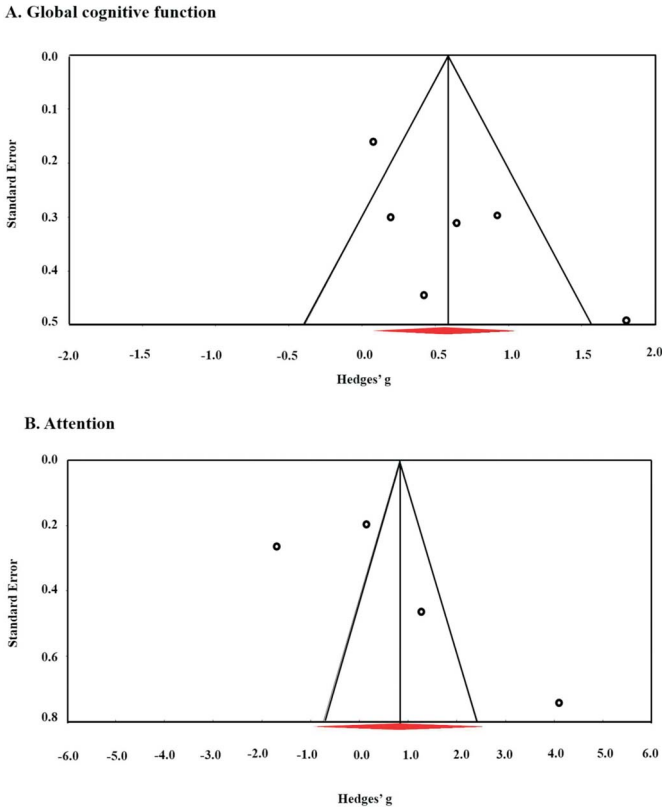
Supplementary Figure 1. Risk of bias graph: authors' judgement about each risk of bias item presented as percentages across all the included studies.



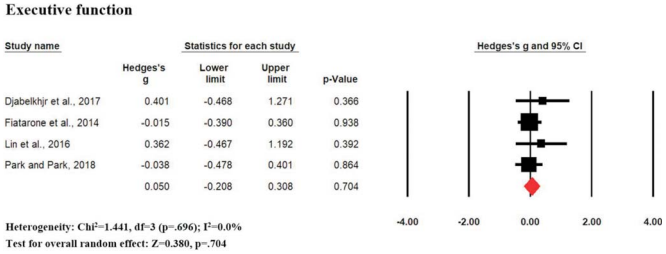
Supplementary Figure 2. Risk of bias summary: authors' judgement about each risk of bias item for each included study.



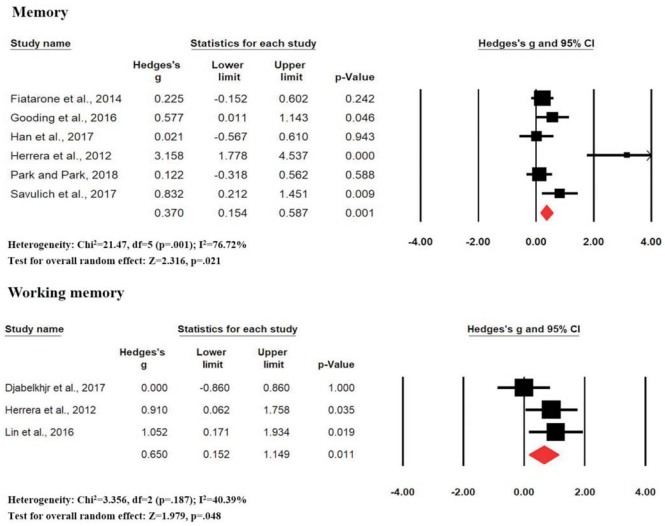
Supplementary Figure 3. Forest plot demonstrating the efficacy of CCT on global cognitive function and attention.



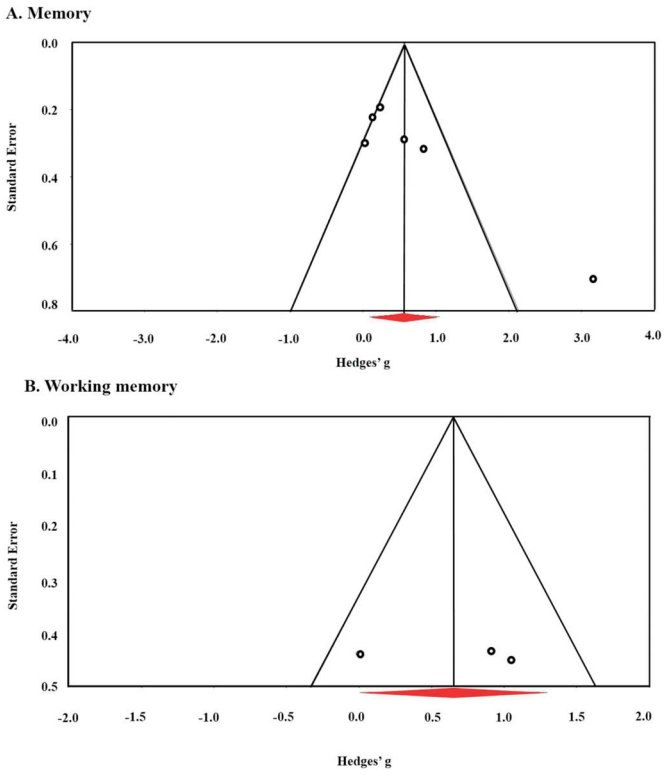
Supplementary Figure 4. (A) Funnel plot demonstrating the bias of CCT on global cognitive function. (B) Funnel plot demonstrating the bias of CCT on attention.



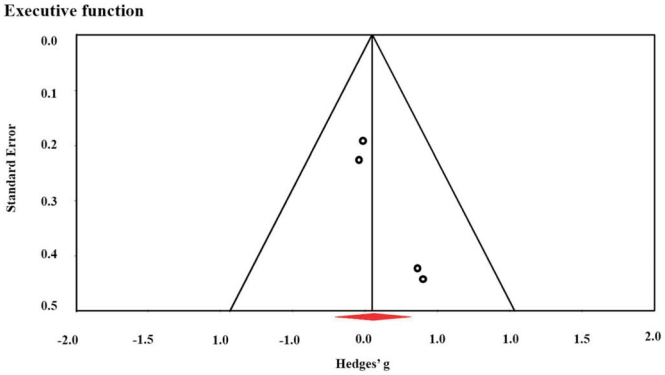
Supplementary Figure 7. Forest plot demonstrating the efficacy of CCT on executive function.



Supplementary Figure 5. Forest plot demonstrating the efficacy of CCT on memory and working memory.



Supplementary Figure 6. (A) Funnel plot demonstrating the bias of CCT on memory. (B) Funnel plot demonstrating the bias of CCT on working memory.



Supplementary Figure 8. Funnel plot demonstrating the bias of CCT on executive function.