Computerized Cognitive Training in Older Adults With Mild Cognitive Impairment or Dementia: A Systematic Review and Meta-Analysis

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Objective: Previous meta-analyses indicate that computerized cognitive training (CCT) is a safe and efficacious intervention for cognition in older adults. However, efficacy varies across populations and cognitive domains, and little is known about the efficacy of CCT in people with mild cognitive impairment or dementia.

Method: The authors searched Medline, Embase, PsychINFO, CINAHL, and CENTRAL through July 1, 2016, for randomized controlled trials of CCT in older adults with mild cognitive impairment or dementia. Overall cognition, individual cognitive domains, psychosocial function, and activities of daily living were pooled separately for mild cognitive impairment and dementia trials.

Results: The overall effect on cognition in mild cognitive impairment across 17 trials was moderate (Hedges' g=0.35, 95% CI=0.20–0.51). There was no evidence of publication bias or difference between active- and passive-controlled trials. Small to moderate effects were found for global cognition, attention, working memory, learning, and memory, with the exception of nonverbal memory, and for psychosocial functioning, including depressive symptoms. In dementia, statistically significant effects were found on overall cognition (k=11, g=0.26, 95% CI=0.01–0.52) and visuospatial skills, but these were driven by three trials of virtual reality or Nintendo Wii.

Conclusions: CCT is efficacious on global cognition, select cognitive domains, and psychosocial functioning in people with mild cognitive impairment. This intervention therefore warrants longer-term and larger-scale trials to examine effects on conversion to dementia. Conversely, evidence for efficacy in people with dementia is weak and limited to trials of immersive technologies.

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Dementia is a progressive neurocognitive disorder characterized by insidious cognitive and functional decline until death. At present, the global prevalence of dementia is estimated at 5%–7% of people over 60 years (1). Mild cognitive impairment often precedes dementia and is characterized by largely intact everyday function despite objective evidence of cognitive decline (2). Mild cognitive impairment is a proximal risk factor for dementia (3), falls (4), and higher health expenditure (5), and risk increases proportionally with the number of impaired cognitive domains and symptom severity (3).

Conversion from mild cognitive impairment to dementia can be conservatively estimated at 5%–10% per year (3, 6, 7), and similar rates have been observed in the opposite direction (i.e., reversion from mild cognitive impairment to normal cognition) (7–9). Thus, mild cognitive impairment is an unstable cognitive state with potential to avert progression to dementia and attendant health and societal sequelae. To date, there is no systematic evidence for the effectiveness of any intervention on the cognitive and psychological symptoms of mild cognitive impairment (10). The current preferred medical treatment, cholinesterase inhibitors, only offer modest short-term cognitive benefits, and their clinical value continues to be debated given the risk of adverse events in clinical trials (11).

Computerized cognitive training (CCT) has generated considerable attention as a safe, relatively inexpensive and scalable intervention that aims to maintain cognition in older adults. CCT involves guided drill-and-practice on standardized tasks designed to load on specific cognitive processes, typically without explicit teaching of memory or problem-solving strategies, which distinguish CCT from other approaches for cognitive remediation (12). CCT can target single or multiple domains and usually adapts task difficulty to individual performance. Recent meta-analyses of randomized controlled trials of CCT have found moderate

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effect sizes on cognition in healthy older adults (13) and in Parkinson's disease (14), as well as on symptom severity, daily functioning, and cognition in major depression (15).

While CCT is a frequent intervention in primary prevention trials (16), the extent to which CCT can benefit cognition in already diagnosed mild cognitive impairment or dementia is unclear. Systematic reviews of cognitive interventions in mild cognitive impairment or dementia have reported mixed results (17–25), but these interventions combined CCT with non-CCT interventions, such as cognitive stimulation or individual rehabilitation strategies, and mixed randomized controlled trials with other designs. We therefore aimed to conduct separate systematic reviews and meta-analyses of narrowly defined CCT in individuals with mild cognitive impairment or dementia in order to chart potential benefits on cognition and behavior across domains and diagnostic groups.

METHOD

This work adheres with PRISMA [Preferred Reporting Items for Systematic Reviews and Meta-Analyses] guidelines (26), was prospectively registered with PROSPERO (CRD42015023679), and follows our published methods for meta-analysis of CCT in older adults (13, 14).

Information Sources and Study Selection

We searched Medline, Embase, PsychINFO, CINAHL, and CENTRAL from inception to July 1, 2016 for randomized controlled trials examining the effects of CCT on one or more cognitive or behavioral outcomes in older adults with mild cognitive impairment or dementia (for the full search strategy, see Table S1 in the data supplement accompanying the online version of this article). We did not apply database limits, and non-English articles were translated. Additional articles were obtained by scanning reference lists of included studies and previous reviews. One reviewer (N.T.M.H. or V.L.C.) conducted initial eligibility screening based on title and abstract, followed by assessment of full-text versions by two independent reviewers (N.T.M.H., V.L.C., or an additional reviewer [see the Acknowledgments]). Disagreements were resolved by a senior reviewer (A.L.), who approved the final list of included studies. When eligibility was unclear, one reviewer (N.T.M.H.) contacted authors for additional information.

Eligibility Criteria

Types of participants. The mean age of participants was ≥60 years old, with a diagnosis of mild cognitive impairment or dementia (of any etiology), confirmed by examining the inclusion criteria or baseline scores against standardized diagnostic criteria (2, 27).

Types of interventions. At least 4 hours of drill and practice, with a clear cognitive rationale, videogames, or virtual reality, had to be completed. Studies combining CCT with other interventions were eligible if the control group received the same adjacent intervention. Studies were excluded if less than 50% of the cognitive intervention was CCT or not involving interaction with a computer (e.g., merely watching stimuli).

Types of controls. Passive (no-contact, wait-list), active (e.g., sham CCT, psychoeducation), or pencil-and-paper cognitive training was required. Physical exercise as a sole control condition was excluded.

Types of outcomes. Outcomes were change from baseline to posttraining in nontrained measures of cognition (global cognition, verbal or nonverbal learning, verbal or nonverbal memory, working memory, processing speed, attention, language, visuospatial skills, and executive function); activities of daily living; instrumental activities of daily living; or psychosocial functioning (neuropsychiatric symptoms, quality of life, and depression). All eligible outcomes per study and domain were included. Index scores were excluded if subdomain scores were available.

Data Collection and Coding

Coding of outcomes into cognitive domains and effect direction were performed independently by two reviewers (N.T.M.H. and L.M.) according to accepted neuropsychological categorization (28) or by consulting with a senior reviewer (A.L.) (for categorization of outcomes by domains, see Table S2 in the online data supplement). Outcomes were recorded as mean and standard deviations for each group at baseline and follow-up with the exception of standardized mean difference and 95% confidence interval (29) or mean change and standard deviation (30).

When studies included mixed cohorts, we asked primary authors for split data by diagnosis and group. Three studies for which split data were not available were coded as dementia according to baseline indications of functional impairment in >50% of the sample (31–33).

Risk of Bias in Individual Studies and Quality Appraisal

The Cochrane Collaboration's risk of bias tool (34) was used to assess risk of bias in individual studies. Studies with high or unclear risk of bias for the blinding of assessors or incomplete outcome data categories were considered as high risk of bias. Methodological quality within studies was further assessed using the PEDro-P scale [Physiotherapy Evidence Database Rating Scale] (35). The original scale consists of 11 items. However, blinding of therapists and patients was not assessed due to nonfeasibility in CCT trials, and thus the maximum obtainable score (reflecting higher quality) was 9. Assessments were conducted by two independent reviewers (N.T.M.H., V.L.C. or an additional reviewer [see Acknowledgments]). A senior reviewer (A.L.) established consensus scores and resolved disagreements.

Data Analysis

We calculated standardized mean differences as Hedges' g and 95% confidence interval of change in outcome measures between the CCT and control groups from baseline to

posttraining and each follow-up. A positive standardized mean difference indicates a therapeutic effect of CCT over and above the control. Pooling of standardized mean differences across studies was performed using a random-effects model. Analogous to Cohen's d (36), Hedges' g estimates of <0.30, ≥ 0.30 and <0.60, and ≥ 0.60 were considered small, moderate, and large, respectively. Analyses were performed for overall cognitive outcomes, as well as for each cognitive or behavioral domain separately. When studies provided more than one outcome per domain for analysis, their standardized mean difference and variance were combined into a single study-level estimate. Finally, standardized mean differences from each arm (CCT and control) were split at the study level and pooled across studies in order to investigate nonspecific effects among control groups and likewise to investigate whether CCT genuinely enhances cognition.

Heterogeneity across studies was quantified using the I^2 statistic, considered as low, moderate, or large when at 25%, 50%, or 75%, respectively (37). Small study effect (publication bias) was assessed by visually inspecting funnel plots of standardized mean differences against standard error for asymmetry (38). When at least 10 studies were available for analysis, Egger's test of the intercepts (39) was used to formally test asymmetry, and the Duval and Tweedie trim and fill (40) was used to quantify the magnitude of small study effect. When less than 10 studies were available and potential asymmetry was found, a sensitivity analysis was performed by recalculating effect size after removal of outliers. A planned series of subgroup analyses based on key study design features (13) was not performed due to null statistical heterogeneity among mild cognitive impairment outcomes (I^2=0% and τ^2=0.001 for the most powered analysis, Figure 1), making redundant tests for further between-study variance. All analyses were performed using Comprehensive Meta-analysis version 3.0.

RESULTS

Study Selection

The initial search provided a total of 22,276 records. After removing duplicates, 14,961 articles were screened based on titles and abstracts, of which 660 full-text versions were assessed for inclusion. Twenty-six studies were eligible for inclusion in the review, of which one was excluded because the summary data were not provided in the original report (41) and could not be obtained from the authors. Four articles (30, 42–44) were split into two studies each, and two articles reporting outcomes from the same trial (45, 46) were combined into one study. Finally, one additional study was obtained from a book chapter (47), resulting in a final data set of 29 independent comparisons (mild cognitive impairment: k=17, dementia: k=12) (Figure 2). We requested additional data from authors of 18 reports, of which six provided data (29, 31, 44, 48–50).

Characteristics of Included Studies

Mild cognitive impairment. The 17 included studies encompassed 686 participants (CCT: N=351, mean group size: N=21; control: N=335, mean group size: N=20) (Table 1). Mean age ranged between 67 and 81 years old, and 51.88% of participants were female. One study (51) did not report gender ratios. Active control was provided in 11/17 studies. The mean PEDro-P score was 7.2/9 (SD=1.03), and 14/17 studies had high or unclear risk of bias (for risk of bias assessments, see Table S3 in the online data supplement). The majority of studies (15/17) administered supervised training.

Dementia. The 12 included studies encompassed a total of 389 participants (CCT: N=201, mean group size: N=17; control: N=188, mean group size: N=16) (Table 1). Mean age ranged between 66 and 81 years old, and 63.5% of participants were female. One study (32) did not report gender ratios. Active control was confirmed in 7/12 studies. The mean PEDro-P score was 7.7/9 (SD=1.25), and 10/12 studies had high or unclear risk of bias (see Table S3 in the online data supplement). The majority of studies provided supervised training (9/12). One study (52) reported only behavioral outcomes.

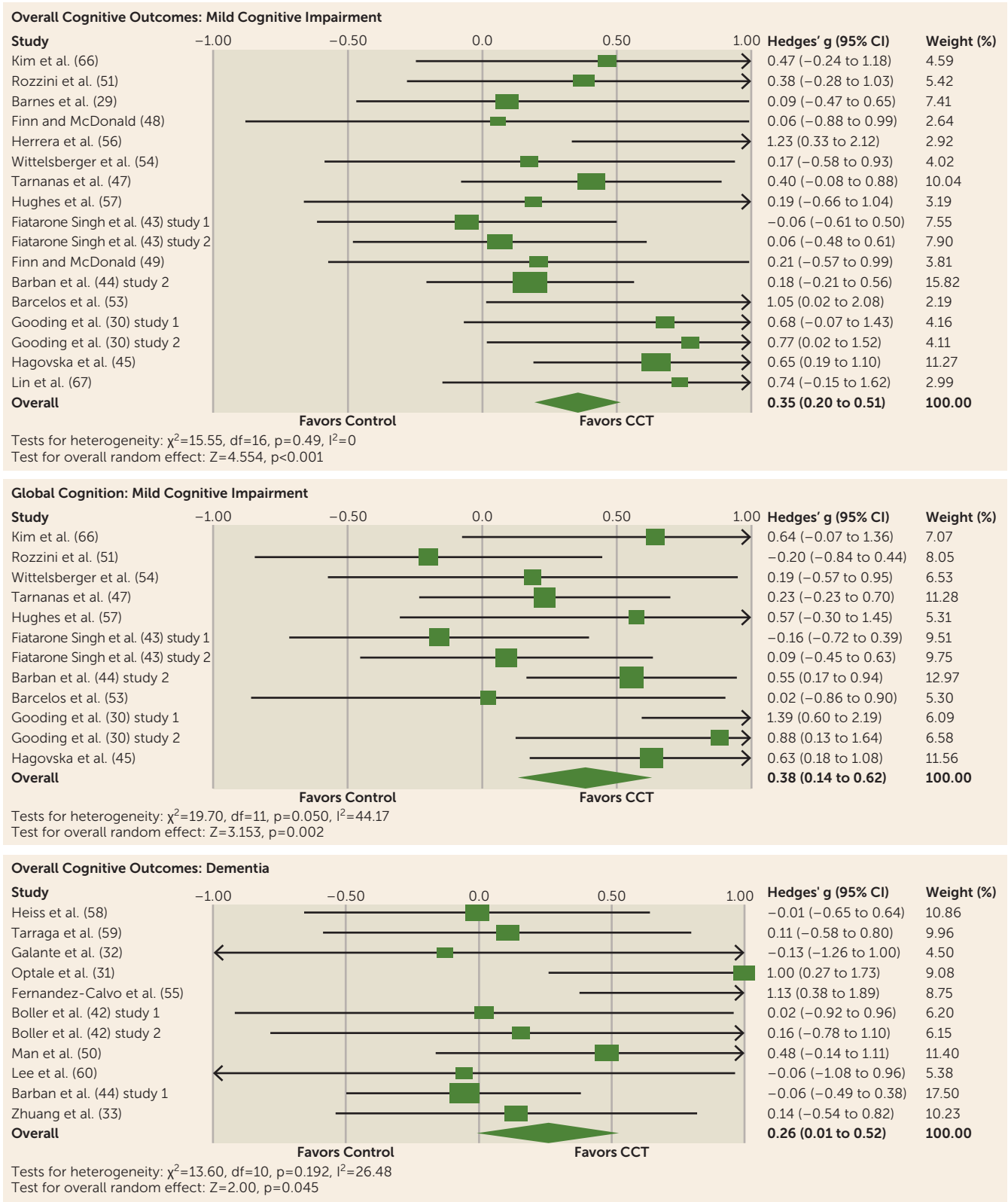
Meta-Analysis of Mild Cognitive Impairment Outcomes

Overall efficacy on cognitive outcomes. The overall effect size was moderate and statistically significant (k=17, g=0.35, 95% confidence interval [CI]=0.20–0.51, $p<0.001$, I^2=0%) (Figure 1). The funnel plot did not reveal significant asymmetry (Egger's intercept=1.39, p=0.11 [see Figure S1 in the data supplement). After splitting arms, CCT groups revealed a statistically significant improvement (g=0.32, 95% CI=0.20–0.44, I^2=28.47%), compared with no change across control groups (g=0.02, 95% CI=–0.08 to 0.11, I^2=0%). The effect size across active-controlled trials (k=11, g=0.40, 95% CI=0.17–0.63, I^2=18.95%) was comparable to that of trials with passive control groups (k=6, g=0.32, 95% CI=0.09–0.55, I^2=0%). Domain-specific effect sizes are summarized in Figure 3.

Global cognition. The global cognition effect size was moderate and statistically significant (k=12, g=0.38, 95% CI=0.14–0.62, p=0.002, I^2=44.17%) (Figure 1). The funnel plot did not reveal asymmetry (Egger's intercept=0.33, p=0.83) (see Figure S1 in the data supplement). Once again, the pooled effect size across CCT groups was significant (g=0.28, 95% CI=0.05–0.51), compared with no change in the controls (g=–0.02, 95% CI=–0.16 to 0.12), and there was no difference between the effect across active (k=8, g=0.41, 95% CI=0.03–0.75) and passive (k=4, g=0.37, 95% CI=0.02–0.72) controlled trials.

Verbal learning. The verbal learning effect size was moderate and statistically significant (k=11, g=0.39, 95% CI=0.14–0.63, p=0.002, I^2=37.3%) (see Figure S2 in the data supplement). The funnel plot revealed significant asymmetry (Egger's intercept=3.95, p=0.04) (see Figure S3 in the data supplement). A trim and fill analysis imputed three studies; the adjusted effect size was small and statistically nonsignificant (g=0.20, 95% CI=–0.08 to 0.49).

FIGURE 1. Meta-Analyses of Overall and Global Cognition Outcomes[a]



[a] Studies are sorted by publication year. CCT=computerized cognitive training.

Verbal memory. The verbal memory effect size was moderate and statistically significant (k=12, g=0.42, 95% CI=0.21–0.63, p<0.001, I^2=33.02%) (see Figure S2 in the data supplement). The funnel plot revealed significant asymmetry (Egger's intercept=2.5, p=0.06) (see Figure S3 in the data supplement). A trim and fill analysis did not impute additional studies.

Nonverbal learning. The nonverbal learning effect size was moderate and statistically significant (k=8, g=0.50, 95% CI=0.25–0.76, p<0.001, I^2=15.32%) (see Figure S2 in the data supplement). The funnel plot did not reveal asymmetry (see Figure S3 in the data supplement).

Working memory. The working memory effect size was large and statistically significant (k=9, g=0.74, 95% CI=0.32–1.15, p<0.001, I^2=63.1%) (see Figure S4 in the data supplement). The funnel plot revealed one outlier (53) (see Figure S3 in the data supplement). A sensitivity analysis after removal of the outlier revealed a moderate and statistically significant effect (g=0.58, 95% CI=0.27–0.90).

Attention. The attention effect size was moderate and statistically significant (k=6, g=0.44, 95% CI=0.20–0.68, p<0.001, I^2=0%) (see Figure S4 in the data supplement). The funnel plot revealed potential asymmetry (see Figure S3 in the data supplement), but asymmetry was not formally assessed due to an insufficient number of studies.

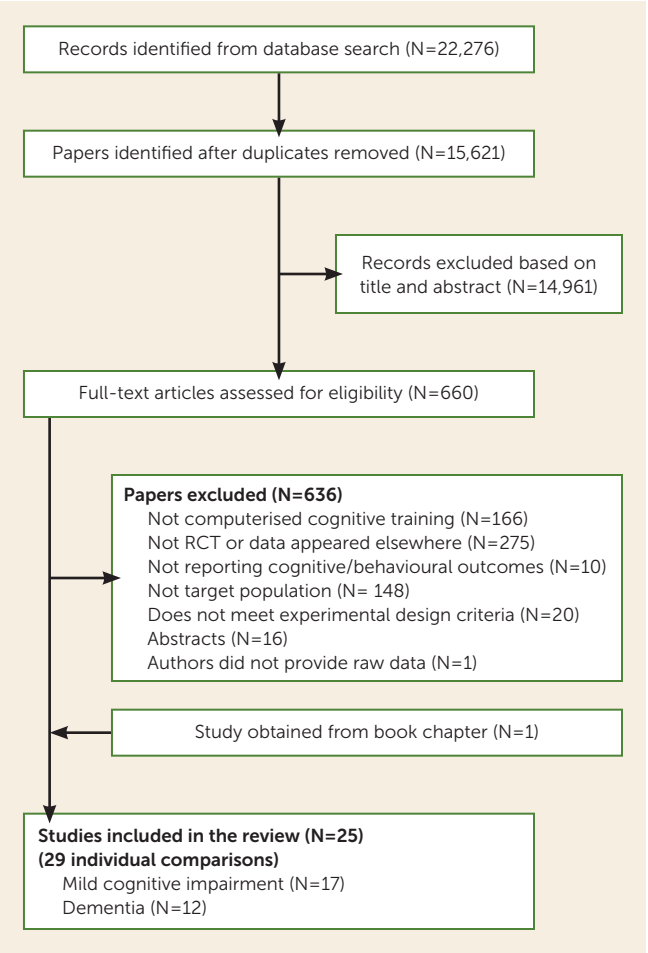
Psychosocial functioning. The psychosocial functioning effect size was moderate and statistically significant (k=8, g=0.52, 95% CI=0.01–1.03, p=0.045, I^2=78.69%) (see Figure S4 in the data supplement). The funnel plot revealed one study outside of the funnel (46), but this was a relatively large study and the rest of the funnel plot did not suggest small-study effect (see Figure S3 in the data supplement). A sensitivity analysis after removal of the outlier revealed a small and statistically significant effect with no evidence of heterogeneity (g=0.27, 95% CI=0.01–0.52, p=0.04, I^2=0%).

Other domains. Statistically nonsignificant results were found for nonverbal memory (k=7, g=0.20, 95% CI=–0.03 to 0.43, I^2=8.79%), executive function (k=13, g=0.20, 95% CI=–0.05 to 0.44, I^2=49.75%), processing speed (k=7, g=0.09, 95% CI=–0.17 to 0.35, I^2=34.1%), visuospatial skills (k=5, g=0.18, 95% CI=–0.23 to 0.60, I^2=64.68%), language (k=6, g=0.41, 95% CI=–0.10–0.92, I^2=80.69%), or instrumental activities of daily living (k=6, g=0.21, 95% CI=–0.18 to 0.61) (see Figure 3). Analysis of activities of daily living outcomes was not performed because only one study (54) was available for analysis.

Meta-Analysis of Dementia Outcomes

Overall efficacy on cognitive outcomes. The overall effect was small and statistically significant (k=11, g=0.26, 95% CI=0.01–0.52, p=0.045, I^2=26.48%) (Figure 1). The funnel plot did not reveal significant asymmetry (Egger's intercept=0.61, p=0.67) (see Figure S3 in the data supplement).

FIGURE 2. Summary of Trial Identification and Selection[a]



[a] RCT=randomized controlled trial.

However, the summary effect was driven by two studies with a g value ≥1.0 (31, 55). Removal of any of these resulted in statistically nonsignificant effect sizes (after removal of Optale et al. [31]: g=0.17, 95% CI=–0.05 to 0.40, I^2=1.61%; after removal of Fernandez-Calvo et al. [55]: g=0.17, 95% CI=–0.06 to 0.39], I^2=0%). A mixed-effects analysis revealed that separating these two studies from the other studies in the analysis created two homogenous subgroups with statistically significant difference in effect sizes (outliers: g=1.07, 95% CI=0.54–1.59, I^2=0%; remaining: g=0.08, 95% CI=–0.15 to 0.31, I^2=0%; Q-between=11.23, df=1, p=0.001).

Efficacy on individual cognitive domains. The effect size on global cognition was moderate and statistically nonsignificant (k=7, g=0.31, 95% CI=–0.11 to 0.72, p=0.15, I^2=56.66%). A moderate and statistically significant effect size was found on visuospatial skills (k=3, g=0.54, 95% CI=0.07–1.01), but this was once more driven by the Optale et al. study (31) (see Figure S4 in the data supplement). There were no other statistically significant effects on any other domain (see Table S4 in the data supplement).

TABLE 1. Characteristics of Included Studies[a]

Study	N	Population Diagnosis	Mean Age (Years)[b]	Sex (% Female)	Mean Mini-Mental State Examination or Equivalent	Delivery
Kim et al. (66)	30 (CCT, N=15; control, N=15)	Mild cognitive impairment	78.7	70	26.7	Supervised
Rozzini et al. (51)	37 (CCT, N=15; control, N=22)	Mild cognitive impairment			26.2	Supervised
Barnes et al. (29)	47 (CCT, N=22; control, N=25)	Mild cognitive impairment	74	40		Home-based
Finn et al. (48)	16 (CCT, N=8; control, N=8)	Mild cognitive impairment	72.69	50	27.76	Home-based
Herrera et al. (56)	22 (CCT, N=11; control, N=11)	Mild cognitive impairment	76.63	50	27.27	Supervised
Tarnanas et al. (47)	71 (CCT, N=32; control, N=39)	Mild cognitive impairment	70.05	60.5	26.5	Supervised
Wittelsberger et al. (54)	27 (CCT, N=17; control, N=10)	Mild cognitive impairment	70.07	48.14	22.88	Supervised
Finn et al. (49)	24 (CCT, N=12; control, N=12)	Mild cognitive impairment	73.95	29.16	27.79	Supervised
Hughes et al. (57)	20 (CCT, N=10; control, N=10)	Mild cognitive impairment	77.4	70	27.1	Supervised
Fiatarone Singh et al. (43) (study 1 [CCT + exercise vs. sham CCT + exercise])	49 (CCT, N=27; control, N=22)	Mild cognitive impairment	70.1	68	27	Supervised
Fiatrone Singh et al. (43) (study 2 [CCT + sham exercise vs. sham CCT + sham exercise])	51 (CCT, N=24; control, N=27)	Mild cognitive impairment	70.1	68	27	Supervised
Barban et al. (44) (study 2, mild cognitive impairment)	106 (CCT, N=46; control, N=60)	Mild cognitive impairment	73.54	47.16	27.74	Supervised
Hagovska et al. (45, 46)	78 (CCT, N=40; control, N=38)	Mild cognitive impairment	66.97	48.75	26.33	Supervised
Barcelos et al. (53)	17 (CCT, N=8; control, N=9)	Mild cognitive impairment	80.6	56	20.8[h]	Supervised
Gooding et al. (30) (study 1 [CCT and ACG])	41 (CCT, N=31; control, N=10)	Mild cognitive impairment	75.59[j]	61.9[j]	50.62[i]	Supervised
Gooding (30) (study 2 [CVT and ACG])	33 (CCT, N=23; CTL, N=10)	Mild cognitive impairment	75.59[j]	61.9[j]	50.84[i]	Supervised
Lin et al. (67)	21 (CCT, N=10; control, N=11)	Mild cognitive impairment	73.0	47.62	25.02[h]	Home-based
Optale et al. (31)	31 (CCT, N=15; control, N=16)	Mixed[k]	80.96	67.74	21.91	Supervised
Galante et al. (32)	11 (CCT, N=7; control, N=4)	Mixed[k]	75.51	Not reported	22.9	Supervised
Zhuang et al. (33)	33 (CCT, N=19; control, N=14)	Mixed[k]	78.07	75.75	10.16	Supervised
Heiss et al. (58)	35 (CCT, N=18; control, N=17)	Dementia	66.29	45.71	21.1	Supervised
Lowenstein et al. (52)	44 (CCT, N=19, control, N=25)	Dementia	76.43	34.09	23.96	Supervised + home-based
Tarraga et al. (59)	31 (CCT, N=15; control, N=16)	Dementia	76.54	87.09	21.55	Supervised

TABLE 1, *continued*

Program and Targeted Domains	Dose[c]	Number of Sessions[d]	Session Length[e]	Sessions/ Week[f]	Control	Risk of Bias[g]	PEDro-P Scale
Virtual reality simulating household tasks	6	12	30	3	Active	High	7
Neuropsychological training: Memory, attention, language, executive function, visuospatial processing	60	60	60	5	Active	Low	8
Posit science brain fitness Speed, verbal memory, working memory	50	30	100	5	Active	High	8
Lumosity Attention, speed, nonverbal memory, executive functions	10	30	20	3–5	Passive	High	7
In-house program Verbal memory, nonverbal memory, verbal learning, non- verbal learning, attention, speed	24	24	60	2	Active	High	8
Virtual reality museum task	60	40	90	2	Active	High	7
Nintendo Wii bowling	12	12	60	2	Passive	High	5
Repetition lag training Verbal learning, verbal memory	9	6	90	2	Passive	High	6
Nintendo Wii	36	24	90	1	Active	High	7
COGPACK Verbal memory, nonverbal memory, executive functions, attention, speed	78	52	90	2	Active	Low	9
COGPACK Verbal memory, nonverbal memory, executive functions, attention, speed	78	52	90	2	Active	Low	9
Sociable Verbal memory, nonverbal memory, executive functions, language, attention, visuospatial processing	24	24	60	2	Passive	High	8
CogniPlus Verbal memory, nonverbal memory, verbal learning, nonverbal learning, working memory, attention, executive functions, visuospatial processing	10	20	30	2	Passive	High	7
In-house virtual reality enhanced recumbent stationary bike coin and dragon collection Visuospatial processing, executive functions, attention	18	24	20–45	2	Active	High	6
BrainFitness by Posit Science Memory, attention, executive functions	30	32	60	2	Active	High	5
BrainFitness by Posit Science Memory, attention, executive functions	30	32	60	2	Active	High	5
Posit Science InSight. Processing speed, visuospatial, attention, executive functions	24	24	60	4	Active	High	7
Virtual reality Virtools platform Nonverbal learning, nonverbal memory, attention, visuospatial processing	18	36	30	3	Active	High	8
Neuropsychological training Memory (domain unspecified), working memory, language, attention, executive functions, visuospatial processing	12	12	60	3	Active	High	9
In-house program Nonverbal learning, Nonverbal memory, executive functions, visuospatial, processing	108	72	90	3	Not Specified	High	8
Rigling Reha-Service Memory, executive functions, visuospatial	48	48	60	2	Active	High	6
Commercial games Language, executive functions, nonverbal learning, nonverbal memory, verbal memory, nonverbal memory, attention	18	24	45	2	Active	High	7
Smart Brain Memory, attention, language, visuospatial processing, working memory, executive functions	24	72	20	3	Active	High	7

continued

TABLE 1, *continued*

Fernandez-Calvo et al. (55)	30 (CCT, N=15; control, N=15)	Dementia	75.7	43.33	19.66	Supervised
Boller et al. (42) (study 1 [recollection + control])	18 (CCT, N=12; control, N=6)	Dementia	80.82	55.5	24.59	Supervised + home-based
Boller et al. (42) (study 2 [recognition + control])	18 (CCT, N=12; control, N=6)	Dementia	81.5	55.5	25.51	Supervised + home-based
Lee et al. (60)	13 (CCT, N=7; control, N=6)	Dementia	77.7	69.23	16.07	Supervised
Man et al. (50)	44 (CCT, N=20; control, N=24)	Dementia	80.29	85	22.03	Supervised
Barban et al. (44) (study 1)	81 (CTT, N=42; control, N=39)	Dementia	76.79	70.37	23.4	Supervised

[a] Abbreviations: ACG=active control group; CCT=computerized cognitive training; CVT=cognitive vitality training; PEDro-P=Physiotherapy Evidence Database Rating Scale.
[b] Weighted mean age.
[c] Total number of training hours.
[d] Total number of CCT sessions.
[e] Session length (minutes).
[f] Number of sessions per week.
[g] Defined has having high or unclear risk of bias for blinding of assessors and/or incomplete outcome data.
[h] Measured using the Montreal Cognitive Assessment (1–30 scale).
[i] Measured using the Modified Mini-Mental State Examination (1–100 scale).
[j] Summary statistics from study 1 and study 2.
[k] Coded as dementia.

Long-Term Outcomes

Four mild cognitive impairment studies from three articles (43, 56, 57) and four dementia studies (32, 58–60) reported outcomes beyond the first follow-up (see Table S5 in the data supplement). Results were not pooled due to an insufficient number of studies and variability of follow-up times, but individual study results indicated a substantial waning of training benefits after training cessation.

DISCUSSION

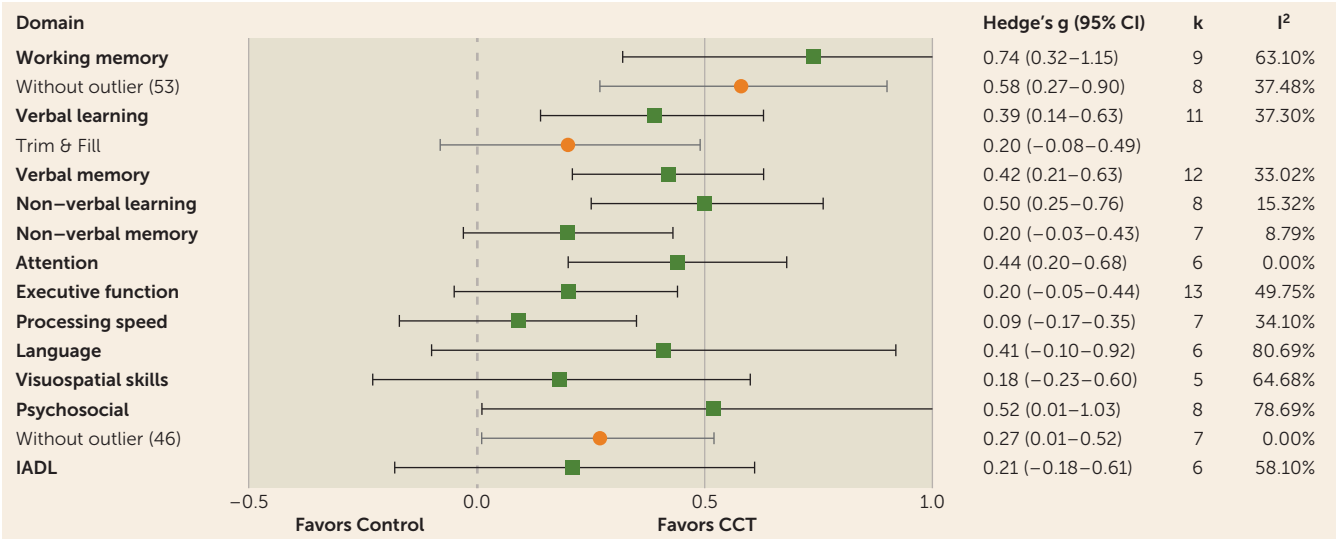
Based on results from 17 randomized controlled trials of moderate quality, we conclude that CCT is a viable intervention for enhancing cognition in people with mild cognitive impairment. The overall effect size on cognition (g=0.35) is larger than effect sizes previously reported for healthy older adults (g=0.22) (13) and for Parkinson's disease (g=0.23) (14). This effect was corroborated by a moderate effect size on common clinical measures of global cognition (mainly the Mini-Mental State Examination and Alzheimer's Disease Assessment Scale-cognitive subscale). Participants in CCT groups improved significantly over the intervention period, while controls did not show any cognitive change, immune to retest effects or nonspecific factors. Most of the trials (70%) used an active control condition, and the effects across active- and passive-controlled trials were comparable. The results of the mild cognitive impairment analysis are therefore robust and indicate a beneficial therapeutic role for CCT in this population. Our analysis updates the benefits on global cognition and memory found in a previous meta-analysis of cognitive training in mild cognitive impairment (17) and is the first, to our knowledge, to focus specifically on randomized trials of CCT.

Moderate effect sizes on most memory and learning domains are encouraging, as amnestic symptoms are the most common presentation of Alzheimer's disease (27), and amnestic mild cognitive impairment profiles are at higher risk for dementia conversion (3). On the other hand, consistent with findings of previous meta-analyses of CCT (13, 15), we report lack of efficacy on executive function, a key predictor of functional decline (61). Since cognitive training gains typically reflect training content (13, 62), this result may be due to insufficient training on executive processes (mainly fluid intelligence, inhibitory control, and reasoning) within studies. Future studies should consider dedicating more time to executive tasks. More surprising is the null effect on processing speed, since CCT exercises are typically timed and this domain was among the most responsive in prior meta-analyses in other populations (13, 14). In healthy older adults, effects on speed are driven by–and limited to–trials of processing speed training (13), and so again training content may help explain this result.

Depression is associated with mild cognitive impairment (63), as well as conversion to dementia (64). It is therefore notable that we found moderate effect sizes on psychosocial functioning (depression, quality of life, and neuropsychiatric symptoms) in mild cognitive impairment, consistent with prior studies (15) and suggestive that CCT may generalize to benefit mood. On the other hand, reliable effects were not seen on

Nintendo Wii Big Brain Academy Nonverbal memory, working memory, executive functions, visuospatial processing	36	36	60	3	Passive	Low	8
Repetition lag training Verbal learning, verbal memory	6	30	20	15	Passive	High	9
Repetition lag training Verbal learning, verbal memory	6	30	20	15	Passive	High	9
In-house computerized errorless learning program Verbal memory, nonverbal memory, working memory, verbal learning, nonverbal learning, attention, executive functions, global cognition	6	12	60	2	Active	High	6
Virtual reality home and shop simulation	5	10	30	2–3	Active	Low	7
Sociable Verbal memory, nonverbal memory, executive functions, language, attention, visuospatial processing	24	24	60	2	Passive	High	8

FIGURE 3. Efficacy of Computerized Cognitive Training (CCT) in Mild Cognitive Impairment Within Individual Domains[a]



[a] IADL=Instrumental activities of daily living.

instrumental activities of daily living outcomes. A limitation in this area is the prevalent use of subjective measures that are insensitive to naturalistic or intervention-related change.

Conversely, the pattern of results in individuals with dementia was weak and driven by two studies. Importantly, clinically meaningful effect sizes were found only for studies that used nontraditional approaches to CCT, namely virtual reality (31, 50) and Nintendo Wii (55) (see Figure 1). It is conceivable that these methods are more stimulating and personally engaging than traditional CCT, an idea that merits further research. Overall, there is no robust evidence that CCT can benefit cognition or function in dementia, in keeping with prior meta-analyses in the field (22, 23).

Limitations

To our knowledge, this is the first meta-analysis focusing exclusively on randomized trials of CCT in people with mild cognitive impairment or dementia. Yet since most trials have focused on short-term cognitive outcomes, we had insufficient data to evaluate the durability of CCT effects and whether these may reduce conversion to dementia. Similarly, functional outcomes were measured mainly using proxy measures that are prone to multiple-source bias, typically requiring long-term follow-up and large samples to detect subtle effects on function.

Methodological differences across mild cognitive impairment studies did not translate into statistically meaningful heterogeneity and thus did not warrant planned moderator analysis such as delivery mode and dose. These factors are critical to CCT outcomes but have yet to be thoroughly investigated in primary studies (13, 65). Notably, while methodological quality across the literature has improved since prior reviews, sample sizes continue to be small. Given an effect size of g=0.36, 80% power, and controlling α at

0.05, the minimal intention-to-treat sample size for CCT trials in mild cognitive impairment is about 64. By contrast, only three studies would have met this criterion (44, 46, 47), and the median sample size across studies was 33.

It is noteworthy that we compared effect size estimates and precision in active- and passive-controlled trials because it has been argued that CCT benefits may be limited to passive-controlled studies (18, 20). As in healthy older adults (13), we did not find any systematic difference in effect sizes. However, since only five of the 17 studies employed a passive-control design, a formal subgroup analysis was underpowered and warrants caution.

CONCLUSIONS

In mild cognitive impairment, CCT is efficacious on global cognition, memory, working memory, and attention and helps improve psychosocial functioning, including depressive symptoms. Effects on other domains such as executive function and processing speed are negligible. Conversely, CCT is not likely to be beneficial for people with dementia, but immersive technologies may be more useful. Future trials should include larger sample sizes and directly compare CCT alternatives in order to optimize outcomes. Finally, there is insufficient data to determine whether training gains can be maintained over the long-term without further training, and thus study of efficient booster regimens is needed in order to examine whether CCT can indeed delay or prevent progression of mild cognitive impairment to dementia.

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