Computerized Cognitive Training in Cognitively Healthy Older Adults: A Systematic Review and Network Meta-Analysis

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ABSTRACT

Background Computerized cognitive training (CCT) is a broad category of drill-and-practice interventions aims to maintain cognitive performance in older adults. Despite a supportive evidence base for general efficacy, it is unclear what types of CCT are most likely to be beneficial and what intervention design factors are essential for clinical implementation.

Methods We searched MEDLINE, Embase, and PsycINFO to August 2019 for randomized controlled trials (RCTs) of any type of CCT in cognitively healthy older adults. Risk of bias within studies was assessed using the Cochrane Risk of Bias 2 tool. The primary outcome was change in overall cognitive performance between CCT and control groups. Secondary outcomes were individual cognitive domains. A series of meta-regressions were performed to estimates associations between key design factors and overall efficacy using robust variance estimation models. Network meta-analysis was used to compare the main approaches to CCT against passive or common active control conditions.

Results Ninety RCTs encompassing 7219 participants across 117 comparisons were included. The overall cognitive effect size across all trials was small (g=0.18, 95% CI 0.14 to 0.23) with considerable heterogeneity (τ^2=0.074, 95% prediction interval -0.36 to 0.73), robust to small-study effect or risk of bias. Effect sizes for individual cognitive domains were small, heterogeneous and statistically significant apart from fluid intelligence and visual processing. Meta-regressions revealed significantly larger effect sizes in trials using supervised training or up to three times per week. Multidomain training was the most efficacious CCT approach against any type of control, with greater benefits in a subset of supervised training studies.

Conclusions The efficacy of CCT varies substantially across designs, independent of the type of control. Multidomain supervised CCT appears to be the most efficacious approach, and should be developed to accommodate for individual needs and remote delivery settings. Future research should focus on identifying the intervention components and regimens that could attenuate aging-related cognitive decline.

INTRODUCTION

While cognitive decline is a highly common aspect of normal aging, interventions that can support cognitive function in older adults may have far-reaching health and societal implications, including delaying or preventing insidious progress towards mild cognitive impairment and dementia.[1] In an evidence commissioned by the National Institutes of Aging, the National Academy of Medicine[2] defined cognitive training as one of the three highest priority areas for prevention research, along with physical activity and blood pressure management. The World Health Organization guidelines for prevention of cognitive decline and dementia[3] was similarly supportive of cognitive training, albeit based on low-quality evidence. Yet these conclusions were drawn based on an array of cognitive training interventions compared to various control conditions, leaving no guidance on how their recommendations might be implemented.

Computerized cognitive training (CCT) is a highly common cognitive training approach, based on repeated exercise repeated and controlled practice on exercises that target specific cognitive processes. CCT can be adapted to individual needs, is inherently safe and can be delivered inexpensively at scale in various clinical and community settings. About a dozen meta-analyses have investigated the efficacy of CCT in healthy older adults, generally reporting benefits for overall cognition.[4] The largest to date, encompassing 51 randomized controlled trials (RCTs),[5] found that efficacy could be moderated by delivery settings and session frequency but did not find differences across types of CCT and control conditions. Regardless, legitimate concerns regarding the overall quality of evidence and variability of methods in the field as well as misleading marketing practices by the “brain training” industry have driven skepticism towards CCT.[6] Lack of clarity regarding which CCT approaches might be beneficial are therefore a clear impediment towards translating the recommendations into practice. Thus, we aimed to update and extend the findings of our previous systematic review of the field,[4] with a particular focus on comparing the main CCT methods to the most common control conditions.

METHODS

We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement[7,8] and prospectively registered the protocol PROSPERO (CRD42018114891). Eligibility criteria and search strategy follow our previous systematic review of the same topic.[5]

Eligibility criteria

We considered randomized trials comparing change from baseline to post-training in one or more cognitive measure between CCT and control conditions in cognitively healthy older adults. CCT was defined as ≥4 h of practice on standardized computerized tasks or video games with clear cognitive rationale, administered on personal computers, mobile devices, or gaming consoles. Eligible controls included wait lists, alternative cognitive activities (e.g., psychoeducation) or sham conditions (e.g., low-level practice). Combinations of CCT with other interventions (e.g., physical exercise) were included if controls received the same adjacent intervention. When combined interventions were compared to passive control, trials were included if CCT comprised at least 50% of intervention time. Outcome measures that closely resembled one of more of the trained tasks were excluded.

Information sources and study selection

We searched MEDLINE, Embase, and PsycINFO using the search terms “cognitive training” OR “brain training” OR “memory training” OR “attention training” OR “reasoning training” OR “computerized training” OR “computer training” OR “video game” OR “computer game”. No search or language limits were applied. The first search was done from inception July 2014.[5] Search updates were applied on November 2015, February 2018 and August 2019. In each update, two or more independent reviewers performed abstract screening and assessment of full-text articles against the inclusion criteria. A senior reviewer [AL, HMG or GP] was responsible for consolidation of eligibility assessments and resolution of disagreements among reviewers. The final set of included studies was reviewed and approved by AL.

Data items and coding

Since CCT studies typically report multiple outcome measures, all eligible measures were collected. Efficacy data were collected as mean and standard deviation (SD) for each group at each time point, or assessed using measures of change (e.g., pre-post mean and SD of change within groups). We contacted authors when reports provided insufficient data to calculate an effect size or when data for certain outcome measures were not reported. In multi-arm studies, all eligible arms were included (for a list of included arms from each study, see Table 1). Definitions of contrasts for the NMA occasionally differed from the pairwise meta-analyses, especially in multi-arm trials to reflect all available comparisons. Coding CCT and active control conditions into specific types was done based on the content of the intervention. Coding of outcome measures into specific cognitive domains was done based on the Cattell-Horn-Carroll- Miyake framework.[9]

Risk of bias within studies

We used the 2019 Cochrane Risk of Bias 2 tool[10] (RoB2) to assess risk of bias across five domains (randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of the reported result). In addition, each study received an overall RoB assessment of high, low or some concerns. In contrast to the original RoB2 macros, studies that did not report assessor blinding or intention-to-treat results were coded as high risk of bias regardless of other RoB2 items.

Statistical analysis

Analyses were conducted using the R packages robumeta,[11] clubSandwich[12] and netmeta.[13] The primary outcome was overall cognition, defined as a composite of all eligible outcomes reported in each trial.[5] Secondary outcomes were individual cognitive domains. Between-group differences in each outcome measure were converted to standardized mean differences and calculated as Hedges' g with 95% CI. Pairwise analyses were performed using robust variation estimation[14] (RVE) with robumeta, based on correlational dependence model with r=0.8. Heterogeneity across studies was quantified using τ^2 and expressed as a proportion of overall observed variance using the I^2 statistic.[15] Prediction intervals were calculated to assess the dispersion of true effects across studies.[16] RVE meta-regressions based on prespecified categorical moderators were performed using robumeta and

formally tested for between-group differences based on F-statistic using clubSandwich. Small-study effect for the primary outcome was investigated by visually inspecting funnel plots of effect size vs standard error and formally tested using the Egger's test as a meta-regression in RVE.[17,18]
Second, random-effects network meta-analysis of the primary and secondary outcomes was performed using a frequentist framework using netmeta. Network geometry was summarized in a network graph and league tables were created to display the relative effect sizes of all available comparisons. Ranking of treatments were estimated using P-scores, representing the extent of certainty that an intervention is more effective than another intervention[19]. Higher P-scores represent higher likelihood of a certain intervention to be the more effective. To examine the transitivity assumptions, we created a table summarizing potential effect modifiers (design characteristics and risk of bias) to explore whether these were similarly distributed across the different comparisons. Sensitivity analysis of the primary outcome were conducted for subsets of supervised and home-based training studies.

RESULTS

After accounting for duplicates within and across searches, we screened 14,361 unique titles, of which 762 full-text articles were assessed against the inclusion criteria, resulting in 90 eligible RCTs encompassing 7219 participants (**Fig 1**). Fourteen RCTs were identified from manual searches and four potentially eligible RCTs were excluded because the reports did not provide sufficient data for analysis and authors did not provide data following our requests.

Characteristics of included studies

Key study characteristics are reported in **Table 1**. The 90 RCTs included 117 eligible CCT and control arms. The most common type of CCT was multidomain training (n=36 RCTs), followed by working memory training (n=21) and attention/dual task CCT (n=10). Fifty-nine trials (66%) compared CCT to at least one active control condition, of which 11 included an additional passive control group, and 7 trials included more than one CCT arm (**Figure 2**). Overall risk of bias was assessed as low in 21 trials, high in 36, and 29 had some concerns (**Table 1**).

Primary outcome: Overall cognition

The pooled overall effect size across all 90 RCTs (1211 effect sizes, median 10 effect sizes per study) was small (g=0.18, 95% CI 0.14 to 0.23) with considerable heterogeneity (τ^2=0.074, I^2=58%). The 95% prediction interval indicated high variability in overall effect sizes across settings (-0.36 to 0.73). There was no evidence for small-study effect (β=0.35, one-tailed p=0.117, Figure 3). There was no evidence for difference across levels of risk of bias ($F_{2,64.8}$=0.391, p=0.678).

Meta-regressions

Results of meta-regressions for the primary outcome are provided in **Table 2**. The pooled effect size was significant larger for supervised vs home-based training ($F_{1,68.5}$=5.8, p=0.019) and for training 1-3 times per week vs more frequent regimens ($F_{1,71.2}$=4.9, p=0.029). Session length, treatment duration and total hours of training were not associated with overall cognitive effect size. Compared to studies that used supervised training, home-based training studies tended to provide more frequent ($t_{74.8}$=8.82, p<0.001) and shorter sessions ($t_{87.5}$=-3.67, p<0.001), as well as more hours of training ($t_{55.4}$=2.19, p=0.032). Multiple meta-regressions did not find interactions between delivery mode and any dosing factor.

Secondary outcomes: Individual cognitive domains

Meta-analyses of individual cognitive domains are provided in **Table 3**. Effect sizes across the six domains were generally small and heterogeneous. There was no evidence for benefit on fluid intelligence, and the pooled estimate for visual processing did not reach statistical significance.

Network meta-analysis: Primary outcome

The 90 RCTs provided 131 pairwise comparisons across 13 CCT or control conditions, resulting in a well-connected network structure (**Figure 2**). Direct evidence was available for 32 comparisons, most notably multidomain vs no contact (20 RCTs), multidomain vs CS/Education (19 RCTs) and working memory training vs sham (14 RCTs). There was evidence for inconsistency for four comparisons; the direct effect size was larger than the indirect estimate for multidomain vs no contact and speed vs casual computer games, and smaller for speed vs no contact (**Table 4**).

Across all trials, multidomain training ranked highest for efficacy on overall cognition, with small and statistically significant effect sizes over and above passive control (g=0.21, 95% CI 0.12 to 0.30) and all active control conditions apart from physical exercise (Table 4). Processing speed training was ranked second with similar but slightly smaller estimates. Working memory training was better than all control conditions apart from cognitive stimulation. There was no evidence for cognitive benefit of any active control condition over and above no contact control.

When separating supervised and home-based training studies, only multidomain training was found to be more efficacious than passive control (g=0.30, 95% CI 0.18 to 0.41) and CS/Education (g=0.25, 95% CI 0.14 to 0.36). There was no evidence of benefit for any home-based condition. Finally, an RVE analysis of the 21 RCTs that used supervised multidomain CCT revealed a similar estimate (g=0.30, 95% CI 0.20 to 0.40), with about half the heterogeneity of the full model (τ^2=0.037, I^2=36%). Of these, 19 provided training up to 3 times per week, resulting in nearly identical estimates (g=0.30, 95% CI 0.19 to 0.41, τ^2=0.038, I^2=38%).

Secondary outcomes

Network meta-analyses ranking for individual domains are presented in Figure 4. The CCT types ranked highest and reported statistically significant benefits were multidomain (g=0.24, 95% CI 0.10 to 0.38) and working memory training (g=0.22, 95% CI 0.06 to 0.38) for executive functions, speed (g=0.36, 95% CI 0.08 to 0.65) and multidomain (g=0.26, 95% CI 0.05 to 0.46) for long-term memory and retrieval, speed (g=0.61, 95% CI 0.38 to 0.83) and multidomain (g=0.36, 95% CI 0.18 to 0.54) for processing speed, and attention/dual task (g=0.46, 95% CI 0.21 to 0.72) and multidomain (g=0.19, 95% CI 0.05 to 0.32) for general short-term memory. Analyses of fluid intelligence and visual processing did not identify statistically significant benefits for any CCT type.

DISCUSSION

This multivariate and network meta-analysis of 90 RCTs has confirmed the efficacy of CCT and narrowed down the conditions in which CCT can result in cognitive benefits in healthy older adults. Our results suggest that multidomain CCT as the most sensible approach to improving global and domain-specific cognitive performance in this population, and that these effects can be further augmented by implementing supervised settings across up to three weekly sessions. However, trials that used supervised CCT were also more likely to provide less frequent sessions, and therefore it was not possible to examine whether these two factors are independent effect modifiers.

Furthermore, comparisons of common active control conditions (general cognitive stimulation, sham CCT and computer games) do not point to a benefit over and above no-contact (passive) control, suggesting that these are ineffectual not only as stand-alone interventions, but also as a means to control for non-specific ('placebo') effects in CCT trials apart from those associated with repeated testing.

The effect size estimates for the primary outcome as well as lack of evidence for small-study effect or association with risk of bias are consistent with our previous meta-analysis,[5] and so are the role of supervision and session frequency as effect modifiers. The current meta-analysis included 40 additional RCTs that meet the same stringent eligibility criteria and used more efficient methods to handle dependent effect sizes in meta-regressions. Thus, these findings are likely to be robust and substantially increase the certainty in the RCT evidence for the general efficacy of CCT.

Given the wealth of RCTs, reasonable certainty in the evidence and lack of evidence to support the efficacy of active or passive control conditions, clinical equipoise assumptions in CCT trials are becoming increasingly difficult to justify. That is, the new knowledge gained from clinical trials comparing CCT programs to inert control may not necessarily be substantial enough to withhold potentially effective intervention from older participants.[20] At the same time, the opportunity cost of testing relatively basic efficacy hypotheses ('does CCT work?') instead of addressing clinical implementation challenges in the field is increasing. Specifically, in order to test the effectiveness of CCT as a means to prevent cognitive decline at scale, research that focuses on maintaining engagement over time, providing remote supervision akin to that of center-based training and personalizing CCT, among other research priorities. These would require larger and longer studies that those typically conducted in the field but allow investigations of novel approaches compared to existing CCT programs.

Our network meta-analysis highlights the importance of multidomain training as the CCT approach most likely to be beneficial. Several meta-analyses of single domain training have shown that training gains tend to be most pronounced within the domains targeted by the program.[21,22] Lack of robust evidence for gains in untrained domains is often cited as a limitation of CCT but in fact this is simply the reality of most interventions targeting a specific physiological or mental process. From a clinical implementation perspective, targeted CCT may be clinically relevant for rehabilitation of specific cognitive deficits, such as a recent FDA-approved attention training program for children with attention-deficit/hyperactivity disorder.[23] However, given age-related cognitive decline affects multiple domains and typically measured using global cognitive batteries, clinicians and researchers should expect the greater generalizability from multidomain CCT. Several methods for adapting training content to individual cognitive profiles have been developed and are currently undergoing clinical trials, especially within multicomponent dementia prevention trials.[24] What methods can increase the efficacy of CCT and, importantly, whether these can slow down cognitive decline remains to be investigated in future trials and more specific meta-analysis methods.

Limitations

To the best of our knowledge, this is the largest systematic review of CCT in older adults to date, and the first to perform a network meta-analysis. Since trials tend to report multiple outcome measures, we used RVE analyses to account for non-independence of effect sizes within studies. Whereas this is an efficient approach that allowed us to detect more heterogeneity and increase the power of meta-regression analyses, a limitation of RVE is that it allows to model dependence due to nesting of multiple outcome measures (correlational model) or groups within studies (hierarchal model), but not both. We used a correlational model as nearly all studies reported multiple outcome measures while only 23 reported more than two eligible arms. Consequently, estimations of weights and heterogeneity did not account for possible differences between subgroups, which may have affected the efficiency of the model specifications.[14] A method for combining the two working models has been very recently proposed[25] and may counter this problem in future meta-analyses.

Accounting for dependency in a network meta-analysis is even more challenging,[26] and we are not aware of viable solutions for generating arm-level composites at this stage. To limit the effect of this problem on our estimates we combined effect sizes within arms into a single estimate using the same correlation-based method[27] used in our previous univariate meta-analysis of CCT.[5] Despite applying a large coefficient (r=0.8, as in the RVE model) for estimated correlated variance within arms, there was no detectable heterogeneity in the full network, limiting the precision of our estimates. Nevertheless, imprecision of the main analysis was not substantially greater than the RVE estimates, and arguably less prone to bias compared to selection of outcome measures.

Finally, we did not include data beyond post-training assessments for two main reasons. First, including such data will introduce selection bias as the majority of studies implemented relatively short training periods and did not report long-term outcomes, with considerable variation in the number and length of follow-ups. Second, while some residual gains can still be apparent several months and perhaps up to a year after a course of CCT, effects are expected to wane over time without further training.[28,29] There is therefore limited value in testing hypotheses related to effect maintenance as the null is the most likely outcome, especially as effects are measured further away from training cessation. Given the ultimate goal of CCT is to delay cognitive decline, implementing and optimizing long-term booster schedules is the key to maintain CCT effects and should be prioritized over more conventional trial designs that focus on modelling the gradual waning of cognitive gains.

CONCLUSIONS

CCT is efficacious for overall and domain-specific cognitive performance in healthy older adults, but effect vary across key intervention design factors. Greater efficacy should be expected from multidomain CCT, applied up to 3 times per week, and provided in supervised settings. Future trials should avoid inert control conditions whenever possible and focus on optimizing training protocol, specifically in home settings. Research synthesis efforts can move away from investigating mere efficacy and focus on detecting more specific intervention components and individual predictors of training response.

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Table 1: Study characteristics

Study	Comparison	n	Mean age	% fem	MMSE	Delivery	CCT type	Program	Dose[a]	Sessions[b]	Length[c]	Sessions/ wk[d]	Control	Risk of Bias[e]
Ackerman 2010[30]	CCT: Wii first Control: Reading first	78 (CCT, n=39; control, n=39)	60.70	46.2	NR	Home	Multidomain	Wii Big Brain Academy	20	20	60	5	CS / Education	High
Anderson 2013[31]	CCT: Auditory training Control: Active control	67 (CCT, n= 35; control, n=32)	63.00	58.2	27.4[f]	Home	Multidomain	PS Brain Fitness	40	40	60	5	CS / Education	Some concerns
Anguera 2013[32]	CCT: Multitasking training Control: Single task training	31 (CCT, n=16; control, n=15)	66.79	64.5	≥26	Home	Attention or Dual task	NeuroRacer	12	12	60	3	Sham CCT	High
Anguera 2013[32]	CCT: Multitasking training Control: Passive control	31 (CCT, n=16; control, n=15)	65.82	67.7	≥26	Home	Attention or Dual task	NeuroRacer	12	12	60	3	No contact	High
Ball 2002[33]	CCT: Processing speed training Control: Passive control	1398 (CCT, n=702; control, n=696)	73.60[g]	75.9[g]	27.3[g]	Supervised	Speed	Speed	11	10	67	2	No contact	Low
Ballesteros 2014[34]	CCT: Video game training Control: Active control	30 (CCT, n=17; control, n=13)	68.97	60.0	28.74	Supervised	Multidomain	Lumosity	60	20	60	2	CS / Education	High
Ballesteros 2017[35]	CCT: Video game training Control: Active control	55 (CCT, n=30; control, n=25)	65.55	NR	28.84	Supervised	Multidomain	Lumosity	12	16	45	1	Strategy video game	High
Barban 2016[36]	CCT: Training first Control: Rest first	114 (CCT, n=61; control, n=53)	70.90	43.0	29.1	Supervised	Multidomain	SOCIABLE	24	24	60	2	No contact	Some concerns
Barban 2017[37]	CCT: Cognitive training Control: Active control	241 (CCT, n=118; control, n=123)	75.07	60.2	≥20	Supervised	Multidomain	SOCIABLE	24	24	60	2	CS / Education	Low
Barban 2017[37]	CCT: Motor + cognitive training Control: Active control	244 (CCT, n=121; control, n=123)	75.26	68.4	≥20	Supervised	Multidomain	SOCIABLE	24	24	60	2	CS / Education	Some concerns
Barnes 2013[38]	CCT: Mental activity/stretching Control: Documentary/stretching	63 (CCT, n=31; control, n=32)	73.85	60.3	28.92[h]	Home	Multidomain	Posit Brain Fitness + Insight	36	36	60	3	CS / Education	Low
Barnes 2013[38]	CCT: Mental activity/exercise Control: Documentary/exercise	63 (CCT, n=32; control, n=31	72.92	65.1	28.38[h]	Home	Multidomain	Posit Brain Fitness + Insight	36	36	60	3	CS / Education	Low

Basak 2008[39]	CCT: Strategy video game Control: Passive control	39 (CCT, n=19; control, n=20	69.56	74.4	29.3	Supervised	Strategy video game	Rise of Nations	23	15	90	3	No contact	Some concerns
Belchior 2013[40]	CCT: Action game Control: Passive control	27 (CCT, n=14; control, n=13)	74.27	40.8	29.1	Supervised	Action video game	Medal of Honour	9	6	90	2-3	No contact	Some concerns
Belchior 2013[40]	CCT: Arcade game Control: Passive control	28 (CCT, n=15; control, n=13)	74.83	50.0	29.21	Supervised	Casual computer game	Tetris	9	6	90	2	No contact	Some concerns
Belchior 2013[40]	CCT: UFOV training Control: Passive control	29 (CCT, n=16; control, n=13)	73.70	58.7	29.11	Supervised	Speed	UFOV Speed of Processing	9	6	90	2	No contact	Some concerns
Belchior 2019[41]	CCT: Commercial videogame Control: Passive control	35 (CCT, n=17; control, n=18)	73.20	63.0	≥24	Home	Action video game	Crazy Taxi	60	60	60	5	No contact	High
Belchior 2019[41]	CCT: Computerized training Control: Passive control	37 (CCT, n=19; control, n=18)	73.20	63.0	≥24	Home	Multidomain	PS InSight	60	60	60	5	No contact	High
Berry 2010[42]	CCT: Visual discrimination training Control: Passive control	30 (CCT, n=15; control, n=15)	71.93	56.3	29.3	Mixed	Speed	PS Sweep Seeker	10	15	40	3-5	No contact	Some concerns
Boot 2013[43]	CCT: Brain fitness game Control: Passive control	40 (CCT, n=20; control, n=20)	72.50	60.0	29	Home	Multidomain	Brain Age 2 (Nintendo DS)	60	60	60	5	No contact	Low
Boot 2013[43]	CCT: Action game Control: Passive control	34 (CCT, n=14; control, n=20)	72.41	52.9	29	Home	Action video game	Action game (Mario Cart)	60	60	60	5	No contact	High
Bottiroli 2009[44]	CCT: Cognitive training Control: Passive control	44 (CCT, n=21; control, n=23)	66.16	NR	27.61	Supervised	Multidomain	Neuropsychological training software (TNP)	6	3	120	1	No contact	Some concerns
Bozoki 2013[45]	CCT: Adaptive online game Control: Active control	60 (CCT, n=32; control, n=28)	68.90	58.4	27.3[i]	Home	Multidomain	My Better Mind	30	30	60	5	CS / Education	Some concerns
Brehmer 2012[46]	CCT: Adaptive training Control: Active control	45 (CCT, n=26; control, n=19)	63.77	60.0	NR	Supervised	Working memory	Cogmed	9	23	26	4	Sham CCT	High

Buitenweg 2017[47]	CCT: Frequent domain switching Control: Active control	106 (CCT, n=56; control, n=50)	67.71	59.4	NR	Home	Multidomain	TAPASS	28.6	57.1	30	5	Sham CCT	Some concerns
Buitenweg 2017[47]	CCT: Infrequent domain switching Control: Active control	83 (CCT, n=33; control, n=50)	67.72	57.8	NR	Home	Multidomain	TAPASS	28.6	57.1	30	5	Sham CCT	Some concerns
Burki 2014[48]	CCT: Working memory training Control: Active control	42 (CCT, n=22; control, n=20)	67.65	76.2	NR	Supervised	Working memory	In-house program	5	10	30	3	Sham CCT	Some concerns
Burki 2014[48]	CCT: Working memory training Control: Passive control	45 (CCT, n=22; control, n=23)	68.14	75.9	NR	Supervised	Working memory	In-house program	5	10	30	3	No contact	Some concerns
Casutt 2014[49]	CCT: Cognitive training Control: Passive control	46 (CCT, n=23; control, n=23)	72.78	28.3	NR	Supervised	Attention or Dual task	In-house program	7	10	40	2	No contact	Some concerns
Casutt 2014[49]	CCT: Cognitive training Control: Simulator training [j]	54 (CCT, n=23; control, n=31)	71.98	31.5	NR	Supervised	Attention or Dual task	In-house program	7	10	40	2	Computer games	High
Chan 2015[50]	CCT: Working memory training Control: Active control	22 (CCT, n=12; control, n=10)	70.60	45.4	28.99	Supervised	Working memory	n-back tasks	10	10	60	7	Sham CCT	High
Colzato 2011[51]	CCT: Video games (Met/-carriers) Control: Documentary	20 (CCT, n=13; control, n=7)	67.60	46.7	28.8	Home	Multidomain	In-house program	25	50	30	7	CS / Education	High
Colzato 2011[51]	CCT: Video games (Val/Val homozygous) Control: Documentary	40 (CCT, n=27; control, n=13)	67.60	46.7	28.8	Home	Multidomain	In-house program	25	50	30	7	CS / Education	High
Dahlin 2008[52]	CCT: Cognitive training Control: Passive control	29 (CCT, n=13; control, n=16)	68.31	62.1	28.76	Supervised	Working memory	In-house program	11	15	45	3	No contact	Some concerns
Desjardins-Crepeau 2016[53]	CCT: Exercise + cognitive training Control: Exercise + computer lessons	38 (CCT, n=22; control, n=16)	71.52	55.3	28.8	Supervised	Attention or Dual task	Dual-task training	12	12	60	1	CS / Education	High
Desjardins-Crepeau 2016[53]	CCT: Stretching + cognitive training Control: Stretching + computer lessons	38 (CCT, n=20; control, n=18)	72.87	84.0	28.97	Supervised	Attention or Dual task	Dual-task training	12	12	60	1	CS / Education	High

Du 2018[54]	CCT: Computerized training Control: Lectures	31 (CCT, n=17; control, n=14)	69.53	NR	NR	Supervised	Working memory	Updating training	12	12	60	3	CS / Education	Some concerns
Dustman 1992[55]	CCT: Videogames Control: Passive control	40 (CCT, n=20; control, n=20)	66.25	60.0	NR	Supervised	Multidomain	Multiple Games	33	33	60	3	No contact	High
Dustman 1992[55]	CCT: Videogames Control: Movies	40 (CCT, n=20; control, n=20)	66.50	67.5	NR	Supervised	Multidomain	Multiple Games	33	33	60	3	CS / Education	High
Edwards 2002[56]	CCT: Speed of processing training Control: Passive control	91 (CCT, n=44; control, n=47)	73.71	56.7	NR	Supervised	Speed	SOP	10	10	60	2	No contact	Some concerns
Edwards 2005[57]	CCT: Speed of processing training Control: Internet training	126 (CCT, n=63; control, n=63)	75.64	NR	28.11	Supervised	Speed	SOP	10	10	60	2	CS / Education	Low
Edwards 2015[58]	CCT: Speed of processing training Control: Passive control	60 (CCT, n=27; control, n=33)	73.07	69.0	28.08	Supervised	Multidomain	PS InSight	15	15	60	2	No contact	Some concerns
Eggenberger 2015[59]	CCT: Walking + verbal memory training Control: Walking	47 (CCT, n=22; control, n=25)	79.72	68.1	28.14	Supervised	Memory	In-house program	17.33	52	20	2	Physical exercise	High
Frankenmolen 2018[60]	CCT: Computerized attention and memory training Control: Memory strategy training	60 (CCT, n=29; control, n=31)	67.07	48.3	NR	Supervised	Multidomain	CogPack	9	6	90	1	CS / Education	Low
Garcia-Campuzano 2013[61]	CCT: Computerized matching tasks Control: Passive control	24 (CCT, n=13; control, n=11)	76.70	79.2	NR	Supervised	Working memory	In-house program	12	24	30	3	No contact	Low
Goghari 2017[62]	CCT: Logic and planning training Control: Passive control	61 (CCT, n=32; control, n=29)	70.63	69.0	28.78	Home	Executive functions	Brain Gymmer	20	40	30	5	No contact	Some concerns
Goghari 2017[62]	CCT: Working memory training Control: Passive control	65 (CCT, n=36; control, n=29)	70.35	64.0	28.93	Home	Working memory	Brain Gymmer	20	40	30	5	No contact	High
Goldstein 1997[63]	CCT: Videogame Control: Passive control	22 (CCT, n=12; control, n=10)	77.70	90.9	NR	Home	Casual computer games	Tetris	26-37				No contact	High
Gronholm-Nyman 2017[64]	CCT: Set shifting training Control: Active control	33 (CCT, n=17; control, n=16)	68.54	57.6	NR	Supervised	Executive functions	In-house program	11.25	15	45	3	Casual computer games	High

Guye 2017[65]	CCT: Working memory training Control: Active control	142 (CCT, n=68; control, n=74)	70.35	43.6	29.22	Home	Working memory	Tatool	16	25		5	Sham CCT	High
Hynes 2016[66]	CCT: Strategy training Control: Passive control	25 (CCT, n=13; control, n=12)	71.02	76.0	NR	Home	Multidomain	In-house program	4.5	18	15	3	No contact	High
Jaeggi 2019[67]	CCT: Working memory training Control: General knowledge	155 (CCT, n=78; control, n=77)	72.86	74.0	28.79	Home	Working memory	n-back task	7	20	20	3-14	CS / Education	High
Ji 2016[68]	CCT: Inhibitory training Control: Lectures	34 (CCT, n=18; control, n=16)	70.06	58.3	NR	Supervised	Executive functions	In-house program	10.5	12	52.5	3	CS / Education	High
Kuhn 2017[69]	CCT: Inhibition game Control: Passive control	33 (CCT, n=18; control, n=15)	69.60	50.9	28.45	Home	Executive functions	In-house program	14	56	15	7	No contact	High
Kuhn 2017[69]	CCT: Tablet-based cognitive training Control: Passive control	30 (CCT, n=15; control, n=15)	69.05	50.9	28.45	Home	Multidomain	In-house program	14	56	15	7	No contact	High
Lampit 2014[70]	CCT: Multidomain cognitive training Control: Active control	77 (CCT, n=39; control, n=38)	72.05	68.8	28	Supervised	Multidomain	COGPACK	36	36	60	3	CS / Education	Low
Lange 2015[71]	CCT: Working memory training Control: Active control	62 (CCT, n=31; control, n=31)	67.54	46.8	NR	Supervised	Working memory	In-house program	12	12	60	2	CS / Education	High
Lange 2015[71]	CCT: Working memory training Control: Passive control	60 (CCT, n=31; control, n=29)	67.74	56.7	NR	Supervised	Working memory	In-house program	12	12	60	2	No contact	High
Lee 2020[72]	CCT: Cognitive training Control: Active control	59 (CCT, n=29; control, n=30)	69.74	61.0	27.60[f]	Home	Multidomain	Posit	35	50	42	5	Casual computer games	Low
Legault 2011[73]	CCT: Cognitive training Control: Health education	33 (CCT, n=16; control, n=17)	75.70	41.7	28.49[h]	Supervised	Working memory	In-house program	18	24	44	2	CS / Education	Some concerns
Legault 2011[73]	CCT: Cognitive training + physical activity Control: Physical activity	34 (CCT, n=18; control, n=16)	77.19	59.5	28.38[h]	Supervised	Working memory	In-house program	18	24	44	2	Physical exercise	Some concerns
Li 2010[74]	CCT: Cognitive dual-task training Control: Passive control	20 (CCT, n=10; control, n=10)	76.15	65.0	26.92[f]	Supervised	Attention or Dual task	Dual-task training	5	5	60	2	No contact	Low

Mahncke 2006[75]	CCT: Cognitive training Control: Active control	106 (CCT, n=53; control, n=53)	71.05	50.0	24	Home	Multidomain	PS Brain Fitness	40	40	60	5	CS / Education	High
Mahncke 2006[75]	CCT: Cognitive training Control: No contact control	109 (CCT, n=53; control, n=56)	70.02	50.0	24	Home	Multidomain	PS Brain Fitness	40	40	60	5	No contact	High
Maillot 2012[76]	CCT: Exergame Control: No contact	30 (CCT, n=15; control, n=15)	73.47	84.4	28.97	Supervised	Multidomain	Exergames (Nintendo Wii)	24	24	60	2	No contact	Some concerns
McAvinue 2013[77]	CCT: Working memory training Control: Active control	36 (CCT, n=19; control, n=17)	70.44	63.9	28.06	Home	Working memory	In-house program	15	25	35	5	Sham CCT	High
Millan-Calenti 2015[78]	CCT: Computerized cognitive training Control: Passive control	142 (CCT, n=80; control, n=62)	74.34	74.6	27.76	Supervised	Multidomain	Telecognitio	8	24	20	2	No contact	High
Miller 2013[79]	CCT: Computerized mental stimulation Control: Passive control	74 (CCT, n=38; control, n=36)	81.86	67.6	27.95	Home	Multidomain	Dakim's Brain Fitness	15	40	23	5	No contact	Some concerns
Mishra 2014[80]	CCT: Distractor training Control: Passive control	31 (CCT, n=16; control, n=15)	68.08	68.1	NR	Home	Attention or Dual task	Distractor training	6	12	30	2	No contact	Some concerns
Nilsson 2017[81]	CCT: Sham tDCS + working memory Control: Sham tDCS + active control	61 (CCT, n=33; control, n=28)	69.72	62.3	≥26	Supervised	Working memory	In-house program	13	19	40	5	Sham CCT	Some concerns
Nilsson 2017[81]	CCT: tDCS + Working memory Control: tDCS + active control	62 (CCT, n=32; control, n=30)	69.58	53.2	≥26	Supervised	Working memory	In-house program	13	19	40	5	Sham CCT	Some concerns
Nouchi 2012[82]	CCT: Cognitive training Control: Active control	28 (CCT, n=14; control, n=14)	69.09	53.6	28.5	Home	Multidomain	Nintendo Brain Age	5	20	15	5	Casual computer games	Low
Nouchi 2016[83]	CCT: Processing speed training Control: Active control	72 (CCT, n=36; control, n=36)	69.01	61.0	28.43	Home	Speed	Processing speed training	5	20	15	5	CS / Education	Some concerns
Nouchi 2019[84]	CCT: Cognitive training Control: Active control	60 (CCT, n=30; control, n=30)	72.40	42.0	28.95	Home	Multidomain	In-house program	10	30	20	5	Sham CCT	Low
Nozawa 2015[85]	CCT: Computerized cognitive training Control: Crossword puzzles	23 (CCT, n=11; control, n=12)	67.99	34.8	28.56	Supervised	Multidomain	In-house program	8	24	20	3	Casual computer games	Low

O'Brien 2013[86]	CCT: Speed of processing training Control: Passive control	22 (CCT, n=11; control, n=11)	71.86	50.0	28.09	Supervised	Multidomain	PS InSight	17	14	70	2	No contact	Low
Payne 2017[87]	CCT: Verbal working memory training Control: Active control	40 (CCT, n=22; control, n=18)	67.87	73.2	27.53[f]	Home	Working memory	iTrain	7.5	15	30	5	Sham CCT	Some concerns
Peng 2012[88]	CCT: Computerized cognitive training Control: Passive control	51 (CCT, n=26; control, n=25)	70.39	80.8	NR	Supervised	Speed	Figure Comparison Task	5	5	50	1	No contact	High
Peng 2012[88]	CCT: Computerized cognitive training Control: Paper and pencil training	53 (CCT, n=26; control, n=27)	68.41	80.8	NR	Supervised	Speed	Figure Comparison Task	5	5	50	1	CS / Education	High
Pereira-Morales 2017[89]	CCT: Computerized cognitive training Control: Passive control	23 (CCT, n=12; control, n=11)	67.53	91.3	≥21	Supervised	Multidomain	In-house program	32	32	60	4	No contact	High
Pereira-Morales 2017[89]	CCT: Psychostimulation program Control: Passive control	28 (CCT, n=17; control, n=11)	64.93	89.3	≥21	Supervised	Multidomain	In-house program	32	32	60	4	No contact	High
Peretz 2011[90]	CCT: Computerized cognitive training Control: Active control	155 (CCT, n=84; control, n=71)	67.80	61.9	28.95	Supervised	Multidomain	CogniFt	16	36	25	3	Casual computer games	Low
Pergher 2018[91]	CCT: Cognitive training Control: Passive control	28 (CCT, n=14; control, n=14)	63.11	53.6	29.43	Supervised	Working memory	n-back	5	10	30	3	No contact	Some concerns
Perrot 2019[92]	CCT: Cognitive training game Control: Passive control	23 (CCT, n=12; control, n=11)	65.09	67.0	NR	Home	Multidomain	Kawashima Brain Training	24	24	60	3	No contact	Some concerns
Perrot 2019[92]	CCT: Action videogame Control: Passive control	23 (CCT, n=12; control, n=11)	64.61	67.0	NR	Home	Action video game	Super Mario Bros	24	24	60	3	No contact	Some concerns
Rasmusson 1999[93]	CCT: Individualized memory training Control: Audiotapes	25 (CCT, n=13; control, n=12)	76.84	NR	28.16	Supervised	Multidomain	CNT	14	9	90	1	CS / Education	Some concerns
Rasmusson 1999[93]	CCT: Individualized memory training Control: Group memory course	23 (CCT, n=13; control, n=10)	78.38	NR	28.13	Supervised	Multidomain	CNT	14	9	90	1	CS / Education	Some concerns

Rasmusson 1999[93]	CCT: Individualized memory training Control: Passive control	24 (CCT, n=13; control, n=11)	79.21	NR	27.8	Supervised	Multidomain	CNT	14	9	90	1	No contact	Some concerns
Richmond 2011[94]	CCT: Working memory training Control: Active control	40 (CCT, n=21; control, n=19)	66.00	80.0	29	Supervised	Working memory	In-house program	10	20	30	4	Sham CCT	High
Rolle 2017[95]	CCT: Computerized cognitive training Control: Active control	40 (CCT, n=20; control, n=20)	68.70	72.5	≥26	Home	Executive functions	Distributed attention task (DAT)	5	10	30	5	Casual computer games	High
Salminen 2015[96]	CCT: Working memory training Control: Passive control	36 (CCT, n=25; control, n=21)	64.89	58.5	28.7	Supervised	Working memory	Brain-Twister	12	14	50	4	No contact	Some concerns
Sandberg 2014[97]	CCT: Executive process training Control: Passive control	30 (CCT, n=15; control, n=15)	69.27	56.7	28.94	Supervised	Multidomain	In-house program	11	15	45	3	No contact	High
Shatil 2013[98]	CCT: Cognitive training Control: Book club	62 (CCT, n=33; control, n=29)	80.47	67.7	≥24	Supervised	Multidomain	CogniFit	32	48	40	3	CS / Education	High
Shatil 2013[98]	CCT: Combined cognitive + physical Control: Physical activity	60 (CCT, n=29; control, n=31)	79.00	70.0	≥24	Supervised	Multidomain	CogniFit	32	48	40	3	Physical exercise	High
Shatil 2014[99]	CCT: Cognitive training Control: Active control	109 (CCT, n=50; control, n=59)	68.00	63.0	28.65	Supervised	Multidomain	CogniFit	8	24	20	3	CS / Education	High
Simon 2018 Study 1[100]	CCT: Cognitive training Control: Active control	38 (CCT, n=18; control, n=20)	75.70	25.6	≥26	Home	Working memory	Cogmed	17	25	40	5	Sham CCT	Some concerns
Simon 2018 Study 2[100]	CCT: Cognitive training Control: Active control	39 (CCT, n=19; control, n=20)	70.70	39.5	≥26	Home	Working memory	Cogmed	17	25	40	5	Sham CCT	Some concerns
Simpson 2012[101]	CCT: Cognitive training Control: Solitaire	31 (CCT, n=17; control, n=14)	62.29	52.9	≥27	Home	Multidomain	mybraintrainer.com	7	21	20	7	Casual computer games	High
Smith 2009[102]	CCT: Computerized cognitive training Control: Active control	487 (CCT, n=242; control, n=245)	75.30	52.4	29.15	Home	Multidomain	Posit Brain Fitness	40	40	60	5	CS / Education	Low
Sosa 2019[103]	CCT: Video game training Control: Passive control	35 (CCT, n=20; control, n=15)	74.71	74.3	NR	Supervised	Multidomain	Brain Age	15	15	60	3	No contact	Some concerns

Souders 2017[104]	CCT: Cognitive training Control: Active control	60 (CCT, n=30; control, n=30)	72.35	56.7	NR	Home	Multidomain	Mind Frontiers	22	30	45	7	Casual computer games	High
Stern 2011[105]	CCT: Video game (emphasis change) Control: Passive control	40 (CCT, n=20; control, n=20)	66.65	59.0	NR	Supervised	Attention or Dual task	Space Fortress (emphasis change)	36	36	60	3	No contact	Some concerns
Stern 2011[105]	CCT: Video game (standard) Control: Passive control	40 (CCT, n=20; control, n=20)	66.25	54.0	NR	Supervised	Attention or Dual task	Space Fortress	36	36	60	3	No contact	Some concerns
ten Brinke 2020[106]	CCT: Computerized cognitive training Control: Active control	79 (CCT, n=39; control, n=40)	72.11	63.9	28.57	Supervised	Multidomain	Fit Brains	48	48	60	6	CS / Education	Low
Toril 2016[107]	CCT: Video game training Control: Meetings with experimenter	39 (CCT, n=19; control, n=20)	71.62	NR	28.02	Supervised	Multidomain	Lumosity	15	15	60	2	No contact	Some concerns
Van het Reve 2014[108]	CCT: Cognitive + physical training Control: Physical training	145 (CCT, n=69; control, n=76)	81.52	69.7	27.65	Supervised	Attention or Dual task	Cogniplus	6	36	10	3	Physical exercise	High
van Muijden 2012[109]	CCT: Cognitive training games Control: Documentary/quizzes	72 (CCT, n=53; control, n=19)	67.64	44.4	28.83	Home	Multidomain	In-house program	25	49	30	7	CS / Education	High
Van Vleet 2016 Study 1[110]	CCT: Alertness/speed of processing training Control: Active control	21 (CCT, n=11; control, n=10)	76.05	47.6	NR	Supervised	Attention or Dual task	Tonic and Phasic Alertness Training, TAPAT	5.4	9	36	3	Sham CCT	High
Van Vleet 2016 Study 2[110]	CCT: Alertness/speed of processing training Control: Active control	24 (CCT, n=12; control, n=12)	74.50	37.5	NR	Supervised	Attention or Dual task	Tonic and Phasic Alertness Training, TAPAT	12	21	36	3	Sham CCT	High
Vance 2007[111]	CCT: Speed of processing training Control: Social contact control	159 (CCT, n=82; control, n=77)	75.13	47.8	28.6	Supervised	Speed	SOP	10	10	60	1	CS / Education	Low
von Bastain 2013[112]	CCT: Working memory training Control: Active control	57 (CCT, n=27; control, n=30)	68.42	40.4	≥25	Home	Working memory	WM training via Tatool	16	20	27	5	Sham CCT	Low

Wang 2011[113]	CCT: Executive functioning training Control: Passive control	52 (CCT, n=26; control, n=26)	64.20	67.3	28.35	Supervised	Attention or Dual task	In-house program	4	5	45	1	No contact	High
Wayne 2016[114]	CCT: Working memory training first Control: Placebo training first	26 (CCT, n=13; control, n=13)	64.96	50.0	≥24[f]	Home	Working memory	Cogmed	19.15	25	45	5	Sham CCT	Some concerns
Weicker 2018[115]	CCT: High-level WM training Control: Low-level WM training	40 (CCT, n=20; control, n=20)	67.75	53.0	NR	Supervised	Working memory	WOME/RehaCom	9	12	45	3	Sham CCT	Low
Weicker 2018[115]	CCT: High-level WM training Control: Passive control	40 (CCT, n=20; control, n=20)	67.65	53.0	NR	Supervised	Working memory	WOME/RehaCom	9	12	45	3	No contact	Low
West 2019[116]	CCT: Computerized cognitive training Control: Active control	69 (CCT, n=39; control, n=30)	85.80	65.2	NR	Home	Multidomain	CogniFit	8	24	20	3	Sham CCT	Low
Wolinsky 2011[117]	CCT: Standard and booster training Control: Crossword puzzles	456 (CCT, n=280; control, n=176)	61.88	62.3	NR	Supervised	Speed	PS On the Road	10	5	120	1	Casual computer games	Low
Zimmerman 2016[118]	CCT: Memory training Control: Active control	67 (CCT, n=36; control, n=31)	67.43	61.2	29.24	Home	Memory	Tatool	19.15	30	37.5	5	Sham CCT	Low

Note:
a = total number of training hours
b = total number of CCT sessions
c = session length (minutes)
d = number of sessions per week
e = defined as having high, some concerns of low risk of bias for the domains missing outcome data and measurement of the outcome
f = Measured with the Montreal Cognitive Assessment (MOCA,1–30scale).
g = For the whole study (including groups that were not included in the analysis).
h = Converted from the Modified Mental State Exam (3MSE, 1–100scale) to Mini-Mental State Examination (1–30scale).
i = Measured with the St Louis University Mental Status exam (SLUMS, 1-30 scale)
j = This arm was not included in the network meta-analysis

Table 2: Tests of moderators (primary outcome)

Moderator	**No. of studies (effect sizes)**	**Summary effect**				**Test of moderation**		
		Hedges' *g* (95% CI)	**t**	**df**	***p***	**F**	**df**	***p***
Delivery						5.8	1,68.5	0.018
Supervised	54 (731)	0.23 (0.17 to 0.28)	7.98	47.3	<0.001			
Home-based	36 (470)	0.12 (0.05 to 0.19)	3.55	32.1	0.001			
Frequency						4.93	1,72.2	0.029
1-3 per week	53 (706)	0.23 (0.17 to 0.28)	7.58	46.2	<0.001			
4-7 per week	37 (495)	0.13 (0.06 to 0.19)	3.91	33.2	<0.001			
Session length						0.57	2,54	0.568
1-30 min	28 (312)	0.15 (0.06 to 0.24)	3.48	24.9	0.002			
>30 – <60 min	23 (373)	0.18 (0.11 to 0.26)	5.19	21.9	<0.001			
≥60 min	39 (516)	0.21 (0.14 to 0.29)	5.65	32.5	<0.001			
Training duration						0.48	2,49.9	0.62
≤9 hours	25 (242)	0.21 (0.11 to 0.31)	4.28	22.0	<0.001			
>9 – 20	42 (591)	0.16 (0.09 to 0.23)	4.94	37.1	<0.001			
>20 hours	23 (368)	0.20 (0.11 to 0.29)	4.87	20.0	<0.001			
Risk of bias								
Low	21 (273)	0.15 (0.09 to 0.22)	4.71	21.2	<0.001	HTZ 1.38	4.95	0.33
Some concerns	29 (421)	0.19 (0.11 to 0.26)	5.20	21.2	<0.001			
High	36 (507)	0.19 (0.13 to 0.26)	5.86	45.1	<0.001			

Table 3: Analyses of individual cognitive domains

Broad CHCM domain	**No. of studies (effect sizes)**	**Hedges' *g***	**t**	**df**	***p***	**τ^2**	**I^2**
Executive functions	59 (535)	0.17 (0.11 to 0.23)	5.82	50.2	<0.001	0.036	32.7
Fluid intelligence	33 (95)	0.08 (-0.04 to 0.20)	1.35	28.1	0.187	0.051	48.3
Long-term memory and retrieval	45 (156)	0.16 (0.06 to 0.26)	3.29	37.5	0.002	0.052	51.7
Processing speed	62 (235)	0.21 (0.12 to 0.31)	4.37	59.6	<0.001	0.231	80.6
General short-term memory	63 (261)	0.17 (0.11 to 0.24)	5.49	53.1	<0.001	0.038	35.9
Visual processing	28 (88)	0.12 (-0.01 to 0.24)	2	25.1	0.057	0.072	45.1

Table 4: Network meta-analysis results (primary outcome)

Multidomain				0.07 [-0.41, 0.56]	0.00 [-0.37, 0.38]	0.07 [-0.57, 0.71]		**0.15 [0.07, 0.24]**	0.26 [-0.21, 0.72]	0.08 [-0.14, 0.30]	**0.30 [0.18, 0.42]**	0.18 [-0.02, 0.38]
0.03 [-0.08, 0.13]	Speed				0.24 [-0.46, 0.95]			**0.20 [0.02, 0.38]**			**0.14 [0.05, 0.23]**	**0.35 [0.17, 0.54]**
0.04 [-0.14, 0.22]	0.01 [-0.18, 0.20]	Attention or Dual task						0.07 [-0.34, 0.48]	0.16 [-0.14, 0.45]	**0.50 [0.07, 0.92]**	0.11 [-0.12, 0.33]	
0.05 [-0.08, 0.19]	0.02 [-0.12, 0.17]	0.01 [-0.19, 0.21]	Working memory			0.03 [-0.40, 0.47]		0.12 [-0.10, 0.33]	0.10 [-0.51, 0.72]	**0.14 [0.00, 0.27]**	0.17 [-0.03, 0.37]	
0.04 [-0.33, 0.42]	0.01 [-0.37, 0.40]	0.00 [-0.41, 0.41]	-0.01 [-0.40, 0.38]	Strategy video game							0.22 [-0.37, 0.80]	
0.07 [-0.23, 0.36]	0.04 [-0.26, 0.34]	0.03 [-0.31, 0.36]	0.02 [-0.30, 0.33]	0.03 [-0.45, 0.50]	Action video game						0.20 [-0.13, 0.54]	-0.21 [-0.89, 0.48]
0.16 [-0.09, 0.40]	0.13 [-0.12, 0.38]	0.12 [-0.18, 0.41]	0.10 [-0.15, 0.36]	0.11 [-0.33, 0.56]	0.09 [-0.28, 0.46]	Executive functions		0.16 [-0.45, 0.77]			-0.02 [-0.39, 0.35]	0.01 [-0.41, 0.43]
0.18 [-0.18, 0.55]	0.16 [-0.21, 0.53]	0.14 [-0.23, 0.52]	0.13 [-0.23, 0.49]	0.14 [-0.38, 0.66]	0.12 [-0.35, 0.58]	0.03 [-0.40, 0.46]	Memory		-0.04 [-0.57, 0.48]	0.04 [-0.40, 0.48]		
0.17 [0.09, 0.24]	**0.14 [0.03, 0.25]**	0.13 [-0.06, 0.31]	0.12 [-0.02, 0.25]	0.12 [-0.26, 0.50]	0.10 [-0.20, 0.40]	0.01 [-0.23, 0.26]	-0.02 [-0.38, 0.35]	CS / Education			0.04 [-0.18, 0.26]	
0.20 [-0.05, 0.44]	0.17 [-0.09, 0.42]	0.16 [-0.08, 0.39]	0.14 [-0.11, 0.40]	0.15 [-0.29, 0.60]	0.13 [-0.25, 0.50]	0.04 [-0.30, 0.37]	0.01 [-0.36, 0.38]	0.03 [-0.22, 0.28]	Physical exercise			
0.18 [0.04, 0.33]	**0.16 [0.00, 0.31]**	0.14 [-0.06, 0.35]	**0.13 [0.01, 0.25]**	0.14 [-0.25, 0.54]	0.12 [-0.20, 0.44]	0.03 [-0.24, 0.29]	0.00 [-0.35, 0.35]	0.02 [-0.13, 0.16]	-0.01 [-0.27, 0.25]	Sham CCT	0.05 [-0.28, 0.39]	
0.21 [0.12, 0.30]	**0.19 [0.10, 0.27]**	**0.17 [0.00, 0.35]**	**0.16 [0.03, 0.29]**	0.17 [-0.21, 0.55]	0.15 [-0.15, 0.44]	0.06 [-0.18, 0.30]	0.03 [-0.34, 0.39]	0.05 [-0.05, 0.14]	0.02 [-0.23, 0.26]	0.03 [-0.12, 0.17]	No contact	-0.45 [-0.99, 0.09]
0.25 [0.11, 0.39]	**0.22 [0.08, 0.36]**	0.21 [-0.01, 0.43]	**0.20 [0.02, 0.38]**	0.21 [-0.19, 0.60]	0.18 [-0.13, 0.50]	0.09 [-0.16, 0.35]	0.07 [-0.32, 0.45]	0.08 [-0.07, 0.23]	0.06 [-0.22, 0.33]	0.07 [-0.12, 0.26]	0.04 [-0.10, 0.18]	Casual computer games

Figure 1: PRISMA flowchart

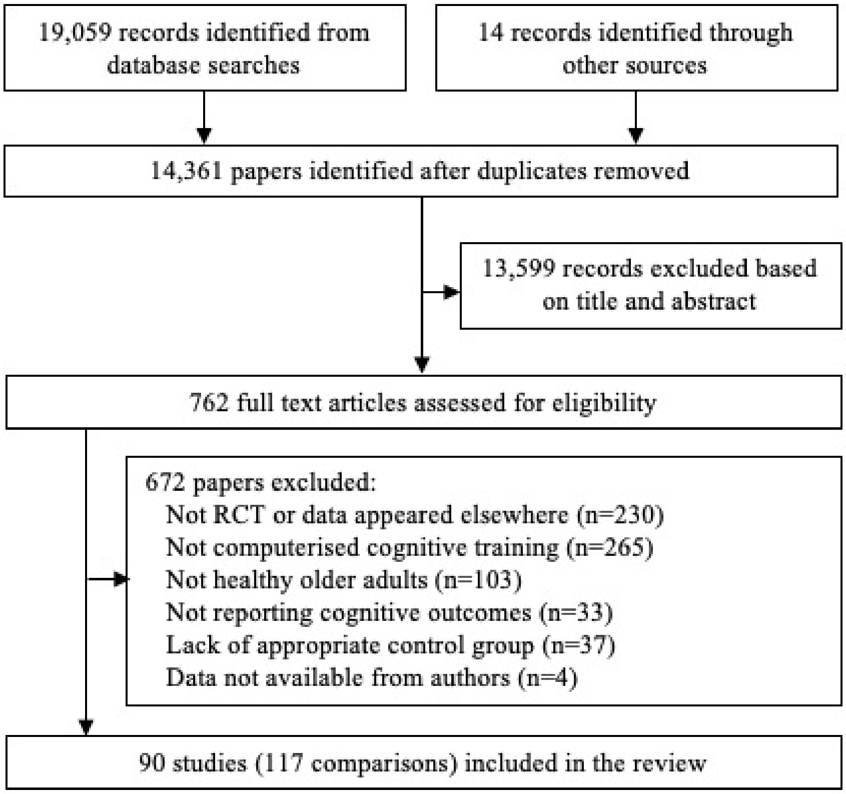

Figure 2: Network structure

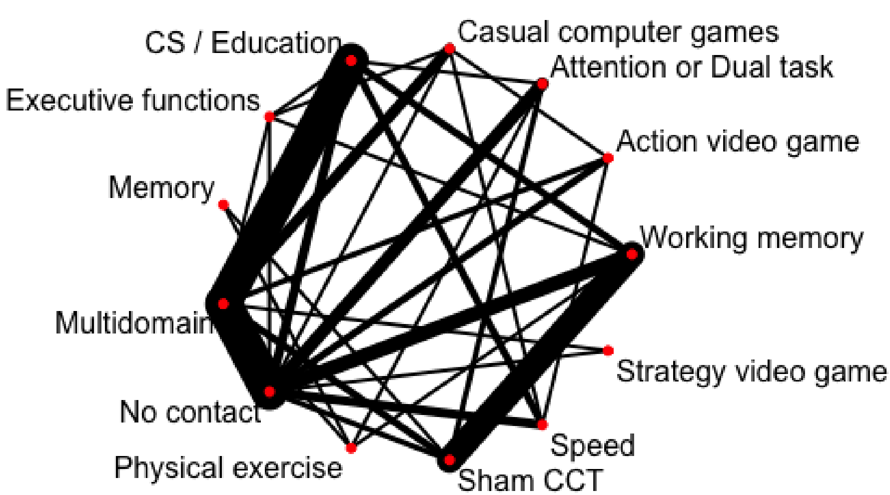

Figure 3: Funnel plot (primary outcome)

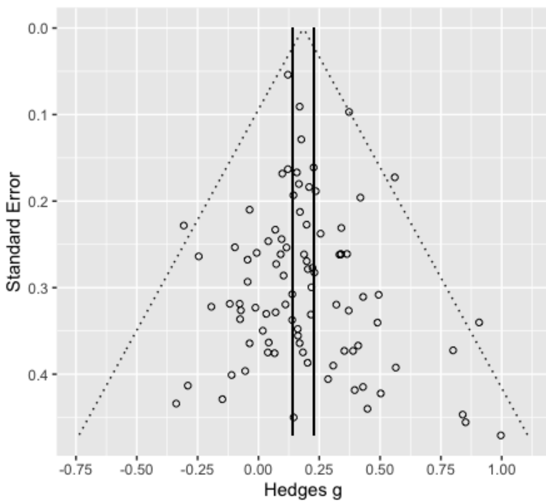

Figure 4: P-scores for primary and secondary outcomes