



Published in final edited form as:

J Am Med Dir Assoc. 2021 November ; 22(11): 2281–2288.e5. doi:10.1016/j.jamda.2021.05.022.

Effectiveness of brain gaming in older adults with Cognitive Impairments: A systematic review and meta-analysis

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Abstract

Objective: This systematic review and meta-analysis is evaluating the evidence from randomized clinical trials (RCTs) that designed brain gaming interventions to improve cognitive functions of older adults with cognitive impairments, including Mild Cognitive Impairments and Dementia.

Design: Systematic review and meta-analysis.

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Conflict of Interest

All authors declare that we have no conflict of interest either financial or personal to disclose.

Setting and Participants: N/A

Measures: N/A

Methods: Data sources- Relevant randomized control trials (RCTs) were identified by a systematic search of databases including Medline, Pubmed, PsycINFO, Embase, CINAHL, Web of Science, and Cochrane. RCTs were selected first based on title and abstract review, and then on full-text review by independent reviewers using pre-defined eligibility criteria. Risk of Bias (RoB) was assessed using the Cochrane RoB tool and funnel plots. The primary outcome variable was the composite score of global cognitive function.

Results: 909 participants with mild cognitive impairment or dementia from 16 RCTs were included in the systematic review. The study quality was modest and the RoB assessment showed bias in blinding the participants and personnel. Funnel plots showed no evidence of publication bias. The meta-analysis of 14 RCTs revealed no superior effect of brain gaming compared to other interventions on global cognitive function (pooled SMD = 0.08, 95% confidence interval [-0.24 – 0.41], $p = 0.61$, $I^2 = 77%$). Likewise, no superior effects were found on cognitive domains of memory, executive function, visuospatial skills, and language.

Conclusion and Implications: This meta-analysis findings suggest that brain gaming compared to control group does not show significant improvement in standardized tests of cognitive function. Because of considerable heterogeneity in sample size, gaming platform, cognitive status, study design, assessment tools, and training prescription, we cannot confidently refute the premise that brain gaming is an effective cognitive training approach for older adults with cognitive impairments. Recommendations for future research are included.

Keywords

Brain gaming; Dementia; Alzheimer's Disease; Mild Cognitive Impairment; cognitive training

Introduction

Dementia is one of the leading causes of disability. An estimated 50 million adults live with the disease worldwide.¹ With the aging population, the global prevalence of dementia is expected to increase to 82 million by the year 2030.² The socio-economic burden of dementia on patients, families and societies is already staggering. Alzheimer's disease (AD), a type of dementia, alone is projected to have cost Medicare and Medicaid \$195 billion in 2019.³ Despite the enormous financial and human cost of dementia, effective pharmacological treatment options remain unavailable.⁴ Therefore, non-pharmacological treatment interventions, including computerized cognitive training (CCT), are receiving increasing attention to prevent, delay, or improve cognitive impairments.^{5,6} The potential benefits of developing effective CCT programs extend beyond people with dementia to include people with mild cognitive impairment (MCI). MCI is considered an at-risk state between healthy aging and dementia that is associated with subjective memory complaints in the absence of objective impairments in cognitive functions and daily-life activities.⁷ The optimal point for delivery of CCT of people living with MCI continues to be investigated.^{8,9}

In particular, brain gaming, a non-immersive, user-friendly form of CCT, has gained tremendous popularity over the past decade. While there are subjective components to define brain gaming (i.e., features that enhance user engagement and motivation), the ability to adapt games based on level of difficulty and therefore provide a challenging or competitive experience to the user is one of the main criteria for inclusion as a brain gaming paradigm.^{9,10} The cognitive tasks must be engineered to enhance the user's engagement and motivation with the game. This adaptability is a core feature that separates basic CCT programs from brain gaming. Electronic brain gaming software may run on desktop and laptop computers, tablets, or mobile devices (i.e. iPad, tablet, phone), and gaming hardware that are accessible and frequently used by older adults.^{11,12} The ease of access to brain gaming through applications on a smartphone has made this industry a billion-dollar business.¹³ Studies that investigate the effectiveness of brain gaming in older adults with and without cognitive impairments are vital to confirm or refute the claims that are made by the industry.

Continuing to understand and advance the utility of effective digital at-home cognitive therapies is also timely given the precautions needed to be taken during COVID-19. Telemedicine and remote rehabilitation are more common during the pandemic – for both patients with COVID-19 as well as those who do not have COVID-19.¹⁴ The potential benefits of engaging in safe, cognitively challenging and motivating activities afforded by brain gaming may play a vital role in post care of patients affected by COVID-19, but also in protecting against accelerated cognitive decline due to detriments on mental health.¹⁵

Although some systematic reviews and meta-analyses demonstrate beneficial effects of CCT on cognitive functions, psychosocial functioning, daily-life activities, and quality of life,¹⁶ no study has evaluated the effectiveness of non-immersive brain gaming on cognitive functions in older adults with MCI and dementia related AD. A scoping review conducted by our group found 13 randomized controlled trials (RCTs) investigating brain gaming in older adults with MCI and AD. The included studies demonstrate that non-immersive electronic brain gaming is a safe, feasible, user-friendly, and potentially effective CCT intervention to maintain or improve cognitive functions among older adults with cognitive impairments.¹⁰ Although some differences were found in intervention dose, type of brain gaming, and cognitive outcome measures among the included RCTs, we concluded that the studies were sufficiently homogeneous in research design to evaluate the effectiveness of brain gaming by performing a meta-analysis.

The primary objective of this systematic review and meta-analysis was to quantify the effects of brain gaming intervention on global cognitive function among older adults with MCI or dementia. Secondary objectives were to (i) assess the effect of brain gaming interventions on the cognitive domains such as memory, executive function, visuospatial skills, and language; and (ii) determine the effect of brain gaming interventions on secondary outcomes, such as Activities of Daily Living (ADL), Instrumental Activities of Daily Living (IADL), depression, and Quality of Life (QoL). In our subgroup analysis, we hypothesized that brain gaming interventions would show larger effect sizes in adults with MCI as compared to dementia. In addition, we evaluated whether intervention dose and type

of setting (home versus controlled settings) would impact the magnitude of the intervention effect.

Methods

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines were followed for this review.¹⁷ The protocol for this review was registered on PROSPERO (Central registration Depository: CRD42015023918).

Search Strategy

The literature search was conducted using Ovid Medline, PubMed, PsycInfo, Embase, CINAHL, Web of Science, and the Cochrane Library to identify RCTs, written in English and published from inception to April 2021. The search strategy was based on four main concepts: (a) cognitive impairment or dementia; (b) outcomes (i.e., cognition, ADL, QoL); (c) non-immersive, electronic brain gaming interventions (e.g., computer gaming, video gaming); and (d) study designs (controlled, randomized). Combination of multiple text words and medical subject headings (MeSH) were used to extract literature with the assistance of a medical librarian (search strategy, Appendix A). Manual search yielded additional articles from reference list of review articles, authors' own literature file, and Google Scholar. Authors of the studies that had insufficient information were contacted directly via email. A comprehensive two-level eligibility process was followed to identify studies for inclusion. Level 1 involved screening titles and abstracts to exclude articles that failed to meet our inclusion criteria and level 2 involved screening full texts of remaining studies. The data were independently extracted by two reviewers, i.e. first reviewer extracted the data and the second reviewer reviewed data for any discrepancies. Disagreements were resolved through study team discussion.

Selection Criteria

Studies included were only RCTs that examined the effect of cognitive interventions using non-immersive, electronic brain gaming methods as defined by Sood et al, 2019 on cognition among older adults with MCI or dementia.¹⁰

Brain gaming technology involves a wide range of computer technologies (hardware and software) such as desktop and laptop computers, mobile computers (i.e. iPad, tablet, phone), and video game technologies.^{12,18} We chose to investigate brain gaming technology as it is relatively easy to access by older adults at home, clinic, or in the research laboratory.¹² Cognitive impairment status, i.e. diagnosis of MCI or dementia, was determined by neuropsychological instruments used to define cognitive status (i.e. Mini-Mental State Examination, MMSE or Montreal Cognitive Assessment, MOCA) or as reported by the authors (based on the criteria or cognitive evaluation) in the original study. Our primary focus was on cognition and domain-specific cognitive functions such as memory, executive functions, visuospatial functions, and language.

Studies were excluded if they were case reports, protocols, commentaries, dissertations, book chapters, letters, or conference abstracts. Decision was made to exclude brain gaming interventions that involved immersive or semi-immersive virtual reality games as these

games required specialized equipment that are harder to access than non-immersive brain games. Additionally, any non-computer-based games such as paper-and-pencil games or board games were excluded.

Risk of Bias and Quality Assessment

Two reviewers (S.L.K. and P.H.) independently completed risk of bias (RoB) assessment using a standardized form and Cochrane Risk of Bias tool.¹⁹ A score of “low risk”, “high risk”, or “unclear” (i.e. lack of information or uncertainty over the potential bias) was assigned to each RoB criterion.²⁰ Disagreements were discussed among the reviewers and research team until an agreement was reached. When the number of studies was at least 10, a comparison-adjusted funnel plot was drawn to assess for publication bias and small study effects. Quality assessment was performed using level-of-evidence hierarchy used in evidence-based clinical medicine as developed by Center for Evidence-Based Medicine.²¹

Type of Outcomes

Primary outcome: Global cognitive function was considered our primary outcome variable and was obtained from either composite scores or scores on the Mini-Mental State Examination. The composite score was calculated as the grand average mean and standard deviation (SD), derived from the post-intervention mean of each cognitive domain measure.

Secondary outcomes: Our secondary outcomes included domain-specific cognitive functions such as memory, executive functions, visuospatial functions, and language, reported in at least two studies. Other secondary outcomes were ADL, iADL, and QoL.

Statistical Analysis

The outcomes in the included studies reported continuous data (mean and SD) and used different outcome measures. Therefore, standardized mean differences (SMDs) with 95% confidence intervals (95% CI) were used to estimate the treatment effect to facilitate comparisons across all outcomes. SMDs were pooled and the inverse-variance random effects model was used considering the variability in methodology, participants, and intervention characteristics across studies. SMD between 0.20 and 0.49 represented a small effect, SMD between 0.50 and 0.79 a moderate effect, and SMD of 0.80 and higher a large effect.²² Review Manager Version 5 was used for data analysis.²³ The Z test was used to determine the treatment effect with a statistical significance threshold of $p < 0.05$. Heterogeneity was assessed using the Chi-square statistic (two-tailed $p < 0.10$) using the Higgins I^2 criteria in accordance with the Cochrane Collaboration thresholds, where 25%, 50%, and 75% imply small, moderate and large heterogeneity, respectively.²⁴ Subgroup analysis was conducted to compare the treatment effects in studies with different diagnoses (MCI versus dementia), intervention dosage (intense versus mild where intense is categorized as more than three formal sessions per week while less intense interventions is categorized as up to three formal sessions per week,²⁵ and intervention setting (home versus lab/clinic).

Results

Included Studies

Figure 1 depicts the PRISMA flowchart of the systematic review and meta-analysis. After duplicate studies were removed, a total of 1291 original studies were initially screened for eligibility. Following title and abstract screening, 207 full-text articles were independently reviewed by two authors. Sixteen studies were included in the systematic review. Two studies were excluded from the meta-analysis. Authors of these two studies were contacted but we could not retrieve the necessary data required to conduct the analysis.^{26,27}

Characteristics of Included Studies: The 16 studies included in this systematic review encompassed 909 participants with mean age ranging from 67 to 82 years. Of those, 461 (51%) participants were males as detailed in Table 1. Twelve studies (75%) included participants with MCI, whereas three studies (19%) included participants with dementia. Only one study focused on both MCI and dementia.

The type of control group varied across studies with sample sizes ranging from 11 to 195 participants. Eleven studies used an active comparison group such as other non-gaming computer-based activities^{26–36} whereas five studies used a passive control group.^{5,35,37–39} One study used both active and passive control groups,³⁶ and another study used a therapist led training program as control intervention.³⁵

Seven out of 16 studies were conducted in the USA, two were conducted in Italy and China, one each in Australia, Eastern Slovakia, Greece, Republic of Korea, and United Kingdom (Supplementary Table 1). Although the type of brain gaming varied considerably across studies, most studies (n=14, 88%) used a computer platform. Intervention periods ranged between 4 to 16 weeks. The training frequency varied between 2 to 15 sessions per week and the duration per session varied between 20 to 100 minutes.

Risk bias assessment and quality of studies: Based on OCEBM level of evidence, all RCTs were rated as level 1B, except one study which was 1C.³⁶ Five studies categorized themselves as pilot studies.^{26,33–35,37}

Eight of the 16 studies specified their randomization method. Some studies used a computer generated randomization method,^{29,31,40} pseudo-randomization method,²⁸ or site specific block method,²⁶ whereas others allocated participants into groups based on order of recruitment,³⁰ or by drawing lots or slips of paper.^{35,37}

Overall, the quality of the studies was modest (Figure 2). The results of RoB assessment revealed that description of blinding of the participant and personnel was mostly unclear or low. In addition, the blinding of outcome assessment (detection bias) was largely unclear or low. Attrition bias was low. The funnel plot suggested no evidence of publication bias for overall cognitive functions from the composite scores (Supplementary Figure 1).

Primary Outcome

Global Cognitive Function from Composite Scores—Fourteen studies were included for calculation of global cognition function (Figure 3). The overall effect size was small (SMD=−0.08, 95% CI= −0.24 to 0.41) and non-significant ($p=0.61$). The heterogeneity across the studies was high ($I^2=77\%$).

Global Cognitive Function from MMSE—Six studies used MMSE as outcome tool to determine global cognition (Supplementary Figure 2). The meta-analysis of global cognition revealed a small (SMD=−0.07, 95% CI= −0.46 to 0.59), non-significant effect size ($p=0.49$) and moderate heterogeneity across the studies ($I^2=70\%$).

Secondary Outcomes: Cognitive Domains

Memory—Seven studies reported memory outcomes and were pooled to determine the effect of brain gaming on memory (Supplementary Figure 3). The overall effect size was small (SMD=−0.17, CI=−0.40, 0.06) and non-significant ($p=0.16$). There was small heterogeneity across the studies ($I^2=21\%$).

Executive Function—As illustrated in Supplementary Figure 4, the pooled data for eight studies demonstrated no superior effect of brain gaming on executive function (SMD=−0.03, CI=−0.30, 0.24; $p=0.82$). The heterogeneity was small across the studies ($I^2=34\%$).

Visuospatial Function—Data from three studies were pooled to determine the effect of brain gaming on visuospatial functions (Supplementary Figure 5). The overall effect size was small (SMD=−0.09, CI=−0.37, 0.18) and non-significant ($p=0.51$). Heterogeneity across the studies was small ($I^2=0\%$).

Language—Supplementary Figure 6 shows the pooled data from three studies, demonstrating a large effect (SMD=1.28, CI=−0.23, 2.78) which was non-significant ($p=0.10$) in favor of the brain gaming intervention on language. However, there was considerable heterogeneity across the studies ($I^2=96\%$).

3.6 Secondary Outcomes: Other

ADL—As shown in Supplementary Figure 7, the pooled data from two studies demonstrating a small (SMD=0.04, CI=−0.78, 0.86), non-significant ($p=0.93$) effect size on ADL, with no heterogeneity across studies ($I^2=0\%$).

IADL—Supplementary Figure 8 pools the data from six studies, showing a small (SMD=0.14, CI=−0.13, 0.42) and non-significant ($p=0.31$) effect size in iADL. There was no heterogeneity across the studies ($I^2=0\%$).

Depression—Supplementary Figure 9 shows a small (SMD=−0.09, CI=−0.56, 0.39) and non-significant ($p=0.72$) effect size on depression based on data from three studies. There was small heterogeneity across the studies ($I^2=13\%$).

Quality of Life—Data from two studies were pooled to demonstrate large heterogeneity across the studies ($I^2=98\%$) on QoL. The overall effect size was small but non-significant ($p=0.75$), equally favoring the brain gaming and the control interventions (Supplementary Figure 10).

Subgroup Analysis on Effects of Brain Gaming

MCI versus dementia—Figure 4 displays the results of brain gaming on overall cognitive function in MCI and dementia, separately. Subgroup analysis based on diagnosis suggest that participants with dementia did not benefit more than participants with MCI from brain gaming on overall cognitive functions (SMD=-0.19, CI=-0.54, 0.16 versus SMD=0.16, CI=-0.23, 0.54 respectively). Studies that focused on MCI demonstrated higher heterogeneity ($I^2=82\%$) versus studies that focused on dementia ($I^2=0\%$).

Weekly Intervention Dosage (sessions per week)—Studies were categorized based on dosage sessions per week similar to the one used by Bahar-Fuchs et al., 2019 as more intense (i.e. more than three formal sessions per week) versus less intense interventions (i.e. up to three formal sessions per week).²⁵ We found no significant differences between intervention dosage of brain gaming (SMD=0.00, CI=-0.30, 0.30 versus SMD=-0.18, CI=-0.37, 0.74, $p=0.57$) on overall cognitive function (Supplementary Figure 11).

Intervention Setting—Subgroup analysis revealed that categorized by setting did not change the benefit of brain gaming (Supplementary Figure 12). Studies focused on clinical and lab settings demonstrated higher heterogeneity ($I^2=87\%$) versus studies focused on home ($I^2=42\%$) and others ($I^2=1\%$).

Discussion

The aim of our systematic review and meta-analysis was to evaluate the effectiveness of brain gaming—a subdomain of computerized cognitive training (CCT)—for adults with cognitive impairments. The evidence base for brain gaming in older adults with cognitive impairments has grown rapidly, partly driven by unsubstantiated claims from commercial application developers that brain gaming can maintain or improve cognitive functions. Based on our systematic review of 16 studies and our meta-analysis of 14 studies, we conclude that brain gaming is not more effective than control interventions in improving cognitive functions among adults with mild cognitive impairment (MCI) or dementia. However, because of considerable heterogeneity of the included studies in terms of study design (e.g., training prescription, gaming platform, and setting), we cannot confidently refute the premise that brain gaming is an effective cognitive training approach in this population.

Our conclusions largely resonate with a recent review on the effectiveness of 12 or more weeks of CCT (including immersive and non-immersive brain gaming) on maintaining or improving cognitive function in MCI.⁴¹ CCT interventions did not prove to be more efficacious compared to other interventions on speed of processing, verbal fluency, and quality of life. The low quality of evidence of the included studies hampered the authors' ability to make firm conclusions about the effectiveness of CCT in MCI.⁴¹ Conversely, two meta-analyses recently reported positive effects of CCT in older adults

with cognitive impairments. Hu and colleagues found that CCT significantly improves cognitive functions especially related to various constructs of memory in participants with subjective cognitive decline and MCI.⁴² Zhang and colleagues reported positive effect sizes in favor of CCT for global cognitive function, memory and working memory in adults with MCI.⁴³ Previous systematic reviews that compared the effectiveness of CCT also found significant, yet modest, improvements on cognitive functions in older adults with cognitive impairments.^{8,16,44}

Methodological differences between the included RCTs, such as inconsistencies in study design, training prescription (duration and intensity), type of training program, outcome measures, and severity of cognitive dysfunction, may have led to the ambiguity of conclusions amongst the systematic reviews and meta-analyses. In particular, the scope of studies included in our systematic review and meta-analysis may be an explanation for discrepancy between our findings are those reported by others.^{8,16,44} Previous reviews did not particularly focus on the brain gaming literature, rather included several CCT paradigms, such as immersive virtual reality technology or CCT without adaptability in difficulty of training. Perhaps the ease of use, adaptability, and engaging elements that typically define brain gaming come at the expense of effectiveness of targeted, immersive CCT interventions or non-adapting training (Flak et al 2019).

Previous systematic reviews also reported a differential effect of CCT on disease severity with adults with MCI benefiting more from CCT compared to those with dementia.^{16,25,45} Hu and colleagues reported CCT to be most beneficial when initiated early in the course of cognitive decline.⁴² Participants with subjective cognitive complaints showed twice as much benefit from CCT compared to participants with MCI. Based on our analyses we found no difference in effectiveness of brain gaming interventions across these subgroups.

There is no consensus amongst reviews whether benefits of CCT generalize to ADLs or QoL measures. Coyle reported significant improvements in depression, but no improvements in ADL and QoL.⁸ Hill, on the other hand, reported most improvements on several psychosocial functions, including depression, QoL, and neuropsychiatric functions, among individuals with MCI.¹⁶ Our review did not reveal any benefits of brain gaming on ADL and QoL outcomes; this was expected since we included studies that only assessed brain gaming as the intervention. As highlighted by Harvey and colleagues, CCT by itself is not the typical strategy aimed at improving functional outcomes in clinical populations.⁴⁶

Strengths of our review include a wide search of the available literature on brain gaming interventions. There was considerable heterogeneity across studies in study design; thus, we advocate that our findings should be interpreted with caution. Although our review included only RCT designs, many of the included RCTs had small sample size, had short-term interventions and were pilot studies. Larger RCTs, with consistent outcome reporting would improve the ability to generate grounded conclusions regarding the effects of brain gaming. For example, for domain analysis, each domain was measured by a variety of outcome measures, which created heterogeneity in the meta-analyses. Another limitation to our work is that we assessed interventions that incorporated only brain gaming in the experimental group. Several studies, not included in our analysis, assessed

multimodal cognitive training, which includes, for example, brain gaming combined with a pharmacological intervention,^{47,48} and other nonpharmacological interventions, such as physical exercise,^{31,49,50} reminiscence therapy,^{51,52} occupational therapy,^{53,54} pencil and paper exercises,^{55,56} general education,⁵³ or video gaming.⁵⁷ Ge et al reviewed many of these multimodal games and concluded more studies are needed to understand the advantages of a multimodal cognitive intervention approach for older adults with MCI.⁴⁴

Conclusions and Implications

The currently available data on brain gaming, designed to improve cognitive function in older adults with MCI and dementia, suggests that this approach does not improve cognitive function compared to the control group. While individual studies continue to suggest a promising effecting, collectively, the data do not bear this out. The considerable heterogeneity among the studies in terms of overall study design, reflects a need for the research community to focus on salient design features and outcomes measurements so that the field can move forward in determining the best CCT to improve cognitive functions of older individuals with cognitive impairments.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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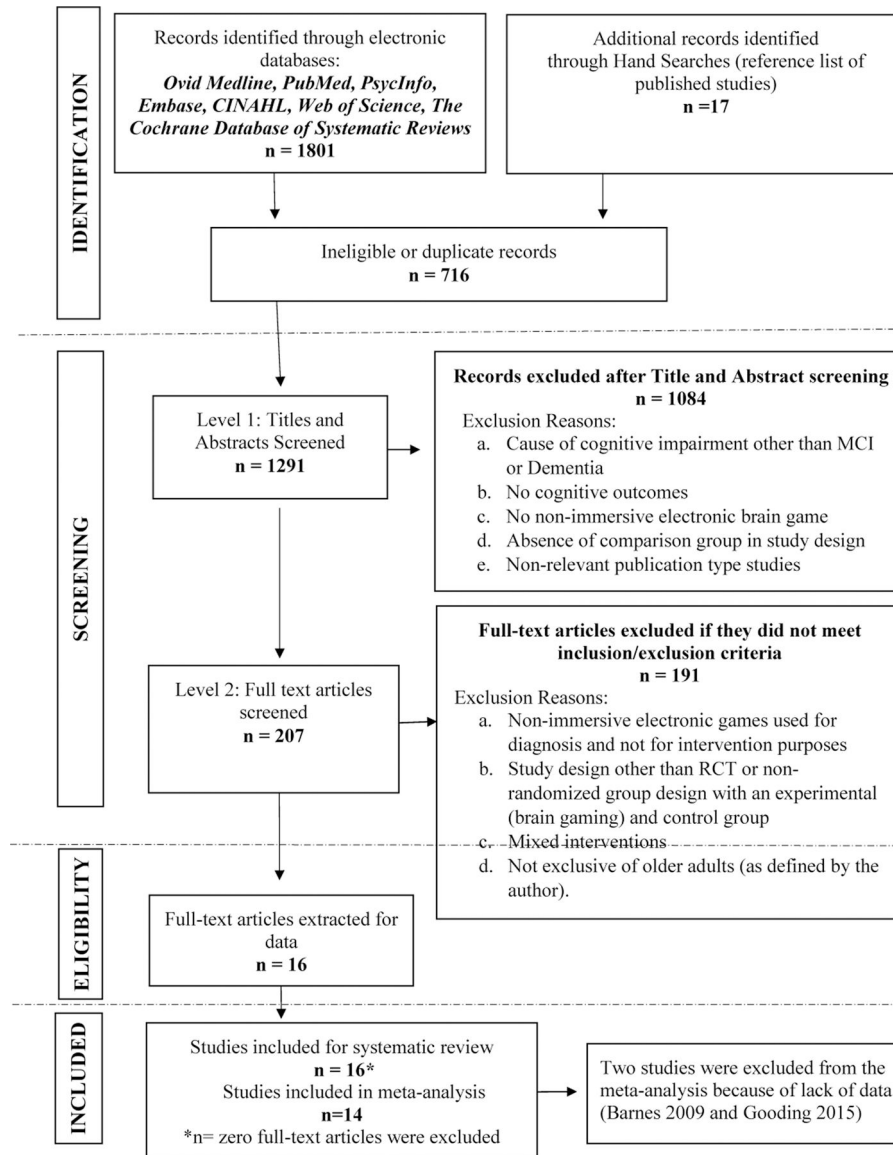


Figure 1. PRISMA flow diagram describing identification and selection of studies for the review

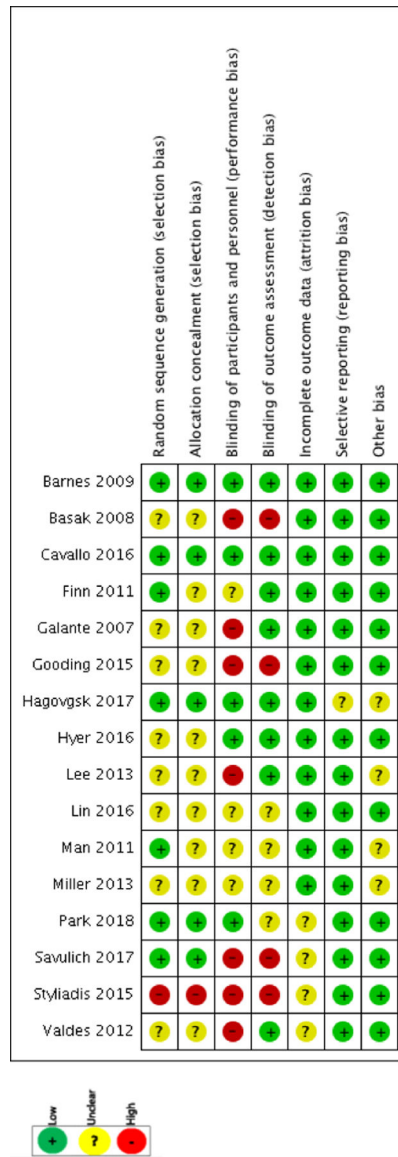


Figure 2.
Risk of bias

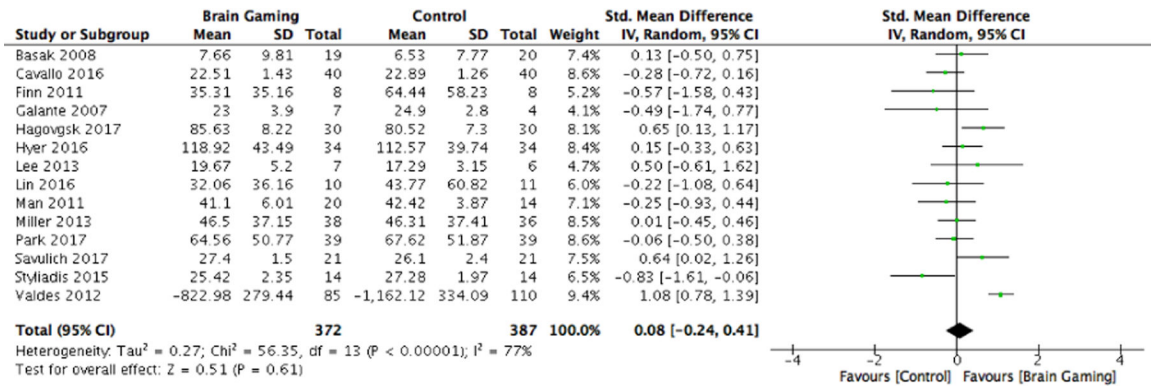


Figure 3.
 Effect of brain gaming on overall cognitive functions in mild cognitive impairment and dementia.

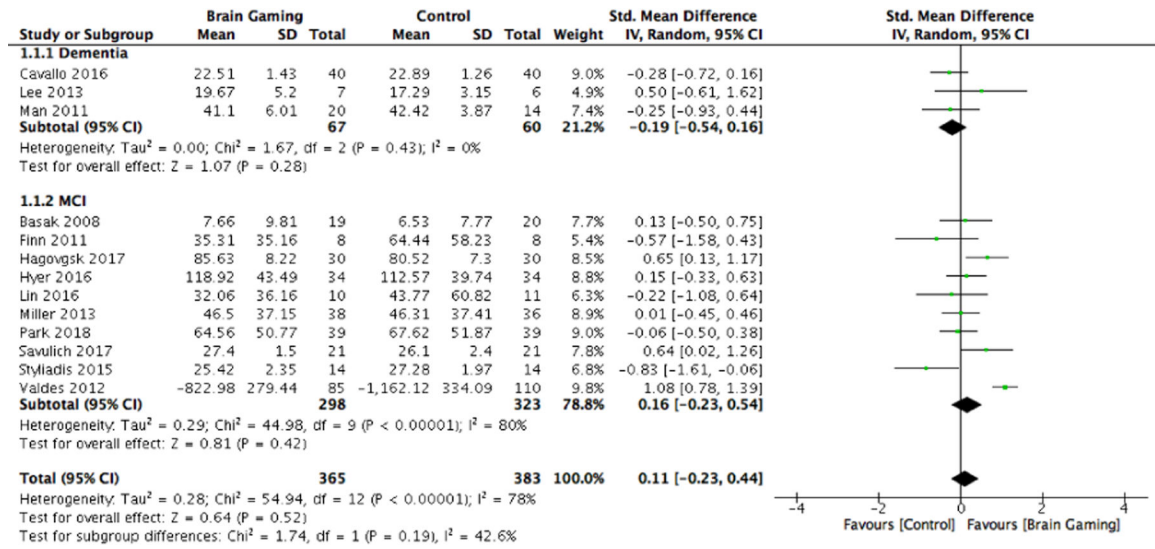


Figure 4.
Effect of brain gaming on overall cognitive functions in mild cognitive impairment and dementia subgroup analysis based on the intervention

Table 1.

Study Sample Characteristics Table According to Cognitive Status

Author (year)	Sample size, n	Mean age, yrs (SD)	Gender, M/F	Mean MMSE score
MCI				
Barnes (2009)	Total=47 (Exp.= 22; Control=25)	Exp.74.1(8.7); Control= 74.8 (7.2)	28/19	N/R
Basak (2008)	Total=39 (Exp.=19; Control=20)	Exp.=70.05 (4.94); Control= 69.10 (6.06)	10/29	Exp.=55.68; Control=55.65 *
Finn (2011)	Total=25 (Exp.=8; Control=8)	Exp.=69 (7.69); Control=76.38 (6.47)	9/16	Both Groups=27.76
Gooding (2015)	Total=74 (Exp.=31; Control=43)	Both Groups= 75.59 (8.75)	43/31	Both Groups=50.58 (2.72) *
Hagovgsk (2017)	Total=60 (Exp.=30; Control=30)	Exp.=67.8 (6.5); Control=68.2 (4.2)	29/31	Exp.=25.6 (2.41); Control=24.9 (2.52)
Hyer (2016)	Total=68 (Exp.=34; Control=34)	Exp.= 75.1(7.4); Control=75.2 (7.8)	32/36	Both Groups=26
Lin (2016)	Total=21 (Exp.=10; Control=11)	Exp.=72.9 (8.2); Control=73.1 (9.6)	11/10	N/R
Miller (2013)	Total=74 (Exp.=38; Control=36)	Exp.=82.2 (4.4); Control=81.5 (7.6)	24/50	Exp=28 (1.5); Control=27.9 (1.7)
Park (2018)	Total=78 (Exp.=39; Control=39)	Exp.=67.64 (4.55); Control=66.95 (4.10)	42/36	Exp.=26.67 (1.68); Control=26.41 (1.94)
Savulich (2017)	Total=42 (Exp.=21; Control=21)	Exp.=75.2 (7.4); Control=76.9 (8.3)	25/17	Exp.=26.6 (2.9); Control=26.8 (2.2)
Styliadis ** (2015)	Total=42 (Exp.=14; Control=28)	Exp.=72.71 (6.57); AC=71.07 (4.38); PC=67.64 (3.97)	15/27	Exp.= 25.14 (3.22); AC=26.21 (1.97); PC=25 (1.77)
Valdes (2012)	Total=195 (Exp.=85; Control=110)	Exp.=76.95 (6.53); Control= 78.34 (6.3)	129/66	N/R
Dementia				
Cavallo (2016)	Total=80 (Exp.=40; Control=40)	Exp.=76.5 (2.88); Control=76.33 (3.82)	29/51	Exp.=22.65 (1.74); Control=23.05 (2.44)
Lee (2013)	Total=13 (Exp.=7; Control=6)	nr	6/13	Exp.=17(3.5); Control=17.6 (4.7)
Man (2011)	Total=34 (Exp.=20; Control=14)	Exp.=80.3 (1.21); Control= 80.22 (1.31)	5/12	Exp.=21 (3.79); Control=23 (3.96)
Both				
Galante (2007)	Total=11 (Exp.=7; Control=4)	Both Groups= 76 (6)	N/R	Exp.=22.9 (3.1); Control=23.1 (1.8)

Abbreviations: AC= active control, Exp.= experimental, MCI= mild cognitive impairment, MMSE = Mini-Mental State Examination, N/R= not reported, PC= passive control.

* Modified MMSE scores

** Styliadis (2015) had two control groups