European Journal of Physical and Rehabilitation Medicine
EDIZIONI MINERVA MEDICA

Active exergames to improve cognitive functioning in neurological disabilities: a systematic review and meta-analysis

Gioia MURA, Mauro Giovanni CARTA, Federica SANCASSIANI, Sergio MACHADO, Luca PROSPERINI

European Journal of Physical and Rehabilitation Medicine 2017 Oct 25
DOI: 10.23736/S1973-9087.17.04680-9

Article type: Systematic reviews and meta-analyses

Article first published online: October 25, 2017
Manuscript accepted: October 25, 2017
Manuscript revised: September 15, 2017
Manuscript received: January 31, 2017

EDIZIONI MINERVA MEDICA

Active exergames to improve cognitive functioning in neurological disabilities: a systematic review and meta-analysis

Gioia Mura[1]*, Mauro G. Carta[1], Federica Sancassiani[1], Sergio Machado[2,3], and Luca Prosperini[4,5].

[1]Department of Medical Sciences and Public Health. University of Cagliari. Italy.

[2]Laboratory of Panic and Respiration, Institute of Psychiatry, Federal University of Rio de Janeiro (IPUB/UFRJ), Rio de Janeiro, Brazil; National Institute of Translational Medicine (INCT-TM).

[3]Physical Activity Neuroscience, Physical Activity Sciences Postgraduate Program - Salgado de Oliveira University, Niterói, Brazil.

[4]Dept. of Neurology and Psychiatry, Sapienza University, Rome, Italy.

[5]Neurology Unit, S. Camillo-Forlanini Hospital, Rome, Italy.

***Corresponding author:**

Dr. Gioia Mura

Department of Medical Sciences and Public Health, University of Cagliari

Policlinico Universitario di Monserrato, SS 554, 09042 Cagliari, Italy

Phone +39 0706093498

Fax +39 0706093498

E-mail: mura.gioia@virgilio.it

Number of words in the Abstract: 272

Number of text words: 4164

Acknowledgement

We wish to thank Dr. Costanza Giannì who provided assistance for English language editing, Ylva Nilsagard and Jen-Wen Hung for data sharing.

Conflicts of Interest and Source of Funding

None declared.

ABSTRACT

INTRODUCTION: Exergames represent a way to perform physical activity through active video games, serving as potentially useful tool in the field of neurorehabilitation. However, little is known regarding the possible role of exergames in improving cognitive functions in persons suffering from neurological disabilities.

EVIDENCE ACQUISITION: A search for relevant articles was carried out on PubMed/Medline, Scopus, PEDro, and Google Scholar. Only randomized controlled studies and non-randomized but controlled studies were retained. The following additional inclusion criteria were applied: studies focused on physical activity interventions carried out by means of exergames; populations targeted were affected by neurological disabilities; and reported results were related to cognitive outcomes. We calculated standardized mean differences (SMD) and pooled results using a random effects meta-analysis.

EVIDENCE SYNTHESIS: Of 520 abstracts screened, thirteen studies met the criteria to be included yielding a total of 465 participants, 233 randomized to exergames, and 232 allocated to the alternative or no intervention. The included studies varied in terms of studied populations (e.g., multiple sclerosis, post-stroke hemiparesis, Parkinson's disease, dementia, dyslexia, Down syndrome), type and duration of interventions, and cognitive outcome measures. Exergames significantly improved executive functions (SMD=0.53, p=0.005; 8 studies, n=380) and visuo-spatial perception (SMD=0.65, p<0.0001; 5 studies, n=209) when compared to the alternative or no intervention. There were no significant differences for attention (SMD=0.57, p=0.07; 7 studies, n=250) and global cognition (SMD=0.05, p=0.80; 6 studies, n=161).

CONCLUSIONS: Exergames are a highly-flexible tool for rehabilitation of both cognitive and motor functions in adult populations suffering from various neurological disabilities and developmental neurological disorders. Additional high-quality clinical trials with larger samples and more specific cognitive outcomes are needed to corroborate these preliminary findings.

Clinical Rehabilitation Impact. Exergames could be considered either as a supplemental treatment to conventional rehabilitation, or as strategy to extend benefits of conventional programs at home.

KEYWORDS: Video games- Neurological disorders- Rehabilitation- Cognition.

INTRODUCTION

Exergames (the portmanteau for “exercise” and “video games”) are comprised of whole-body physical exercises performed through active video games that require gross motor and visual-spatial coordination, balance, and energy expenditure comparable to a moderate-intensity physical activity [1].

To participate in exergames, the player must engage in full motor involvement in the non-immersive, smaller-scale, bi-dimensional virtual reality environment of the video game, through the use of the player’s selected virtual shape (avatar). Using devices such as handheld remote controls, balance boards, and infrared cameras, the avatar reproduces the player’s movement on the screen in order to give an immediate visual feedback of motion accuracy. Handheld controllers have to be wielded and moved the same way sports equipment (e.g., a tennis racket) is held in reality. Moreover, sensation is enhanced by vibration of the handheld controller and auditory feedback, thus giving the player full immersion in the virtual reality of the game (the so-called “haptic or kinesthetic communication”). Common exergames are those marketed by Nintendo® (Nintendo Wii Fit™ and Dance Dance Revolution™), Microsoft® (Microsoft Xbox Kinect®), and Sony® (Sony Eye Toy®).

Exergames were created as low-cost entertainment tools, mostly dedicated to able-bodied younger persons. Nevertheless, more recently, exergames have been considered by researchers as a possible intervention strategy to prevent and treat obesity [2], cardiac diseases [3], and to improve postural control and balance in elderly populations [4,5], as well as in persons with neurological disabilities [6]. Several studies have considered the role of exergames in physical rehabilitation to improve balance, gait, speed and mobility in populations with neurological disabilities, such as persons affected by stroke [7], multiple sclerosis [8], Parkinson’s disease [9], and in children suffering with cerebral palsy [10-12], degenerative ataxia [13,14], Down syndrome [15], developmental coordination disorders [16], and spina bifida [17].

Besides disease-specific motor symptoms, neurological disabilities are often also characterized by cognitive impairment, represented by congenital or acquired deficits either in global intellectual performances or in one or more specific cognitive domains, such as memory, attention, orientation, verbal fluency, executive functions, learning, reasoning, visual-spatial abilities, problem solving and planning [18].

Playing exergames has been proposed as an integrated and adaptable training paradigm to improve not only motor function, but also cognitive abilities [19], by promoting processes of learning and experience-dependent plasticity [20]. Exergaming encompasses most of the principles underlying experience-dependent neural plasticity [21], such as high-intensity repetition of task-oriented exercises, incrementally increased task difficulty, real-time feedback, salience, motivation and reward, and even transfer effects [22]. This latter concept, the so-called “far transfer effect” or “transfer of training”, refers to transferring improved performance in a specific function to a different, untrained functional domain, implying little overlap between the two abilities [23]. Previous reviews of the literature emphasized the effects of exergames on physical rehabilitation [9; 24-26], without investigating the effectiveness in ameliorating cognitive deficits. There is evidence that video games provide a transfer effect from motor to cognitive skills in the able-bodied populations, including older adults [27-30]. More recently, the benefits of exergames on global cognition and individual cognitive domains (executive functions, attentional processing, and visuo-spatial skills) were demonstrated in both healthy and clinical populations [31]. Considering the growing interest on the potential role of exergames in the field of neurological rehabilitation, we performed a systematic literature review and meta-analysis to establish whether exergames are efficacious for improving cognitive deficits in persons with neurological disabilities.

EVIDENCE ACQUISITION

Search strategy and articles selection

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guided the methodology and reporting of this systematic review and meta-analysis [32]. PubMed/Medline, Scopus, PEDro, and Google Scholar were used to search for relevant articles using free-text and MeSH terms shown in **TABLE 1**. No time period restrictions were applied.

- - - Please insert Table 1 about here - - -

To avoid the risk of missing relevant articles, we searched for additional papers on the grey literature (i.e., generic web search) and through the bibliography of previous reviews. One reviewer (GM) ran the search and screened the initial titles after removing duplicates. Three authors (FS, SM and LP) independently examined potential relevant articles, using the following criteria as defined by PICO model [33]: (i) population: persons affected by congenital or acquired neurological disabilities; (ii) intervention: exergames delivered by commercial devices; (iii) comparison: no intervention (i.e., wait-list control group) or conventional treatments or rehabilitation interventions; (iv): outcomes: improvement in cognitive functions assessed by either widely-accepted neuropsychological tests, specific questionnaire(s), or dual-task measures, i.e., performance change in a motor task while simultaneously performing a cognitive task [34]. We only included papers published in peer-reviewed journals, which reported findings from experimentally controlled studies, i.e., both randomized and non-randomized controlled trials. We excluded conference posters, articles not available in English or unpublished, as well as papers reporting findings of non-experimental studies, or involving non-exergaming interventions (e.g., “action” video games involving only hand-eye coordination).

The search was carried out from January through August 2017.

Quality of studies assessment

Two authors (GM and MGC) independently assessed the methodological quality of included studies through the PEDro (Physiotherapy Evidence Database) scale [35]. Studies scoring 9-10 on the PEDro scale are considered to be of “excellent” methodological quality. Scores ranging from 6 to 8 are considered to be of “good” quality, studies scoring 4 or 5 are of “fair” quality, and studies scoring below 4 are deemed to be of “poor” quality. Disagreements between authors were resolved by consensus.

Data synthesis and analysis

For each included article we collected and recorded the following in an electronic spreadsheet: 1) first author’s name and year of publication; 2) samples in intervention and control group; 3) design and duration of the study; 4) topic (i.e., neurological disability covered by the study); 5) type of intervention; 6) assessments; 7) post-intervention outcomes.

Outcomes of interest~~s~~ were expressed as the mean and standard deviation (SD) of post-intervention scores [36]. When applicable, we reverse coded the score for some outcomes so that higher scores represented better cognitive functioning.

As the included studies used different scales to measure cognitive functioning, only post-intervention scores in outcomes measuring similar constructs were pooled as standardized mean differences (SMD) with the accompanying 95% confidence intervals (CIs). Positive SMDs indicated a difference in results favoring exergames; by convention, a SMD of 0.20 is considered small, 0.50 medium, and ≥0.80 a large effect [37]. Data were analyzed using a generic inverse variance with random-effect models in Review Manager 5.3.5 (The Cochrane Collaboration, 2014). Heterogeneity of studies was addressed by the estimation of τ^2 and I^2, considering an I^2 value <40% as an indicator of marginal heterogeneity [36]. Potential publication bias of included studies was determined by the Egger p-value and by checking Funnel plots [36].

EVIDENCE SYNTHESIS

Results from the search

From 4,364 titles originally identified through database searching, and 49 additional titles identified from the bibliography of previous reviews, we were able to assess 187 full-text articles for eligibility. **FIGURE 1** shows the process of study inclusion for qualitative and quantitative review.

- - - Please insert Figure 1 about here - - -

We found thirteen articles published from 2011 to 2017 that fulfilled our inclusion criteria, including eight randomized controlled trials [38-45], two post-hoc analyses from a randomized controlled trial [46, 47], and three non-randomized but controlled studies [48-50]. Among the included studies, two were conducted in Italy [46,49], two in the USA [42, 43], two in Taiwan [45-48], and one each in Brazil [40], Germany [50], Korea [38], Israel [47], Sweden [39], Switzerland [41], and Turkey [44]. **TABLE 2** shows the main characteristics of the included studies.

- - - Please insert Table 2 about here - - -

Samples

Samples in the studies ranged from 20 [39,49] to 155 participants [48]. As expected, the mean age of the participants varied according to neurological disease. Four studies targeted post-stroke survivors [38, 44, 45, 47], three targeted persons affected by multiple sclerosis [39, 46, 50], two targeted Parkinson’s disease [40, 41], one targeted youth population of children with Down Syndrome [48], another youth population with dyslexia [49], one targeted Alzheimer’s disease [42], and one targeted persons with mild cognitive impairment [43]. The severity of all these neurological disabilities was generally mild-to-moderate.

Interventions

Interventions consisted of exergames available on Nintendo Wii Sports or Nintendo Wii Fit, which require balance, motor and cognitive skills similar to actual sports. In most cases, the balance board device was used to perform balance training [39-42, 45-47, 50]. Studies on post-stroke hemiparesis, mild cognitive impairment, Down syndrome and dyslexia [38,43,44,49] required a motion-sensitive remote controller (the so-called “nunchuck”), which provides haptic or kinesthetic communication to the user.

Only one study had participants interact with different commercial devices (Xbox Kinect, Nintendo Wii Fit, Sony PlayStation 2 EyeToy, Sony PlayStation 3 MOVE) [47].

Alternative interventions performed by control groups were quite heterogeneous and included: conventional occupational therapy and/or conventional rehabilitation therapy [38, 48]; global and balance individual [40] or group [47] exercise; computer-assisted cognitive training delivered by the CogniPlus package [41]; supervised indoor walking [42]; health education programming [43]; Bobath neurodevelopmental treatment [44]; non-commercial device or conventional weight-shift training [45]; single-task balance exercises performed on an unstable platform or conventional balance training on a stable surface [50]. Franceschini and colleagues [49] used the same game (Wii Rayman Raving Rabbids) for both the exergaming and the control groups, selecting 10 active mini-games for children in the exergaming group and 10 non-active mini-games for controls. Two studies had a wait-list group without any alternative intervention [39, 46].

Duration, length and frequency of interventions

Duration of interventions ranged from 2 weeks [49] to 24 weeks [43]. Length and frequency of interventions varied from 30 [38, 39, 42, 45, 46, 50] to 90 [43] minutes per session, and once weekly [43] to 5-daily sessions per week [38, 46]. One study provided twice per week individually-tailored time, preceded by a warm-up phase of therapist-led global motility exercises [40].

Outcomes and assessments

Cognitive functioning was the main outcome in six studies [41, 43, 45-47, 49], the secondary or exploratory outcome~~s~~ in five studies [38,39,42,44,48], while the remaining two studies analyzed dual-task performance in gait and balance [40, 50]. One study reported both dual-task measures and a global cognitive test [40] (see **TABLE 3**). Overall, we identified four cognitive domains for meta-analytic purposes: global cognition, attention, executive function (including dual-task performance), and perception (including visuo-spatial abilities). Few studies explored language [45,49] and memory [41,45]; therefore, these cognitive domains were not meta-analyzed.

Measures of general functioning in primary and secondary activities of daily living were reported in four studies, none of which found exergaming-induced changes [38, 42-44].

Post-intervention follow-up assessments ranging from 8 weeks [40, 49] to 12 weeks [45, 47] after the intervention ended were reported in four studies, and one cross-over study provided a 12-week post-training follow-up in the group which was initially randomized to the active intervention [46]. While two studies showed no clear long-term retention of training-induced improvement, three studies demonstrated that the benefit of exergames on executive functions of persons with Parkinson's disease and stroke survivors was maintained at follow-up [40,45,47].

- - - Please insert Table 3 about here - - -

Quality of studies

Quality assessment of the included studies through the PEDro scale [35] is shown in **TABLE 4**.

According to the PEDro scale, most studies were considered to be of good quality: rating 8/11 in four cases [38, 39,45, 47]; 7/11 in three cases [40, 41, 44]; 6/11 in five cases [42, 43, 46, 48, 50]. Only one study was considered to be of fair quality [49], rating 4/11 on the PEDro scale. Higher scores were obtained by randomized controlled trial studies, when allocation to intervention or control group was concealed and at least one category, among therapists or assessors, was blinded to the allocation. Blinding of participants and therapists was not done in any study.

- - - Please insert Table 4 about here - - -

Findings from meta-analysis

The thirteen studies selected for inclusion [38-50] yielded a total of 465 persons, 233 randomized to exergames and 232 allocated to the alternative or no intervention. Three studies included more than two groups [45, 48, 50]; thus, for the meta-analysis, we choose to only include the exergaming group and the groups allocated to a conventional rehabilitation, while the untreated group (n=50) [48], and groups treated with non-commercial devices (n=50) [45] or single-task balance training (n=20) [50] were excluded.

Forrest plots summarizing findings of the meta-analysis are shown in **FIGURE 2**. Mean and SD post-intervention scores were not reported in three studies [39, 41, 45]. These data were inserted after asking the lead author for the data [39, 45], or from using the median and interquartile ranges [41] or appropriate computations [36] to obtain the data.

Although we found no effect on global cognition (SMD=0.05, p=0.80), exergames significantly improved perception (SMD=0.65, p<0.0001) and executive functions (SMD=0.53, p=0.005) when compared with the alternative intervention. Despite an effect size in favor of exergames on attention, the statistical comparison with the alternative or no intervention did not reach statistical significance (SMD=0.57, p=0.07).

Significant heterogeneity was identified in the analyses for attention, and executive functions (I^2≥80%, p-values<0.01), while there was no heterogeneity in the remaining analyses for global cognition and dual-task performance (I^2≤25%, p-values>0.20). There was no evidence for significant publication bias (Egger p-values>0.15). Visual inspection of the Funnel plot revealed a rather symmetrical distribution in the presence of bias because one study on Down syndrome [48] produced an exaggerated effect estimate in favor of the exergaming group on perception and executive functions, while another study on Alzheimer's disease [42] produced an exaggerated effect in favor of the alternative intervention on global cognition (see **FIGURE 3**). Despite these outliers, the main findings did not change even after removing these two studies from the meta-analysis, which resulted a better effect of exergames on executive functions (SMD=0.33, p=0.007) and perception (SMD=0.42, p=0.03) without significant heterogeneity (I^2<1%, p-values>0.65).

- - - Please insert Figures 2 and 3 about here - - -

Discussion

We meta-analyzed thirteen studies investigating the effect of exergames on cognitive functioning as primary or secondary outcomes in persons with neurological disabilities. Results indicated that exergames exhibited a medium effective size in improving some specific cognitive domains, such as executive functions (including dual-task performance) and perceptual/visuo-spatial abilities. In contrast, there were no significant differences between exergames and alternative interventions (or no intervention) for global cognition and attention. The present meta-analysis should be interpreted with caution, given the variability in the assessment of cognitive functions, including generic screening tool [38, 40, 42-45] or dual-task experiments [39, 42, 50], rather than more specific and sensitive tests [41, 46, 47, 49].

Our findings suggest that exergames increase the ability to allocate cognitive resources in time and space, by enhancing decision/prioritization processes (executive functions) and visuo-spatial perception. Exergaming could be considered a dual-task strategy to train persons to automate the motor task, allowing the allocation of more resources to other tasks [51]. Dual-task execution requires prioritization of a task, i.e., to hierarchically select the relevant task [52]. According to the TOTE (Test-Operate-Test-Exit) model, when planning for intentional actions, persons collect information to reach the desired result (T), then operate in practice (O), test the result (T) and exit (E) the program if the goal is reached [53]. During information processing, multiple sources of information must be recorded to integrate all available data and execute a final decision. This process occurs for both deliberate and automatic tasks, such as simple sensory-motor tasks [54], which could be trained through the immediate feedback provided by exergames.

Regarding the lack of significant results for attention, this could be attributed to a power issue given the small number of studies included in this meta-analysis. Unlike our results, the meta-analysis by Stanmore et al. [31] found benefits of exergaming interventions on executive functions, attentional processing, and visuo-spatial skills, as well as an improvement in overall cognitive functioning. However, among the seventeen studies included in the review by Stanmore and colleagues, only five studies included populations of persons with neurological disorders, with merely four on exergaming with commercial devices. Thus, future studies are warranted to better elucidate the relationship between exergames and attention in various populations.

In addition to findings related to cognitive outcomes, exergaming was more efficacious compared to no-intervention [39, 46], and comparable to other therapist-led programs [40, 42-46, 50] at improving motor functions such as balance performance and walking ability. This was also evident for upper extremity motor impairment in persons with hemiparesis [38, 44]. Noticeably, one study performed on persons with multiple sclerosis detected a correlation between improved balance and better performance on a test of information processing speed [46], supporting the hypothesis that a far transfer effect can occur from balance to cognition through exergames [23].

Almost all the included studies considered the exergame programs feasible, safe, enjoyable and motivating. Some of the studies included in this review reported no or minor adverse events related to exergaming, with almost all participants in the exergaming groups completing the programs [38, 39, 40, 41, 42, 43, 44, 48]. Nilsagård and colleagues [39] stated that playing exergames "*functioned as a self-trigger to continue the exercise*", and Şimşek & Çekok [44] reported that "*patients stated that watching themselves enabled them to see and correct their faults during playing the games …they looked forward to play the next session and came to the therapy more willingly in order to improve their scores*". Independently from the objectively measured improvements, exergame-related motivation and salience could explain why this rehabilitation tool is appreciated by therapists and persons with neurological disabilities.

Prior research showed that virtual environment training allows people to develop spatial navigation tasks indistinguishable from those acquired from training in the real world, and that those skills could be transfer into real-world situations [55]. Such transfer from the virtual reality training might be also obtained with exergames, as suggested by their effect on the functional reach test [56], improvement in self-perceived walking ability [39], and in activities of daily living [40].

Implications

Among the thirteen studies included in this review, exergames have been used in different clinical contexts such as persons affected by post-stroke hemiparesis, Parkinson’s disease, multiple sclerosis, Alzheimer’s disease, mild cognitive impairment, and in children with intellectual disabilities or learning disorders, reflecting the unique versatility of this tool. Availability of multiple games and devices encourage creating tailored rehabilitation programs. Moreover, the flexibility of devices permits the framework for making ‘ad-hoc’ modifications to video games to optimize them for use in different clinical settings. For example, Pau and colleagues [57] suggested that specific video games should be developed to exploit the full potential of video game-based rehabilitation; Choi and colleagues [38] developed a forearm orthosis to enable persons with hemiparesis to hold the Wii remote control; dos Santos Mendes and colleagues [56] highlighted the importance of training persons with Parkinson’s disease using only games in which they exhibit no learning deficit.

Although none of the included studies performed a cost-efficacy analysis of exergames compared to conventional or other interventions, some authors assumed that exergames are less expensive than traditional therapies that are typically delivered on a regular basis by therapists in a hospital setting or at home [38, 39, 41, 44, 46].

In few studies, exergames were delivered in addition to conventional treatment, including pharmacotherapy in persons with Parkinson’s disease [40, 41, 56]. It has been demonstrated that exercise is an effective add-on strategy to impact cognitive outcomes in persons suffering from Parkinson’s disease [58], and dementia [59], and to enhance antidepressant-related neurotrophic action on hippocampal atrophy in people with severe depression [60].

While it is not possible to recommend exergames instead of conventional rehabilitation therapies, we strongly support further investigations on the effectiveness of exergames. Specifically, exergames could be proposed as an add-on intervention to conventional rehabilitation, and/or as strategy to avoid deconditioning during temporary discontinuation of physiotherapy, thus extending benefits of conventional programs.

Study limitations

Major limitations of this review mainly encompass the small sample sizes of the selected studies, the dissimilarity in outcomes and assessments used to measure cognitive functioning, and the heterogeneity of populations included in the analysis. We meta-analyzed persons with a wide range of ages, and disparate neurological conditions, such as subacute stroke, Parkinson’s disease, multiple sclerosis, mild dementia, and children with Down syndrome or learning disorders.

Because of these heterogeneities, we are aware that it is not possible to draw univocal conclusions about the efficacy of exergames in improving cognitive functioning in persons with neurological disabilities. Moreover, because exergames were not specifically designed for cognitive rehabilitation, our preliminary findings strongly support the need for high-quality studies, such as randomized controlled trials, with an appropriate sample size calculation.

Lastly, we were not able to extrapolate the metabolic equivalents (METS) spent during exergaming from selected studies. This is relevant information that should be implemented in future studies, since exergames are, by definition, supposed to correspond to moderate intensity training [1], i.e., 40% to <60% oxygen uptake reserve, or heart rate reserve of 3 to <6 METS, according to the American College of Sport Medicine (ACSM) [61].

CONCLUSIONS

The results of this meta-analysis confirm prior literature highlighting the potential role of exergames in enhancing cognitive skills in older adults [62, 63] in school children [64], and in persons affected by developmental disorders [11]. Nevertheless, to the best of our knowledge, this is the first review of experimental studies exclusively devoted to establish the efficacy of exergames on cognition in persons with neurological disabilities.

Exergames could provide a potential rehabilitation tool for improving both cognitive and motor functions by means of unique training, with the hypothesis that playing action video games can modulate the activity of brain regions serving both motor and cognitive domains [65]. Moreover, rehabilitation in neurological disabilities by means of exergaming has been confirmed to be safe, flexible, and is characterized by high rates of adherence. However, quality research including larger samples are needed to better establish the type of games, the frequency, and the intensity upon which exergames could be beneficial for cognition in persons with neurological disabilities.

Funding.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

REFERENCES

[1] Read JL, Shortell SM. Interactive games to promote behavior change in prevention and treatment. JAMA 2011; 305: 1704-1705.

[2] Gao Z, Chen S. Are field-based exergames useful in preventing childhood obesity? A systematic review. Obes Rev. 2014 Aug;15(8):676-91.

[3] Ruivo JA. Exergames and cardiac rehabilitation: a review. J Cardiopulm Rehabil Prev. 2014 Jan-Feb;34(1):2-20.

[4] Laufer Y, Dar G, Kodesh E. Does a Wii-based exercise program enhance balance control of independently functioning older adults? A systematic review. Clin Interv Aging. 2014 Oct 23;9:1803-13.

[5] Hasselmann V, Oesch P, Fernandez-Luque L, Bachmann S. Are exergames promoting mobility an attractive alternative to conventional self-regulated exercises for elderly people in a rehabilitation setting? Study protocol of a randomized controlled trial. BMC Geriatr. 2015 Sep 7;15:108.

[6] Goble DJ, Cone BL and Fling BW. Using the Wii Fit as a tool for balance assessment and neurorehabilitation: the first half decade of “Wii-search”. J Neuroeng Rehabil 2014; 11: 12.

[7] Wüest S, van de Langenberg R, de Bruin ED. Design considerations for a theory-driven exergame-based rehabilitation program to improve walking of persons with stroke. Eur Rev Aging Phys Act. 2014;11(2):119-129.

[8] Taylor M, Griffin M. The use of gaming technology for rehabilitation in people with multiple sclerosis. Mult Scler. 2015 Apr;21(4):355-371.

[9] Barry G, Galna B, Rochester L. The role of exergaming in Parkinson's disease rehabilitation: a systematic review of the evidence. J Neuroeng Rehabil. 2014 Mar 7;11:33.

[10] Luna-Oliva L, Ortiz-Gutiérrez RM, Cano-de la Cuerda R, Piédrola RM, Alguacil-Diego IM, Sánchez-Camarero C, Martínez Culebras Mdel C. Kinect Xbox 360 as a therapeutic modality for children with cerebral palsy in a school environment: a preliminary study. NeuroRehabilitation. 2013 Jan 1;33(4):513-21.

[11] Jannink MJ, van der Wilden GJ, Navis DW, Visser G, Gussinklo J, Ijzerman M. A low-cost video game applied for training of upper extremity function in children with cerebral palsy: a pilot study. Cyberpsychol Behav. 2008 Feb;11(1):27-32.

[12] Deutsch JE, Borbely M, Filler J, Huhn K, Guarrera-Bowlby P. Use of a low-cost, commercially available gaming console (Wii) for rehabilitation of an adolescent with cerebral palsy. Phys Ther. 2008 Oct;88(10):1196-207.

[13] Ilg W, Schatton C, Schicks J, Giese MA, Schöls L, Synofzik M. Video game-based coordinative training improves ataxia in children with degenerative ataxia. Neurology. 2012 Nov 13;79(20):2056-60.

[14] Synofzik M, Ilg W. Motor training in degenerative spinocerebellar disease: ataxia-specific improvements by intensive physiotherapy and exergames. Biomed Res Int. 2014;2014:583507.

[15] Berg P, Becker T, Martian A, Primrose KD, Wingen J. Motor control outcomes following Nintendo Wii use by a child with Down syndrome. Pediatr Phys Ther. 2012 Spring;24(1):78-84.

[16] Ferguson GD, Jelsma D, Jelsma J, Smits-Engelsman BCM. The efficacy of two task-orientated interventions for children with Developmental Coordination Disorder: Neuromotor Task Training and Nintendo Wii Fit training. Research in Developmental Disabilities. 2013; 34: 2449-2461.

[17] Widman LM, McDonald CM, Abresch RT. Effectiveness of an upper extremity exercise device integrated with computer gaming for aerobic training in adolescents with spinal cord dysfunction. J Spinal Cord Med. 2006;29(4):363-70.

[18] Thakur KT, Albanese E, Giannakopoulos P, Jette N, Linde M, Prince MJ, Steiner TJ, Dua T. Neurological Disorders. In: Patel V, Chisholm D, Dua T, Laxminarayan R, Medina-Mora ME, editors. Mental, Neurological, and Substance Use Disorders: Disease Control Priorities, Third Edition (Volume 4). Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2016 Mar 14. Chapter 5.

[19] Bavelier D, Green CS, Han DH, Renshaw PF, Merzenich MM, Gentile DA. Brains on video games. Nat Rev Neurosci. 2011 Nov 18;12(12):763-8.

[20] Bavelier D, Green CS, Pouget A, Schrater P. Brain plasticity through the life span: learning to learn and action video games. Annu Rev Neurosci 2012; 35:391-416.

[21] Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. J Speech Lang Hear Res 2008; 51(1):S225–239.

[22] Levin MF. Can virtual reality offer enriched environments for rehabilitation? Expert Rev. Neurother. 2011; 11(2):153–155.

[23] Barnett SM, Ceci SJ. When and where do we apply what we learn? A taxonomy for far transfer. Psychol Bull 2002; 128(4):612–37.

[24] Weiss PL, Tirosh E, Fehlings D. Role of virtual reality for cerebral palsy management. J Child Neurol. 2014 Aug;29(8):1119-24.

[25] Harris DM, Rantalainen T, Muthalib M, Johnson L, Teo WP. Exergaming as a Viable Therapeutic Tool to Improve Static and Dynamic Balance among Older Adults and People with Idiopathic Parkinson's Disease: A Systematic Review and Meta-Analysis. Front Aging Neurosci. 2015 Sep 7;7:167.

[26] Taylor MJ, Griffin M. The use of gaming technology for rehabilitation in people with multiple sclerosis. Mult Scler. 2015 Apr; 21(4): 355-71.

[27] Green CS, Bavelier D. Action video game modifies visual selective attention. Nature. 2003; 423 (6939): 534–7.

[28] Anderson-Hanley C, Arciero PJ, Brickman AM, et al. Exergaming and older adult cognition: a cluster randomized clinical trial. Am. J. Prev. Med. 2012; 42(2):109–119.

[29] Anguera JA, Boccanfuso J, Rintoul JL, et al. Video game training enhances cognitive control in older adults. Nature. 2013; 501(7465):97–101.

[30] Chao YY, Scherer YK, Montgomery CA. Effects of using Nintendo Wii™ exergames in older adults: a review of the literature. J Aging Health. 2015 Apr;27(3): 379-402.

[31] Stanmore E, Stubbs B, Vancampfort D, de Bruin ED, Firth J. The effect of active video games on cognitive functioning in clinical and non-clinical populations: a meta-analysis of randomized controlled trials. Neurosci Biobehav Rev. 2017 Jul;78:34-43. doi: 10.1016/j.neubiorev.2017.04.011.

[32] Moher D, A. Liberati A, Tetzlaff J, Altman DG, and PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009 Jul 21;339:b2535.

[33] O'Sullivan D, Wilk S, Michalowski W, Farion K. Using PICO to align medical evidence with MDs decision making models. Stud Health Technol Inform 2013;192:1057.

[34] Della Sala S, Baddeley AD, Papagno C, Spinnler H. Dual-task paradigm: a means to examine the central executive. Ann NY Acad Sci 1995; 769: 161-171.

[35] Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. Physical Therapy, 2003; 83 (8): 713–721.

[36] http://handbook.cochrane.org/front_page.htm (accessed on January 2017).

[37] Cohen J. A power primer. Psychol Bull 1992; 112 (1):155-159.

[38] Choi JH, Han EY, Kim BR, Kim SM, Im SH, Lee SY, Hyun CW. Effectiveness of commercial gaming-based virtual reality movement therapy on functional recovery of upper extremity in subacute stroke patients. Ann Rehabil Med. 2014 Aug;38(4):485-93.

[39] Nilsagård YE, Forsberg AS, von Koch L. Balance exercise for persons with multiple sclerosis using Wii games: a randomised, controlled multi-centre study. Mult Scler. 2013 Feb;19(2):209-16.

[40] Pompeu JE, Mendes FA, Silva KG, Lobo AM, Oliveira Tde P, Zomignani AP, Piemonte ME. Effect of Nintendo Wii™-based motor and cognitive training on activities of daily living in patients with Parkinson's disease: a randomised clinical trial. Physiotherapy. 2012 Sep;98(3):196-204.

[41] Zimmermann R, Gschwandtner U, Benz N, Hatz F, Schindler C, Taub E, Fuhr P. Cognitive training in Parkinson disease: cognition-specific vs nonspecific computer training. Neurology. 2014 Apr 8;82(14):1219-26.

[42] Padala KP, Padala PR, Malloy TR, Geske JA, Dubbert PM, Dennis RA, Garner KK, Bopp MM, Burke WJ, Sullivan DH. Wii-fit for improving gait and balance in an assisted living facility: a pilot study. J Aging Res. 2012; 2012:597573.

[43] Hughes TF, Flatt JD, Fu B, Butters MA, Chang CH, Ganguli M. Interactive Video Gaming compared to Health Education in Older Adults with MCI: A Feasibility Study. Int J Geriatr Psychiatry 2014; 29 (9): 890-898.

[44] Şimşek TT, Çekok K. The effects of Nintendo Wii(TM)-based balance and upper extremity training on activities of daily living and quality of life in patients with sub-acute stroke: a randomized controlled study. Int J Neurosci. 2016; 126(12):1061-70.

[45] Hung JW, Chou CX, Chang HF, Wu WC, Hsieh YW, Chen PC, Yu MY, Chang CC, Lin JR. Cognitive effects of weight-shifting controlled exergames in patients with chronic stroke: a pilot randomized comparison trial. Eur J Phys Rehabil Med. 2017; doi: 10.23736/S1973-9087.17.04516-6.

[46] Prosperini L, Petsas N, Sbardella E, Pozzilli C, Pantano P. Far transfer effect associated with video game balance training in multiple sclerosis: from balance to cognition? J Neurol. 2015 Mar;262(3):774-6.

[47] Rozental-Iluz C, Zeilig G, Weingarden H, Rand D. Improving executive function deficits by playing interactive video-games: secondary analysis of a randomized controlled trial for individuals with chronic stroke. Eur J Phys Rehabil Med. 2016 Aug;52(4):508-15.

[48] Wuang YP, Chiang CS, Su CY, Wang CC. Effectiveness of virtual reality using Wii gaming technology in children with Down syndrome. Res Dev Disabil. 2011; 32(1):312-21.

[49] Franceschini S, Gori S, Ruffino M, Viola S, Molteni M, Facoetti A. Action Video Games Make Dyslexic Children Read Better. Curr Biol 2013; 23, 462–466.

[50] Kramer A, Dettmers C, Gruber M. Exergaming with additional postural demands improves balance and gait in patients with multiple sclerosis as much as conventional balance training and leads to high adherence to home-based balance training. Arch Phys Med Rehabil. 2014 Oct;95(10):1803-9.

[51] Fritz NE, Cheek FM, Nichols-Larsen DS. Motor-Cognitive Dual-Task Training in Persons With Neurologic Disorders: A Systematic Review. J Neurol Phys Ther. 2015 Jul;39(3):142-53.

[52] Yogev-Seligmann G, Hausdorff JM, Giladi N. The role of executive function and attention in gait. Mov Disord 2008; 23(3): 329-342.

[53] Miller GA, Galanter E, Pribram KH. Plans and the structure of behavior. Holt, Rinehart and Winston, Inc. (1960).

[54] Gold JI, Shadlen MN. The neural basis of decision making, Annu. Rev. Neurosci. 2007; 30: 535–74

[55] Waller D, Hunt E, Knapp D. The transfer of spatial knowledge in virtual environment training. Presence, *Vol. 7, No. 2, April 1998,* 129-143.

[56] dos Santos Mendes A, Pompeu JE, Modenesi Lobo A, Guedes da Silva K, Oliveira Tde P, Peterson Zomignani A, Pimentel Piemonte ME. Motor learning, retention and transfer after virtual-reality-based training in Parkinson's disease- effect of motor and cognitive demands of games: a longitudinal, controlled clinical study. Physiotherapy. 2012 Sep;98(3):217-23.

[57] Pau M, Coghe G, Corona F, Leban B, Marrosu MG, Cocco E. Effectiveness and Limitations of Unsupervised Home-Based Balance Rehabilitation with Nintendo Wii in People with Multiple Sclerosis. Biomed Res Int. 2015. ~~2015:916478.~~ doi: 10.1155/2015/916478

[58] Reuter I, Mehnert S, Sammer G, Oechsner M, Engelhardt M. Efficacy of a multimodal cognitive rehabilitation including psychomotor and endurance training in Parkinson's disease. J Aging Res 2012; 2012:235765.

[59] Heyn P, Abreu BC, Ottenbacher KJ. The effects of exercise training on elderly persons with cognitive impairment and dementia: a meta-analysis. Arch Phys Med Rehabil. 2004;85:1694–1704

[60] Mura G, Moro MF, Patten SB, Carta MG. Exercise as an add-on strategy for the treatment of major depressive disorder: a systematic review. CNS Spectrums. 2014; 19: 496-508.

[61] http://www.acsm.org/public-information/acsm-journals/guidelines (accessed on 27 January 2017).

[62] Chao YY, Scherer YK, Montgomery CA. Effects of using Nintendo Wii™ exergames in older adults: a review of the literature. J Aging Health. 2015 Apr;27(3):379-402.

[63] Bamidis PD, Vivas AB, Styliadis C, Frantzidis C, Klados M, Schlee W, Siountas A, Papageorgiou SG. A review of physical and cognitive interventions in aging. Neurosci Biobehav Rev. 2014 Jul;44:206-20.

[64] Mura G, Vellante M, Machado S, Nardi AE, Carta MG. Effects of school-based physical activity intervention on cognition and academic achievement: a systematic review. CNS Neurol Disord Drug Targets. 2015;14(9):1194-208.

[65] Prosperini L, Castelli L, De Luca F, Fabiano F, Ferrante I, De Giglio L. Task-dependent deterioration of balance underpinning cognitive-postural interference in MS. Neurology. 2016 Sep 13;87(11):1085-92.

TABLE 1. Search strategy.

CATEGORY	TERMS USED ("OR" TERMS)
Population	Nervous System Diseases; Nervous System Diseases/rehabilitation; stroke; Multiple Sclerosis; Parkinson Disease; Alzheimer Disease; Dementia; Trauma, Nervous System; Chorea; Neurodevelopmental Disorders; Intellectual Disability; Cerebral Palsy.
Intervention	Video Games*; Video Games/therapeutic use; computer game*; computer interact*; virtual reality*; VR; virtual reality exposure therapy/methods*; User-Computer Interface; serious game; Exergam*; Active video games; Nintendo Wii; Wii; Microsoft Kinect; Kinect; Dance Dance Revolution; Sony EyeToy.
Comparison	Randomized; Controlled; Control group*; RCT; Clinical trial; Control condition
Outcomes	Cognit*; Neurocognitive; Neuropsychological; Neurological; Executive Function*; Brain function* Attention; Memory; Problem Solving; Processing; Learning; Language

TABLE 2. Main characteristics of the included studies (in alphabetic order).

AUTHORS, YEAR	TOPIC	SAMPLE SIZE	AGE, YRS mean±SD	DESIGN	DURATION	FREQUENCY	INTERVENTIONS	MAIN RESULTS
Choi et al., 2014 [38]	Stroke	20	64.3±10.3 64.7±11.3	RCT	4 weeks	30-min/session, 5 sessions/week	**Exergames (n=10):** Nintendo Wii Sports Resort (swordplay, table tennis, and canoe) + conventional rehabilitation therapy **Control (n=10):** conventional occupational therapy + conventional rehabilitation therapy	Exergames was as effective as conventional occupational therapy on the upper extremity motor function. Exergames was as effective as conventional occupational therapy on the MMSE score and number of correc detections at the auditory CPT. The number of commission errors at th auditory CPT and number of correct detections in the visual CPT improved only in the exergaming group.
Franceschini et al., 2013 [49]	Dyslexia	20	9.8±1.4	controlled	2 weeks + 8-week follow-up	9 sessions lasting 80 minutes, for a 12 hours of total training	**Exergames (n=10):** active mini-games of Wii Rayman Raving Rabbids **Control (n=10):** non-active mini-games of Wii Rayman Raving Rabbids	General reading abilities improved with active and not non-active video games In the reading speed of pseudo-word decoding tasks and in word text readin skills, the exergaming group showed a bigger improvement. The reading improvements after the active video games training were characterized by the increased reading speed without a cost in accuracy.
Hughes et al. 2015 [43]	Mild cognitive impairment	20	77.4±5.8	RCT	24 weeks	90-min/session, once weekly	**Exergames (n=10):** interactive video games of Wii Sports and Sports Resort **Control (n=10):** passive cognitive stimulation consisting of learning and discussing about age-specific health-related topics with professionals	All participants completed the intervention and 90% of them attendec at least 80% of the scheduled sessions Exergames improved cognitive and physical functioning, but these effects did not reach the statistical significance
Hung et al. 2017 [45]	Stroke	37	56 range: 43-64	RCT	12 weeks + 12-week follow-up	30-min/session, 2 sessions/week	**Exergames (n=12):** **Control 1 (n=13):** non-commercial device equipped with a force platform providing real-time visual feedback (Tetra biofeedback system) **Control 2 (n=12):** conventional weight-sift training without video games	There were no between-group differences in change of global cognition after the intervention. Exergames improved some aspects of cognitive functions, namely abstract-judgement and language. Only the improvement in abstract-judgement wa maintained at 3-month follow-up.
Kramer et al., 2014 [50]	Multiple sclerosis	61	47±9	non- randomized matched group	3 weeks	9 sessions lasting 30 minutes	**Exergames (n=21):** Wii Sports/Sports Resort/Fit performed on an unstable platform **Control 1 (n=20):** single-task exercises performed on an unstable platform **Control 2 (n=20):** conventional balance training on a stable surface	All groups showed significantly improved balance and gait scores, but only the exergame training group showed significantly higher improvements in the dual-task conditio of the gait test than in the single-task condition.

Nilsagård et al., 2013 [39]	Multiple sclerosis	84	50.0±11.5 49.4±11.1	RCT	6 weeks	30-min/session, 2 sessions/week	**Exergames (n=42):** Supervised Nintendo Wii Fit plus games with Nintendo Balance Board **Control (n=42):** no intervention	No statistical between-group differenc in several balance measures. A significant improvement in the TUG-cognitive test was observed only in exergaming group.
Padala et al., 2012 [42]	Alzheimer's disease	22	79.3±9.8 81.6±5.2	RCT	8 weeks	30-min/session, 5 sessions/week	**Exergames (n=11):** supervised Wii Fit games (including strength, yoga and balance training) **Control (n=11):** supervised walking (in group of 3 or 4 subjects)	Exergaming group improved on balanc and gait measures. No significant intra-group change, nor group-by-time interaction on MMSE score were detected in both groups.
Pompeu et al., 2012 [40]	Parkinson's disease	32	67.4±8.1	RCT	7 weeks + 8-week follow-up	60-min/session, 2 sessions/week	**Exergames (n=16):** 30 minutes of global exercises + 30 minutes of Nintendo Wii Fit games, with motor, balance and cognitive demands **Control (n=16):** 30 minutes of global exercises + 30 minutes balance exercise therapy without the provision of external cues, feedback and cognitive stimulation	No additional advantages associated with exergames on UPDRS-II. Both groups showed a significant improvement on global cognitive skills after training that was maintained at follow-up.
Prosperini et al., 2015 [46]	Multiple sclerosis	21	35.1±8.4	Cross-over trial	12 weeks + 12 weeks follow-up	30-min/session, 5 sessions/week	**Exergames (n=10):** home-based video games selected from Nintendo Wii Fit Plus **Control (n=11):** no intervention	Exergames was associated with improvement of speed of information processing and sustained attention, tha was not maintained at follow-up.
Rozental-Iluz et al., 2016 [47]	Stroke	39	59.2±10.1	RCT	12 weeks + 12 weeks follow-up	60-min/session, 2 sessions/week	**Exergames (n=20):** video games selected from consoles (Xbox Kinect, Nintendo Wii Fit, Sony PlayStation 2 EyeToy, Sony PlayStation 3 MOVE) **Control (n=19):** Goal-directed motor activities	Both groups showed a significant improvement on executive functions after training that was maintained at follow-up.
Simsek et al., 2016 [44]	Stroke	42	58.04±16.56	RCT	10 weeks	45-60 min/day, 3 days/week	**Exergames (n=20):** games selected from the Wii sports and Wii Fit packages for upper limb and balance training **Control (n=22):** Bobath neurodevelopmental treatment	Exergames were as effective as Bobat treatment on daily living functions and quality of life. Participants in exergaming group were more satisfied from the intervention.
Wuang YP et al. 2011 [48]	Down syndrome	155	Range: 7-12 years	non- randomized matched group	24 weeks	60-min/session, 2 days/week	**Exergames (n=52):** sports games from Nintendo Wii Sports Resort **Control 1 (n=53):** standard occupational therapy **Control 2 (n=50):** no intervention	Participants in the exergaming group had a better pre-post change on motor proficiency, visual-integrative abilities, and sensory integrative functioning.
Zimmermann et al., 2014 [41]	Parkinson's disease	39	69.9±6.3 66.3±9.7	RCT	4 weeks	40 min/session, 3 times/week	**Exergames (n=20):** sports games from Nintendo Wii Sports Resort (each 10 minutes lasting): Table Tennis, Swordplay, Archery, and Air Sports **Control (n=19):** CogniPlus consisting of	There was a significantly greater enhancement of attention after Wii training compared with CogniPlus. A positive trend in favor of Wii training compared with CogniPlus was showed for visuo-construction and episodic

	4 modules training different cognitive domains: FOCUS, focused attention; NBACK, working memory; PLAND, planning and action skills (executive functions); HIBIT, response inhibition (executive functions)	memory. Changes in working memory and executive functions (flexibility) were no different.

egend. CPT: Continuous Performance Test; MMSE: Mini-Mental State Examination; RCT: randomized controlled trial; SD: standard deviation; TUG: Timed Up-and-Go est; UPDRS-II: Unified Parkinson's Disease Rating Scale, section II.

TABLE 3. Cognitive outcome measures assessed in the included studies (in alphabetic order) according to their construct.

	Global cognition	**Attention**	**Visuo-spatial abilities /perception**	**Executive functions /dual-task performance**
Choi et al., 2014 [38]	Korean version of Mini-Mental State Examination (K-MMSE)	Auditory Continuous Performance Test (A-CPT)	Visual Continuous Performance Test (V-CPT)	-
Franceschini et al., 2013 [49]	-	Cross-modal Temporal Attention task, reaction time	Distributed and Focused Attention tasks, spatial attention	-
Hughes et al. 2015 [43]	Computerized Assessment of Mild Cognitive Impairment (CAMCI)	CAMCI, Tracking A	-	CAMCI, Tracking B
Hung et al. 2017 [45]	Cognitive Abilities Screening Instrument Chinese, version 2.0 (CASI-C)	Attention subscale (CASI-C)	Orientation subscale (CASI-C)	Abstract/judgement subscale (CASI-C)
Kramer et al., 2014 [50]	-	-	-	Both-legs postural sway in dual-task condition
Nilsagård et al., 2013 [39]	-	-	-	Cognitive Timed up-and Go-Test (TUG-C)
Padala et al., 2012 [42]	Montreal Cognitive Assessment (MCA)	-	-	Unipedal Stance Test in dual-task condition
Pompeu et al., 2012 [40]	Mini-Mental State Examination (MMSE)	-	-	-
Prosperini et al., 2015 [46]	-	Paced Auditory Serial Addition Test	-	
Rozental-Iluz et al., 2016 [47]	-	-	-	Executive Function Route-finding Task (EFRT Executive Function Performance Test (EFPT) Trail-Making Test (TMT)
Simsek et al., 2016 [44]	Functional Independent Measures (FIM), cognitive	-	-	-
Wuang YP et al. 2011 [48]	-	Test of Sensory Integration Function, attention and activity	Developmental Test of Visual Motor Integration (VIM), visual perception	Test of Sensory Integration Function, emotion behavioral reactivity
Zimmermann et al., 2014 [41]	-	Test of Attentional Performance (TAP), Alertness	Block-Design Test	Trail-Making Test (TMT)

TABLE 4. Assessment of methodological quality of the included articles using the PEDro Scale.

AUTHOR, YEAR	**1. Eligibility criteria ***	**2. Random allocation**	**3. Concealed allocation**	**4. Baseline comparability**	**5. Blinding of subjects**	**6. Blinding of therapists**	**7. Blinding of assessors**	**8. Adequate follow-up**	**9. Intention-to-treat analysis**	**10. Between-group statistical comparison comparisons**	**11. Point estimates and variability**	**Score**
Choi et al., 2014 [38]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8/11
Franceschini et al., 2013 [49]	N	N	N	Y	N	N	N	Y	Y	Y	Y	4/11
Hughes et al., 2015 [43]	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	6/11
Hung et al., 2017 [45]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8/11
Kramer et al., 2014 [50]	Y	N	N	Y	N	N	Y	Y	Y	Y	Y	6/11
Nilsagård et al., 2013 [39]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8/11
Padala et al., 2012 [42]	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	6/11
Pompeu et al., 2012 [40]	Y	Y	N	Y	N	N	Y	Y	Y	Y	Y	7/11
Prosperini et al., 2015 [46]	Y	Y	Y	Y	N	N	Y	N	N	Y	Y	6/11
Rozental-Iluz et al., 2016 [47]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8/11
Şimşek TT et al., 2016 [44]	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	7/11

Wuang et al., 2011 [48]	Y	N	N	Y	N	N	Y	Y	Y	Y	Y	6/11
Zimmermann et al., 2014 [41]	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	7/11

* Eligibility criteria item does not contribute to total score.

FIGURE 1. Flow diagram of literature search and selection of publications.

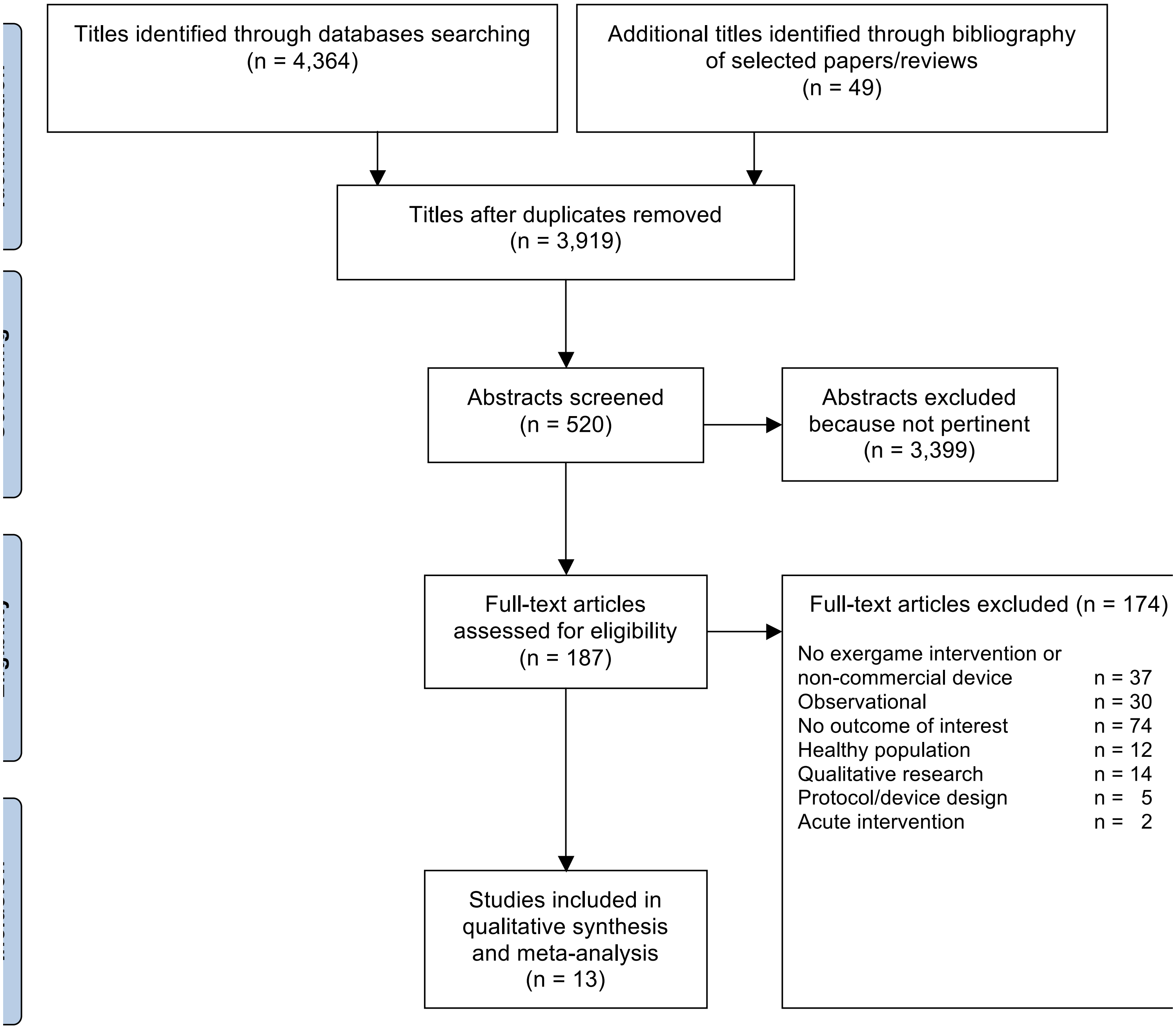
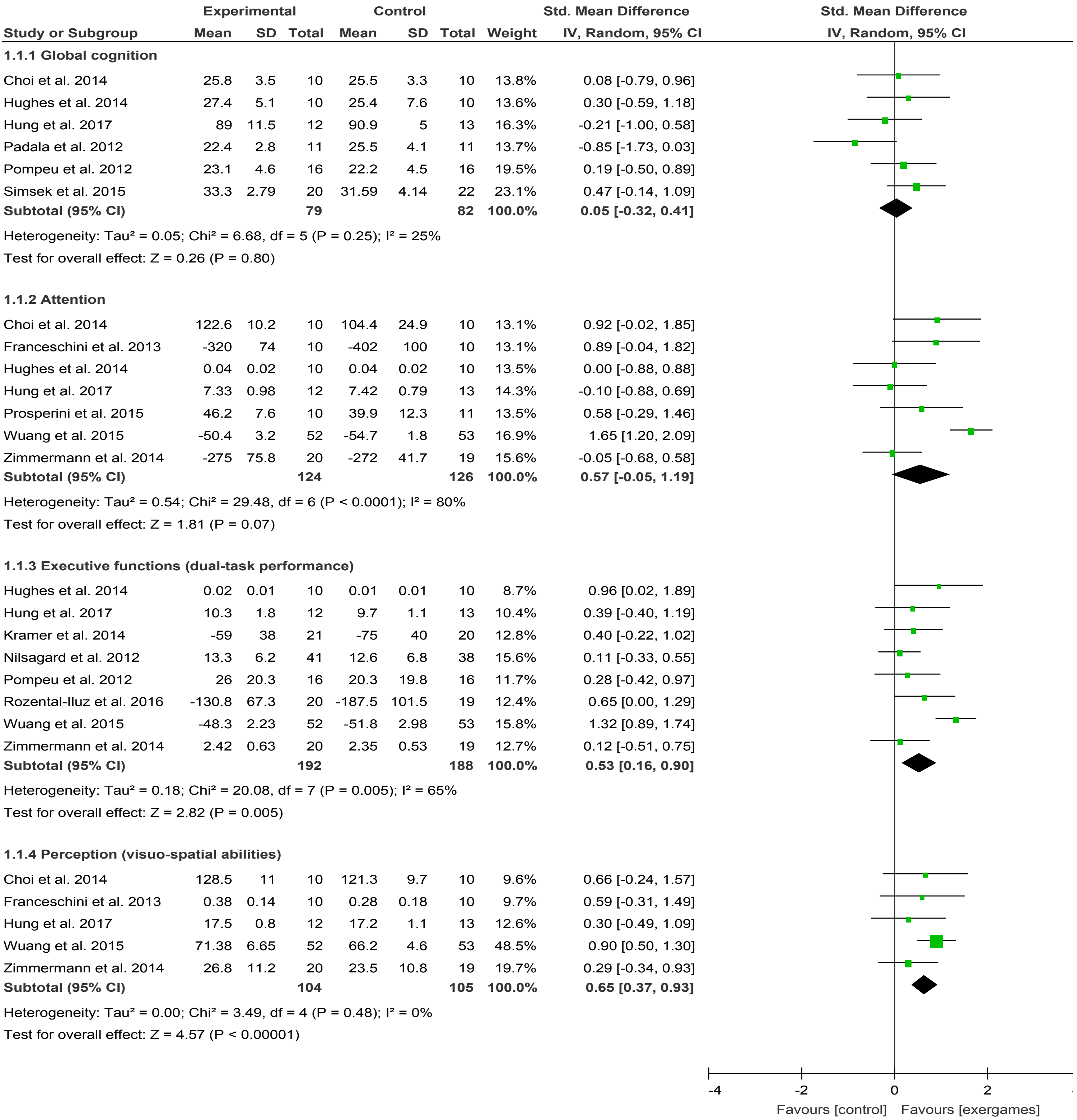
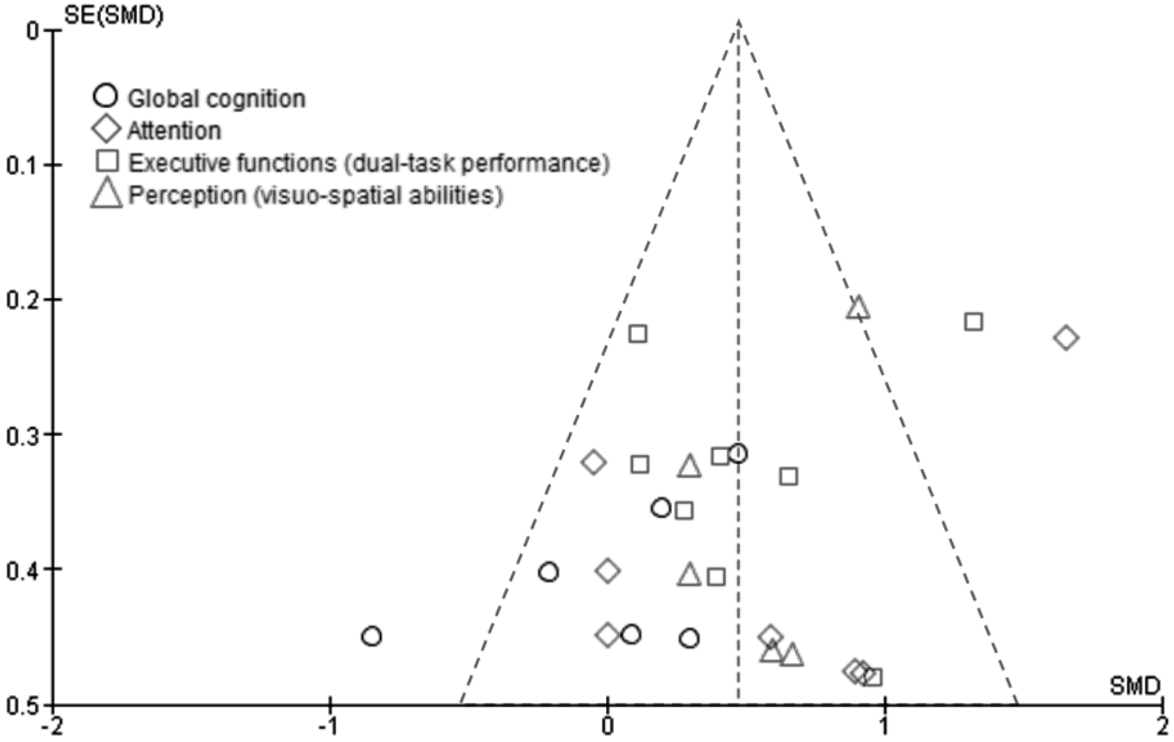


FIGURE 2. Forest plots of included studies.



	Experimental			Control				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
1.1.1 Global cognition								
Choi et al. 2014	25.8	3.5	10	25.5	3.3	10	13.8%	0.08 [-0.79, 0.96]
Hughes et al. 2014	27.4	5.1	10	25.4	7.6	10	13.6%	0.30 [-0.59, 1.18]
Hung et al. 2017	89	11.5	12	90.9	5	13	16.3%	-0.21 [-1.00, 0.58]
Padala et al. 2012	22.4	2.8	11	25.5	4.1	11	13.7%	-0.85 [-1.73, 0.03]
Pompeu et al. 2012	23.1	4.6	16	22.2	4.5	16	19.5%	0.19 [-0.50, 0.89]
Simsek et al. 2015	33.3	2.79	20	31.59	4.14	22	23.1%	0.47 [-0.14, 1.09]
Subtotal (95% CI)			**79**			**82**	**100.0%**	**0.05 [-0.32, 0.41]**
Heterogeneity: Tau² = 0.05; Chi² = 6.68, df = 5 (P = 0.25); I² = 25%								
Test for overall effect: Z = 0.26 (P = 0.80)								
1.1.2 Attention								
Choi et al. 2014	122.6	10.2	10	104.4	24.9	10	13.1%	0.92 [-0.02, 1.85]
Franceschini et al. 2013	-320	74	10	-402	100	10	13.1%	0.89 [-0.04, 1.82]
Hughes et al. 2014	0.04	0.02	10	0.04	0.02	10	13.5%	0.00 [-0.88, 0.88]
Hung et al. 2017	7.33	0.98	12	7.42	0.79	13	14.3%	-0.10 [-0.88, 0.69]
Prosperini et al. 2015	46.2	7.6	10	39.9	12.3	11	13.5%	0.58 [-0.29, 1.46]
Wuang et al. 2015	-50.4	3.2	52	-54.7	1.8	53	16.9%	1.65 [1.20, 2.09]
Zimmermann et al. 2014	-275	75.8	20	-272	41.7	19	15.6%	-0.05 [-0.68, 0.58]
Subtotal (95% CI)			**124**			**126**	**100.0%**	**0.57 [-0.05, 1.19]**
Heterogeneity: Tau² = 0.54; Chi² = 29.48, df = 6 (P < 0.0001); I² = 80%								
Test for overall effect: Z = 1.81 (P = 0.07)								
1.1.3 Executive functions (dual-task performance)								
Hughes et al. 2014	0.02	0.01	10	0.01	0.01	10	8.7%	0.96 [0.02, 1.89]
Hung et al. 2017	10.3	1.8	12	9.7	1.1	13	10.4%	0.39 [-0.40, 1.19]
Kramer et al. 2014	-59	38	21	-75	40	20	12.8%	0.40 [-0.22, 1.02]
Nilsagard et al. 2012	13.3	6.2	41	12.6	6.8	38	15.6%	0.11 [-0.33, 0.55]
Pompeu et al. 2012	26	20.3	16	20.3	19.8	16	11.7%	0.28 [-0.42, 0.97]
Rozental-Iluz et al. 2016	-130.8	67.3	20	-187.5	101.5	19	12.4%	0.65 [0.00, 1.29]
Wuang et al. 2015	-48.3	2.23	52	-51.8	2.98	53	15.8%	1.32 [0.89, 1.74]
Zimmermann et al. 2014	2.42	0.63	20	2.35	0.53	19	12.7%	0.12 [-0.51, 0.75]
Subtotal (95% CI)			**192**			**188**	**100.0%**	**0.53 [0.16, 0.90]**
Heterogeneity: Tau² = 0.18; Chi² = 20.08, df = 7 (P = 0.005); I² = 65%								
Test for overall effect: Z = 2.82 (P = 0.005)								
1.1.4 Perception (visuo-spatial abilities)								
Choi et al. 2014	128.5	11	10	121.3	9.7	10	9.6%	0.66 [-0.24, 1.57]
Franceschini et al. 2013	0.38	0.14	10	0.28	0.18	10	9.7%	0.59 [-0.31, 1.49]
Hung et al. 2017	17.5	0.8	12	17.2	1.1	13	12.6%	0.30 [-0.49, 1.09]
Wuang et al. 2015	71.38	6.65	52	66.2	4.6	53	48.5%	0.90 [0.50, 1.30]
Zimmermann et al. 2014	26.8	11.2	20	23.5	10.8	19	19.7%	0.29 [-0.34, 0.93]
Subtotal (95% CI)			**104**			**105**	**100.0%**	**0.65 [0.37, 0.93]**
Heterogeneity: Tau² = 0.00; Chi² = 3.49, df = 4 (P = 0.48); I² = 0%								
Test for overall effect: Z = 4.57 (P < 0.00001)								

Table 3. Funnel's plot of included studies.



SE: standard error; SMD: standardized mean difference.