



King's Research Portal

DOI:

[10.1016/j.neubiorev.2017.04.011](https://doi.org/10.1016/j.neubiorev.2017.04.011)

Document Version

Publisher's PDF, also known as Version of record

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Stanmore, E., Stubbs, B., Vancampfort, D., de Bruin, E. D., & Firth, J. (2017). The effect of active video games on cognitive functioning in clinical and non-clinical populations: a meta-analysis of randomized controlled trials. *Neuroscience and Biobehavioral Reviews*, 78, 34-43. DOI: 10.1016/j.neubiorev.2017.04.011

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.



Review article

The effect of active video games on cognitive functioning in clinical and non-clinical populations: A meta-analysis of randomized controlled trials

Emma Stanmore^{a,*}, Brendon Stubbs^{b,c}, Davy Vancampfort^{d,e}, Eling D. de Bruin^f, Joseph Firth^g^a Division of Nursing, Midwifery and Social Work, University of Manchester, UK^b Physiotherapy Department, South London and Maudsley NHS Foundation Trust, UK^c Health Service and Population Research Department, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK^d KU Leuven Department of Rehabilitation Sciences, Leuven, Belgium^e KU Leuven Department of Neurosciences, UPC KU Leuven, Belgium^f Department of Health Sciences and Technology, Institute of Human Movement Sciences and Sport, ETH Zürich, Switzerland^g Division of Psychology and Mental Health, University of Manchester, UK

ARTICLE INFO

Keywords:

Physical activity

Exercise

Cognitive impairment

Alzheimer's

Parkinson's disease

Dementia

ABSTRACT

Physically-active video games ('exergames') have recently gained popularity for leisure and entertainment purposes. Using exergames to combine physical activity and cognitively-demanding tasks may offer a novel strategy to improve cognitive functioning. Therefore, this systematic review and meta-analysis was performed to establish effects of exergames on overall cognition and specific cognitive domains in clinical and non-clinical populations. We identified 17 eligible RCTs with cognitive outcome data for 926 participants. Random-effects meta-analyses found exergames significantly improved global cognition ($g = 0.436$, 95% CI = 0.18–0.69, $p = 0.001$). Significant effects still existed when excluding waitlist-only controlled studies, and when comparing to physical activity interventions. Furthermore, benefits of exergames were observed for both healthy older adults and clinical populations with conditions associated with neurocognitive impairments (all $p < 0.05$). Domain-specific analyses found exergames improved executive functions, attentional processing and visuospatial skills. The findings present the first meta-analytic evidence for effects of exergames on cognition. Future research must establish which patient/treatment factors influence efficacy of exergames, and explore neurobiological mechanisms of action.

1. Introduction

Cognition can be broadly defined as the actions of the brain involved in understanding and functioning in our external environment (Hirschfeld and Gelman, 1994). As it is generally accepted that cognition requires multiple mental processes, this broader concept has been theoretically separated into multiple 'cognitive domains' (Hirschfeld and Gelman, 1994). Although definitions vary, and the boundaries between domains often overlap, examples of distinct areas of cognitive functioning include the processes for learning and remembering verbal and spatial information, attentional capacities, response speed, problem-solving and planning (Strauss et al., 2006).

Various neuropsychological tests have been developed as tools for assessing and quantifying an individual's overall cognitive functioning (or 'global cognition') along with their performance within the separable domains of cognition (Strauss et al., 2006). Performance in these

various cognitive tests has been found to be relatively stable over time in healthy adults, and moderately accurate predictors of real-world functioning and occupational performance (Chaytor and Schmitter-Edgecombe, 2003; Hunter, 1986). Furthermore, neuropsychological tests can detect the deficits in cognitive functioning which arise as a consequence of various psychiatric and neurological diseases (Mathuranath et al., 2000; Nuechterlein et al., 2004). For example, people with Parkinson's disease show marked impairments in planning and memory tasks (Dubois and Pillon, 1996), whereas those with schizophrenia have cognitive pervasive deficits, 1–2 standard deviations below population norms, which also predict the severity of disability in this population (Green et al., 2000). Additionally, cognitive abilities decline naturally in almost all people during healthy ageing (Van Hooren et al., 2007). In an ageing population, the functional consequences of cognitive decline may ultimately have a severe social and economic impact. Thus, interventions which improve cognition

* Corresponding author at: Division of Nursing, Midwifery and Social Work, School of Health Sciences, University of Manchester, Jean McFarlane Building, Oxford Road, Manchester, M13 9PL, UK.

E-mail address: emma.stanmore@manchester.ac.uk (E. Stanmore).

<http://dx.doi.org/10.1016/j.neubiorev.2017.04.011>

Received 5 February 2017; Received in revised form 9 March 2017; Accepted 11 April 2017

Available online 23 April 2017

0149-7634/ Crown Copyright © 2017 Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

hold promise for the treatment of psychiatric and neurological diseases, and have positive implications for population health.

Fortunately, interventions which stimulate the brain and/or body can improve cognition, or attenuate decline. For instance, physical exercise has been shown to significantly improve global cognition, along with working memory and attentional processes, in both clinical and healthy populations (Firth et al., 2016; Smith et al., 2010; Zheng et al., 2016). Interventions can also be designed to target cognition directly, as computerized training programs for memory and other functions have been found to provide significant cognitive benefits, at least in the short term (Hill et al., 2017; Melby-Lervåg and Hulme, 2013). Furthermore, ‘gamification’ of cognitive training programs can maximize their clinical effectiveness, as more complex and interesting programs are capable of better engaging patients in cognitively-demanding tasks while also training multiple cognitive processes simultaneously (Anguera et al., 2013).

Previous studies have found that providing both aerobic exercise and cognitive training together may have additive effects, preventing ageing-related cognitive decline more effectively (Shatil, 2013). This may be due to aerobic and cognitive activity stimulating neurogenesis through independent but complementary pathways; as animal studies show that while exercise stimulates cell proliferation, learning tasks support the survival of these new cells (Kempermann et al., 2010), such that combining these two types of training results in 30% more new neurons than either task alone (Fabel et al., 2009).

Rather than delivering aerobic and cognitive training in separate training sessions, recent advances in technology has presented an opportunity for combining physical activity with cognitively-challenging tasks in a single session through ‘exergames’. Exergames are considered as interactive video-games which require the player to produce physical body movements in order to complete set tasks or actions, in response to visual cues (Oh and Yang, 2010). Common examples include the ‘Nintendo Wii’ (along with ‘Wii Fit’ or ‘Wii Sports software’) or the ‘Microsoft Xbox Kinect’. Additionally, virtual reality systems which use exercise bikes and/or treadmills as a medium for players to interact with three-dimensional worlds have also been developed to provide immersive training experiences (Sinclair et al., 2007).

Along with their popular usage for leisure and entertainment, there is growing interest in the application of exergame systems to improve clinical outcomes. Recent systematic reviews and meta-analyses of this growing literature have provided preliminary evidence that exergames can improve various health-related outcomes, including reducing childhood obesity, improving balance and falls risk factors in elderly adults, facilitating functional rehabilitation in people with parkinson’s disease, and even reduce depression (Barry et al., 2014; Li et al., 2016; van’t Riet et al., 2014). However, the effects of exergames on cognitive functioning have not been systematically reviewed, despite many individual studies in this area.

Therefore, the aim of this study was to systematically review all existing trials of exergames for cognition, and apply meta-analytic techniques to establish the effects of exergames on global cognition along with individual cognitive domains. We also sought to (i) examine the effects of exergames on cognition in healthy and clinically-impaired populations, and (ii) investigate if the effects of exergames differed from those of aerobic exercise alone, by comparing exergames to traditional physical activity control conditions.

2. Methods

This meta-analysis followed the PRISMA statement (Moher et al., 2009) to ensure comprehensive and transparent reporting of methods and results.

2.1. Search strategy

An electronic database search of Cochrane Central Register of Controlled Trials, Health Technology Assessment Database, Allied and Contemporary Medicine, Embase, Health Management Information Consortium, MEDLINE and PsycINFO was conducted on 4th January 2017. A search algorithm was developed to identify all RCTs assessing the effects of exergames and similar technologies on cognitive functioning. The terms used in the algorithm are presented in Supplement 1. The reference lists of retrieved articles were also searched and a further search of Google Scholar was also conducted using the same keywords to identify any additional relevant articles.

2.2. Selection criteria

Only English-language research articles published in peer-reviewed journals were included. No restrictions were placed on populations studied or sample type. For the purpose of this review, exergames were defined as any video game for which required upper- or lower-body physical activity for user interaction. Video games controlled entirely via joysticks or handheld controllers were not classified as exergames. Eligible studies were randomized controlled trials (RCTs) which compared the effects of exergame interventions to non-exergame control conditions on performance in untrained cognitive tasks (i.e. performance in cognitive tasks which varied from those directly practiced within the exergame itself). This includes clinically-validated measures of global cognition, or specific tests of individual domains of cognitive functioning. Studies which combined exergaming with other therapeutic aspects were also eligible for inclusion, provided that (a) the exergame was identified as a primary component of a multi-modal intervention, and (b) the intervention dedicated as much/more time to the exergame component as any other aspect of the intervention. Single-session studies which examined acute effects of exergames on cognitive functioning were excluded from this review.

2.3. Data extraction

Articles were screened for eligibility by two independent reviewers (JF and BS). Disagreements were resolved through discussion until consensus was reached. Where further information or study data was required to determine eligibility or for meta-analyses, the corresponding authors of respective articles were contacted twice over the period of 1 month to request this. A systematic tool was used to extract the following data from each study:

(i) Primary outcome – Global cognition: This was defined as total change in any clinically-validated measures of overall cognitive functioning following an exergame intervention (or control condition). Where the total change in an overall measure of cognition was not reported, a composite change score was calculated as a combined average of the mean change (and variance) across all individual cognitive outcomes/tasks reported in the study. This method for calculating overall changes in cognition has widely been applied in previous meta-analyses examining cognitive outcomes of various training interventions (Hill et al., 2017).

(ii) Secondary outcomes – Individual cognitive domains: Effects of exergames in individual cognitive domains were examined with respect to the categories established by accepted neuropsychological domains (Strauss et al., 2006). Where cognitive tasks used in the studies were not listed by accepted neuropsychological categorization, the most suitable cognitive domain was determined through discussion between two reviewers (JF and BS) and consulted with senior reviewer (ES) for agreement to be reached. Executive functioning was examined as an individual domain, with subdomain analyses performed for individual executive functions of working memory, inhibitory control, task switching/flexibility and reasoning/problem solving. Other cognitive domains included visuospatial skills, verbal learning and memory, visual learn-

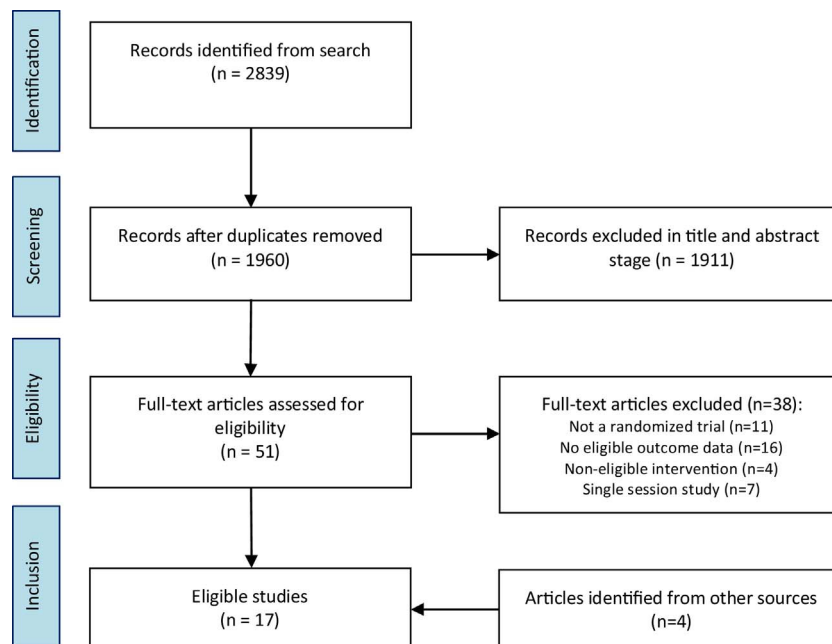


Fig. 1. PRISMA flow diagram of systematic search and study selection.

ing and memory, attention and processing speed (Strauss et al., 2006).

(iii) Potential moderators: Data on factors which may influence the effect size of exercise interventions were also extracted from each study, including sample characteristics (clinical population and status, age, gender distribution), exergame intervention characteristics (intervention length in weeks, number of sessions per week, session duration and total number of sessions during intervention) and study design (control condition used and trial quality).

2.4. Statistical analyses

Meta-analyses were performed in Comprehensive Meta-Analysis 2.0 (Borenstein et al., 2005). To account for the expected heterogeneity between studies, a random-effects model was applied (DerSimonian and Kacker, 2007). A pooled effect size (ES) of exergame interventions was calculated as Hedges' G for both global cognition and each individual cognitive domain, using the mean difference in change scores (and standard deviations) between exergame and control conditions. Where studies measured changes within an individual cognitive domain using more than task, the baseline-to-post-training change across all measures used were pooled to calculate an average change score for the respective domain. If raw means and standard deviations were not reported, the Hedges' G was computed from F- or t-values. Computed effect sizes were classified as small (< 0.2), moderate ($> 0.2, < 0.8$) or large (> 0.8). Statistical heterogeneity between studies was quantified using Cochran's Q and I^2 values; providing estimates of the degree of heterogeneity resulting from between-study variance, rather than by chance. Each study was also individually examined for risk of bias using the Cochrane's Collaboration "Risk of Bias Tool" (Higgins et al., 2011), which assesses six aspects of trial methodology (allocation sequence concealment, sequence generation, blinding of participants and personnel, blinding of outcome assessment, selective outcome reporting incomplete outcome data) that could introduce bias into study findings. For the primary analyses, funnel-plots were generated to inspect for the possibility of publication bias influencing the results. Furthermore, Begg & Mazumdar's test was applied to quantify the risk of publication bias, and where this was found to be significant, a 'Fail-Safe N' (Orwin, 1983) was calculated to determine the number of unpublished null studies which would invalidate the findings (i.e. the number of unpublished null studies required to cause $p > 0.05$). We also

performed sensitivity analyses to assess if comparable effects were still observed when only including RCTs which used complete outcome data (i.e. from intention-to-treat (ITT) or full set analyses) and following the removal of studies at moderate/high risk of bias.

The impact of categorical moderators, such as study population and comparator type, were assessed using subgroup analyses to generate pooled effect sizes of exergames in comparison to active control conditions, and in samples with/without clinical conditions associated with neuropsychological impairments. The relationship between continuous moderators and effect sizes were explored with meta-regression analyses for sample and treatment characteristics which may impact upon the cognitive outcomes of exergame interventions. Patient moderators included age and gender. Treatment moderators considered were intervention length (weeks), sessions per week, session length (minutes) and total number of exergame sessions over the intervention.

3. Results

3.1. Search results

The search returned 2839 results, reduced to 1960 after duplicates were removed. A further 1911 articles were excluded after reviewing the titles and abstracts for eligibility. Full versions were retrieved for 51 articles, of which 13 articles were eligible for inclusion. Four additional eligible articles were retrieved from an additional search of Google Scholar. Thus, a total of 17 unique studies with independent samples were included in this review. The article screening process is detailed in Fig. 1.

3.2. Included studies and participant details

Study details and intervention summaries are displayed in Table 1. Seven studies were conducted in the United States, four in Switzerland, and one each in Brazil, Australia, China, South Korea and Turkey, and one across five different countries. Eligible outcome data was available from a total of 926 participants across the 17 studies; 464 were assigned to exergame intervention, 462 to control conditions. The mean age was 69 years (range = 17–85 years) and 49.3% were male. The majority of studies were conducted in healthy older adults ($N = 9$). Six studies were conducted in clinical samples associated with cognitive impair-

Table 1
Details of included studies.

	Sample characteristics				Exergame Intervention			Study Details		
	Exergame n =	Control n =	Population	Mean age	% male	Session content	Weeks + Sessions	Comparator	Cognitive outcomes	Risk of Bias ^a
Ackerman et al. (2010)	39	39	Healthy older adults	60.7	53.8	60 min of completing 15 different interactive 'brain training' tasks using the Nintendo Wii system and Wii Big Brain Academy software.	4 weeks 5 per week	Educational reading sessions	- Executive function(s) - Processing speed - Language - Visuospatial skills	Unclear
Anderson-Hanley et al. (2012)	38	41	Healthy older adults	75.7	78.5	45 min of interactive 'Cybercycle' video game; pedalling on stationary bike to outpace ghost-racers around a virtual track.	12 weeks 3 per week	Stationary cycling	- Executive function(s) - Processing speed - Verbal memory - Spatial memory	High
Barcelos et al. (2015)	8	9	Healthy older adults	84.8	60	20–45 min of interactive, cognitively demanding cycling: pedalling around virtual track while collecting correspondingly-coloured tokens.	12 weeks 3–5 per week	Stationary cycling	- Language - Executive function(s)	High
Chan et al. (2010)	12	15	Schizoph- renia	66.1	66.0	30 min of exergame co-ordination training, playing catching and throwing games in VR environment.	5 weeks 2 per week	Waitlist	- Global score - Processing speed - Verbal memory	Unclear
Eggenberger et al., 2015	24	22 25	Healthy older adults	78.8	35.2	60 min of interactive dance video game, performing stepping motions on a pressure-sensitive dance platform in response to visual cues.	24 weeks 2 per week	Memory training or Treadmill	- Language - Executive function(s) - Attention - Processing speed	Moderate
Eggenberger et al. (2016)	19	14	Healthy older adults	74.9	36.0	30 min of interactive dance video game, performing stepping motions on a pressure-sensitive dance platform in response to visual cues.	8 weeks 3 per week	Balance and stretching training	- Global score - Executive function(s)	Moderate
Hughes et al. (2014)	10	10	Mild cognitive impairment	77.4	30	75 min of practicing interactive sports games using the 'Wii Sports' software on the Nintendo Wii, with tournaments between participants to increase motivation.	24 weeks 1 per week	Health education sessions	- Processing speed - Global score - Executive function(s)	Unclear
Kimby et al. (2015)	16	17	Schizoph- renia	36.9	64	60 min of whole-body aerobic training using Microsoft Kinect's "Your Shape: Fitness Evolved" software, along with treadmill and elliptical training.	12 weeks 3 per week	Waitlist	- Processing speed - Global score - Executive function(s)	Low
Maillot et al. (2012)	15	15	Healthy older adults	73.5	15.6	60 min of paired training using the Nintendo Wii and Balance Board for physically-demanding games: Wii Sports, Wii Fit and Wii Olympic Games.	12 weeks 2 per week	Waitlist	- Processing speed - Verbal memory - Spatial memory - Executive function(s) - Processing speed - Spatial memory - Visuospatial skills	Unclear
Mirelman et al. (2016)	146	136	Parkinson's, MCI, Recent falls	73.8	64.5	45 min of walking on treadmill in virtual environment; requiring continual stride adjustment in response to obstacles, pathway changes and distractors	6 weeks 3 per week	Treadmill walking	- Executive function(s) - Attention	Moderate
Park et al., (2015)	36	36	Healthy older adults	73.5	6.0	30 min of conventional exercise then 20 min of VR kayaking, requiring co-ordination and physical effort to paddle in a 3D lake.	6 weeks 2 per week	Physical exercise	- Global score	Low
Pompeu et al. (2012)	16	16	Parkinson's disease	67.4	53.0	30 min of conventional exercise then 30 min of aerobic fitness	7 weeks	Balance training and	- Global score	Low

(continued on next page)

Table 1 (continued)

	Sample characteristics				Exergame Intervention			Study Details		
	Exergame n =	Control n =	Population	Mean age	% male	Session content	Weeks + Sessions	Comparator	Cognitive outcomes	Risk of Bias ^a
Schatin et al. (2016)	13	14	Healthy older adults	80	55.5	exergaming using the 'Wii Fit' software. 30 min of interactive dance video game, performing stepping motions on a pressure-sensitive dance platform in response to visual cues.	2 per week 8 weeks 3 per week	exercise Balance training	- Executive function(s) - Processing speed function(s)	Moderate
Schoene et al. (2013)	15	17	Healthy older adults	77.5	-	15–20 min of interactive dance video game, performing stepping motions on a pressure-sensitive dance platform in response to visual cues.	8 weeks 3 per week	Waitlist	- Executive function(s)	Moderate
Simsek et al. (2015)	20	22	Sub-acute stroke	58.0	69.0	45–60 min of 5 interactive video games for upper limbs and balance on the Nintendo Wii, using the Wii Fit and Wii Sports software.	10 weeks 3 per week	Balance, gait and strength training	- Global score	High
Staniano et al. (2012)	18	18	Healthy adolescent	16.5	42.6	30 min of co-operative or competitive activity using the Nintendo Wii "EA Sports Active" whole body workout software.	10 weeks 1 per week	Waitlist	- Executive function(s)	Unclear
Zimmerman et al. (2014)	19	20	Parkinson's disease	66.3	64	40 min of seated interactive gaming using Wii Sports Resort, requiring movement co-ordination and upper-body activity.	4 weeks 3 per week	'CogniPlus' cognitively-demanding tasks	- Executive function(s) - Processing speed - Verbal memory - Visuospatial skills	Moderate

^a Assessed with 'Cochrane Risk of Bias' tool.

ments, including Parkinson's disease (N = 2), mild cognitive impairment (N = 1), sub-acute stroke (N = 1), schizophrenia (N = 2). One study was conducted in healthy adolescents, and one in a mixed clinical and non-clinical sample.

Exergame interventions lasted an average of 10 weeks (range = 4–24 weeks), with an average of 3.2 sessions per week, ranging from 15 to 60 min of exergaming per session. Seven studies used the Nintendo Wii exergaming system with a variety of software packages (Ackerman et al., 2010; Hughes et al., 2014; Maillot et al., 2012; Pompeu et al., 2011; Şimşek and Çekok, 2016; Staiano et al., 2012; Zimmermann et al., 2014), four used interactive dance games with pressure-sensitive dance platforms used to response to visual cues for foot movements (Eggenberger et al., 2016; Eggenberger, 2015; Schattin et al., 2016; Schoene et al., 2013), three used interactive cycling/treadmill training wherein participants completed various tasks or avoided obstacles while pedaling/walking around virtual tracks (Anderson-Hanley et al., 2016; Barcelos et al., 2015; Mirelman et al., 2016) one used virtual-reality kayaking requiring coordinated upper-body movement to navigate virtual lakes/ivers (Park and Yim, 2016), one used the Microsoft Kinect system to deliver an aerobic exercise routine (Kimhy et al., 2015), and one used interactive co-ordination training involving throwing/catching games in a virtual environment (Chan et al., 2010). Control conditions were waitlist/usual treatment (N = 5), aerobic exercise (N = 5), balance, stretching and strengthening exercises (N = 4) and health education sessions, reading, cognitive remediation or memory training (all N = 1).

Risk of bias assessments found that all but two trials (Kimhy et al., 2015; Pompeu et al., 2011) had either introduced sources of bias through study design/conduct, or reported insufficient details to rule out potential bias. Only seven studies had collected outcome data from all randomized participants or applied ITT analyses which sufficiently accounted for study attrition. Full results of the bias assessments for each of the individual studies are displayed in Supplement 2.

3.3. Effects of exergames on cognitive functioning

The effect of exergame interventions on global cognition is displayed in Fig. 2 (N = 17, n = 926). This shows exergame interventions improved overall cognitive functioning significantly more than control conditions (g = 0.436, 95% CI = 0.18–0.69, p = 0.001), although there was significant heterogeneity among study findings (Q = 47.8, p = 0.001, I² = 66.5%). The risk of publication bias was not statistically significant (Kendall's t = 0.32, p = 0.07, Supplement 3). A fail-safe N was also calculated finding that 112 unpublished null studies would be required to exist for the observed p-value to exceed 0.05.

A sensitivity analysis was performed on the RCTs which used time- and attention-matched control conditions i.e. excluding studies with only waitlist/usual treatment comparisons (see Table 2). Among these rigorously controlled RCTs (N = 12, n = 758), the effect size was slightly smaller, but still statistically significant (g = 0.363, 95% CI = 0.06–0.67, p = 0.020) with no significant publication bias but high heterogeneity between studies (Kendall's t = 0.38, p = 0.09, Q = 39.5, p = 0.001, I² = 72.1%).

To examine if the benefits exergames extend beyond regular exercise, a further subgroup analysis was performed to examine effects on overall cognition in comparison to physically-active control conditions. Results are displayed in Fig. 3. Moderate cognitive benefits were observed from exergame interventions in comparison to physical activity alone (N = 9, n = 632, g = 0.435, 95% CI = 0.04–0.83, p = 0.03); again without publication bias but significant heterogeneity (Kendall's t = 0.19, p = 0.47, Q = 36.7, p = 0.001, I² = 78.2%).

3.4. Factors associated with intervention efficacy

Subgroup analyses were performed to examine effects of exergames on overall cognitive functioning in (i) non-clinical/healthy populations,

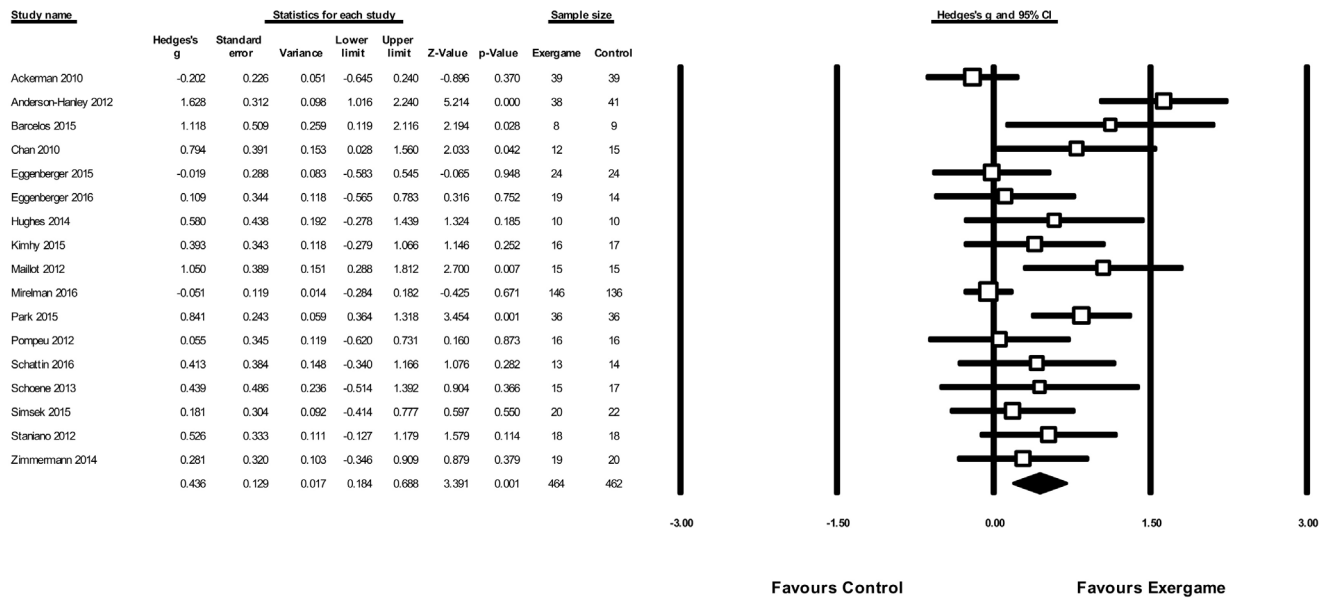


Fig. 2. Meta-analysis of exergames effects on global cognition in comparison to control conditions. Box size represents study weighting. Diamond represents overall effect size and 95% confidence intervals.

and (ii) clinical conditions associated with cognitive impairments. Assessments for publication bias found no indication for any of the subgroup analyses (all $p > 0.1$). Exergame interventions had moderately-large positive effects on cognition in non-clinical samples ($N = 10$, $n = 403$, $g = 0.565$, 95% CI = 0.17–0.96, $p = 0.005$, $Q = 32.8$, $I^2 = 72.5$). Significant benefits of exergames were also observed in the subgroup of trials which studied only healthy older adults ($N = 9$, $n = 415$, $g = 0.573$, 95% CI = 0.14–1.01, $p = 0.01$, $Q = 32.8$, $I^2 = 75.6$). Effects observed in clinical populations were smaller, but still statistically significant ($N = 6$, $n = 193$, $g = 0.34$, 95% CI = 0.06–0.62, $p = 0.017$) with no indication of heterogeneity affecting results ($Q = 2.66$, $p = 0.75$, $I^2 = 0.00\%$).

Meta-regression analyses found no significant associations between effect size and sample characteristics (age, gender distribution) or

intervention details (weeks in length, session length, session frequency) (all $p \geq 0.1$). A post-hoc subgroup analysis was also conducted to compare interventions which were 12 weeks or longer ($N = 6$, $n = 226$, mean length = 16 weeks) to those which were less than 12 weeks long ($N = 11$, $n = 700$, mean length = 7 weeks) (Table 2). Exergame interventions ≥ 12 weeks long had moderately-to-large effects on cognition ($g = 0.759$, 95% C.I. = 0.23–1.29, $p = 0.005$), whereas those which were > 12 weeks had only a small effect ($g = 0.255$, 95% C.I. = 0.02–0.49, $p = 0.03$). Comparative analyses found only a trend-level difference between these two groups ($p = 0.086$).

Table 2
Meta-analyses examining the effect of exergame interventions on cognitive functioning.

	Sample		Meta-analysis			Heterogeneity			
	Studies	Total n	Hedge's g	95% CI	P value	Q-value	P value	I^2	
Global cognition	17	926	0.436	0.18	0.69	0.001	47.8	0.001	66.5
Waitlist controls excluded	12	768	0.363	0.06	0.67	0.020	39.5	0.001	72.1
Compared to physical activity	8	632	0.435	0.04	0.83	0.030	36.7	0.001	78.2
ITT analyses only	7	554	0.554	0.08	1.03	0.023	33.2	0.001	81.9
Clinical populations	6	193	0.340	0.06	0.62	0.017	2.66	0.752	0.00
Non-clinical populations	10	451	0.565	0.17	0.96	0.005	32.8	0.001	72.5
Healthy older adults	9	415	0.573	0.14	1.01	0.010	32.8	0.001	75.6
Length: Less than 12 weeks	11	700	0.255	0.02	0.49	0.030	18.4	0.048	45.7
Length: 12 or more weeks	6	226	0.759	0.23	1.29	0.005	16.3	0.006	68.4
Individual Cognitive Domains									
Executive functions: all	13	745	0.256	0.002	0.510	0.048	29.8	0.003	59.7
Task-switching/flexibility	8	245	0.348	0.002	0.694	0.049	14.1	0.05	51.1
Inhibitory control	5	139	0.900	0.48	1.33	< 0.001	5.05	0.28	20.8
Working Memory	4	171	0.032	-0.26	0.33	0.831	2.55	0.64	0.00
Reasoning and problem solving	3	134	0.393	-0.74	1.52	0.495	17.7	< 0.01	88.7
Other domains									
Attentional processing speed	11	688	0.298	0.03	0.56	0.027	24.1	0.01	58.5
Verbal learning and memory	4	171	0.526	-0.07	1.13	0.085	7.33	0.06	59.7
Spatial learning and memory	3	135	1.230	-0.93	3.39	0.264	55.4	< 0.01	96.4
Visuospatial skills	4	226	0.345	0.03	0.66	0.033	4.21	0.24	28.7
Language	3	184	0.570	-0.65	1.79	0.360	28.5	< 0.01	93.0

Notes: ITT, intention to treat. BOLD represents statistically significant benefit of exergames interventions over control conditions.

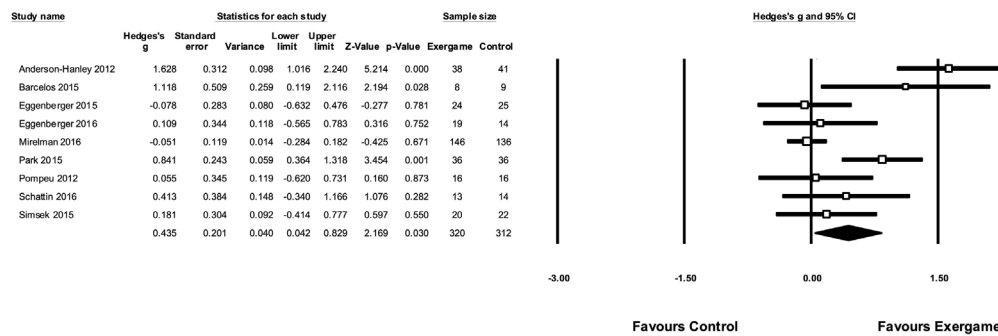


Fig. 3. Meta-analysis showing effects of exergame interventions on global cognition in comparison to physically-active control conditions. Box size represents study weighting. Diamond represents overall effect size and 95% confidence intervals.

3.5. Effects of exergames on individual cognitive domains

We also examined the effects of exergame interventions on individual domains of cognitive functioning, as recognized by established neurocognitive categorization (Strauss et al., 2006). Effects across all domains are displayed in Table 2. The most widely assessed was 'executive functioning' (N = 13, n = 735), which was improved by exergame interventions significantly more than control conditions ($g = 0.256$, 95% CI = 0.002–0.510, $p = 0.048$) but with evidence of heterogeneity ($Q = 29.8$, $p = 0.003$, $I^2 = 59.7\%$). When examining effects on individual executive functions, large positive effects of exergames were observed for inhibitory control (N = 5, n = 139, $g = 0.90$, 95% CI = 0.48–1.33, $p < 0.001$) without heterogeneity between studies ($Q = 5.05$, $p = 0.28$, $I^2 = 20.8$) and task-switching/flexibility (N = 8, n = 245, $g = 0.388$, 95% CI = 0.002–0.694, $p = 0.049$, $Q = 14.1$, $p = 0.05$, $I^2 = 51.1$). Fewer studies examined working memory (N = 4, n = 171) and reasoning/problem solving (N = 3, n = 134) and no effects were found for these executive functions.

Among other domains of cognitive functioning, exergames significantly improved only attentional processing (N = 11, n = 688, $g = 0.298$, 95% CI = 0.03–0.56, $p = 0.027$) and visuospatial skills (N = 4, n = 226, $g = 0.345$, 95% CI = 0.03–0.66, $p = 0.033$). No significant effects of exergames were found for verbal learning/memory or spatial learning/memory (all $p > 0.1$).

4. Discussion

4.1. Effects of exergames on overall cognition

To the best of our knowledge, the current meta-analysis is the first to examine the effects of exergames on cognitive functioning in both clinical and non-clinical populations. Seventeen RCTs with outcome data from 926 participants were eligible for inclusion. Pooled effect-sizes from all cognitive outcomes found that exergame interventions have moderately-large positive effects (ES = 0.44) on global cognition in comparison to control conditions (Fig. 2). Although there was evidence of heterogeneity between studies, there was no significant publication bias, and significant benefits of exergames were still observed when including only the RCTs with time- and attention-matched control conditions (Table 2). Subgroup analyses also found that exergames had significant effects on cognition in both clinical and non-clinical samples.

Analyses within individual domains of cognition found most evidence for the benefits of exergames for 'executive functioning', specifically for improving inhibitory control (ES = 0.9) and cognitive flexibility (ES = 0.35). Improvements in executive functioning may be particularly beneficial outcomes of exergaming for clinical populations, such as those with mild cognitive impairment or Alzheimer's disease, as declines in these specific areas of cognition are strongly correlated with functional disability and disease progression (Marshall et al., 2011). Thus novel interventions, such as exergames, which can target these areas to attenuate deterioration and sustain these capacities offer promise to these patient groups (Hughes et al., 2014). Furthermore,

as executive functioning generally declines with ageing, which impedes on social and physical functioning in these populations also, exergames may present a feasible and acceptable strategy for maintaining health and independence in older age (Carlson et al., 1999; Grigsby et al., 1998).

Whereas significant benefits of exergames were also observed for visuospatial skills, attention and processing speed, no effects were found on language, spatial learning and memory or verbal learning and memory. However, further research is required to establish whether these observations are genuinely the result of domain-specific effects of exergaming within the brain, or if the null findings can simply be ascribed to the fewer number of studies reporting data for the non-significant analyses.

4.2. Effects of exergames in comparison to physical activity

Along with improving cognition more than usual care, exergames outperformed physically-active control conditions, such as stationary cycling or stretch and balance training. Subgroup analyses of the nine RCTs with comparison conditions which administered equal amounts of physical activity found moderately greater effects on cognition from exergames in comparison to aerobic exercise alone ($ES = 0.44$). It has been previously established that physical exercise can produce cognitive improvements, along with increasing hippocampal volume, in both human and animal experimental studies (Erickson et al., 2011), perhaps due to increased levels of ‘brain-derived neurotrophic factor’ (BDNF), the primary neurotrophic hormone in the human brain which is upregulated in response to exercise (Vaynman et al., 2004). It has been further postulated that the additive cognitive benefits observed when combining aerobic exercise with cognitive-demanding (Shatil, 2013) is a result of the complimentary physiological effects these two types of training exert for stimulating and preserving new neurons in the brain (Fabel et al., 2009; Kempermann et al., 2010) – which may also explain the findings of this meta-analysis, as to why exergames outperformed physical activity for cognitive enhancement.

However, there is currently no evidence of exergames outperforming control conditions which demand cognitive (rather than physical) activity, since studies comparing exergames to book reading (Ackerman et al., 2010), memory training (Eggenberger et al., 2015) and cognitive remediation (Zimmerman et al., 2014) found no significant differences in effects on global cognition (Fig. 1). Although these null findings could be ascribed to the limited number of studies examining this, it is equally possible that exergames are no more effective than cognitive training for improving global cognition. Either way, the ‘non-inferiority’ of exergames in comparison to cognitively-demanding control conditions can be considered a positive outcome in itself. Given the known benefits of physical activity for fitness and functionality (Warburton et al., 2006), improving overall well-being (Stewart et al., 1994), reducing falls risk in older age (Chang et al., 2004), and increasing life expectancy through reducing cardio-metabolic risk (Kodama et al., 2013), it could be envisaged that clinical interventions for preventing cognitive decline would favor exergame interventions over sedentary cognitive training, even if the effects of these interventions on cognition itself are equal. However, as technologies for both exergames and standard cognitive training continue to develop, and present new and engaging training systems (e.g. Anguera et al., 2013), unbiased non-inferiority RCTs are required to determine the relative merits and drawbacks of each, and establish prescriptive guidelines for optimal prevention/treatment of cognitive decline.

4.3. Limitations and conclusions

One limitation of this meta-analysis is that we included RCTs which did not use intention-to-treat analyses and those which failed to report complete outcome data from all participants. This introduces the possibility of a ‘survival bias’; whereby perhaps only the participants

who benefit from exergames are retained in the trial, and thus included in final analyses. Therefore, it is possible that the observed main effect is driven by results from only the proportion of participants who can actually adhere to and/or benefit from exergame interventions, and thus does not generalize to the overall population. Nonetheless, a sensitivity analyses of RCTs which did use ITT analyses (or reported full outcome data) found an equally large effect of exergames on cognition (Table 2), although only a minority of the total studies were eligible for this analysis ($N = 7$), which again limits the strength of findings. It should also be considered that variance in participant adherence to the difference interventions could not be accounted for in our analyses (as adherence/engagement variables were insufficiently reported across the eligible studies). This raises the possibility that the significantly greater cognitive improvements observed from exergames in comparison to standard physical activity could simply be due to the novel and game-based nature of exergames engaging participants in greater amounts physical activity, rather than a genuine difference in neuro-physiological response to these alternative interventions. Future studies should aim to determine the differences in participant engagement with exergames, physical activity, and other forms of cognitive training, along with examining the impact that intervention adherence has on cognitive outcomes.

A further limitation is that substantial heterogeneity was found in primary analyses (i.e. significant Cochran’s Q values with high I^2 values). This between-study heterogeneity is unsurprising, given the clear differences between exergame studies in terms of the interventions/control conditions used, populations studied and outcome measures applied. Although this statistical heterogeneity is accounted for in the pooled effect estimated by the random-effects models applied, future research should aim to establish which sample and/or intervention characteristics alter exergame effectiveness. It should also be noted that several of our subgroup analyses with observed significant effects of exergames with little-to-no heterogeneity for (i) the subgroup of studies which used clinical populations, and (ii) specific domains of inhibitory control and visuospatial skill. The moderately large effect size of exergames and p -value of 0.001 in the main analysis adds further weight to the overall findings.

A final limitation is that besides examining the frequency, time and type of the interventions, we could not examine how exergame efficacy was related to the physical intensity of training sessions, due to inadequacies and inconsistencies in the way this was reported in included studies. Future studies should apply the ‘FITT’ components (frequency, intensity, time and type) in both the design and reporting of exergame intervention trial, in order to enable optimal consideration of training components such as specificity, overload, progression, initial values, reversibility and diminishing returns (Knols et al., 2016).

Despite the limitations, this systematic review of RCTs provides the first meta-analytic findings of cognitive benefits from exergame interventions, a rapidly growing area of new research interest. Overall, the existing evidence indicates exergames are a promising new development for both treating cognitive impairments in clinical populations and reducing the decline associated with ageing. Furthermore, the domain-specific effects infer potential for developing exergames which target individual cognitive domains, in order to resolve or re-train isolated deficits, in a personalized medicine approach for the treatment of various neurodegenerative conditions which can impair particular areas of cognition. The current popularity of exergames for leisure/entertainment purposes attests to their acceptability, especially for the impending population of older adults familiar with video-game play. Considering that these technologies will almost certainly continue to improve in coming years, particularly with increased access and usability of virtual-reality gaming systems (Kooiman and Sheehan, 2015), exergames present a novel and scalable intervention which can be readily personalized and administered at relatively low-cost. Given the potential benefits, ongoing research is required to establish the neurobiological mechanisms and effective components of exergames for

cognition, and apply this understanding in the development of evidence-based exergame interventions.

Acknowledgments

We would first like to acknowledge the assistance of both Dr. Anat Mirelman (Sourasky Medical Center, Tel Aviv, Israel) and Dr. Patrick Eggenberger (Swiss Federal Institute of Technology, Zurich, Switzerland) for kindly agreeing to share their additional study data required for the meta-analysis. JF is funded by an MRC Doctoral Training Grant. DV is funded by the Research Foundation – Flanders (FWO-Vlaanderen). BS is funded by Stanley Medical Research Institute Grant 13T-006. ES receives funding from Innovate UK GrantR119047.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.neubiorev.2017.04.011>.

References

- Ackerman, P.L., Kanfer, R., Calderwood, C., 2010. Use it or lose it? Wii brain exercise practice and reading for domain knowledge. *Psychol. Ageing* 25, 753–766.
- Anderson-Hanley, C., Maloney, M., Barcelos, N., Striegnitz, K., Kramer, A., 2016. Neuropsychological benefits of neuro-exergaming for older adults: a pilot study of an interactive physical and cognitive exercise system (iPACESTM). *J. Ageing Phys. Act.* 1–32.
- Anguera, J.A., Boccanfuso, J., Rintoul, J.L., Al-Hashimi, O., Faraji, F., Janowich, J., Kong, E., Larraburo, Y., Rolfe, C., Johnston, E., 2013. Video game training enhances cognitive control in older adults. *Nature* 501, 97–101.
- Barcelos, N., Shah, N., Cohen, K., Hogan, M.J., Mulkerin, E., Arciero, P.J., Cohen, B.D., Kramer, A.F., Anderson-Hanley, C., 2015. Aerobic and Cognitive Exercise (ACE) pilot study for older adults: executive function improves with cognitive challenge while exergaming. *J. Int. Neuropsychol. Soc.* 21, 768–779.
- Barry, G., Galna, B., Rochester, L., 2014. The role of exergaming in Parkinson's disease rehabilitation: a systematic review of the evidence. *J. Neuroeng. Rehabil.* 11 (1) (no pagination).
- Borenstein, M., Hedges, L., Higgins, J., Rothstein, H., 2005. *Comprehensive Meta-analysis Version 2*. Biostat, Englewood, NJ, pp. 104.
- Carlson, M.C., Fried, L.P., Xue, Q.-L., Bandeen-Roche, K., Zeger, S.L., Brandt, J., 1999. Association between executive attention and physical functional performance in community-dwelling older women. *J. Gerontol. Ser. B: Psychol. J. Soc. Sci.* 54, S262–S270.
- Chan, C.L., Ngai, E.K., Leung, P.K., Wong, S., 2010. Effect of the adapted virtual reality cognitive training program among Chinese older adults with chronic schizophrenia: a pilot study. *Int. J. Geriatr. Psychiatry* 25, 643–649.
- Chang, J.T., Morton, S.C., Rubenstein, L.Z., Mojica, W.A., Maglione, M., Sutton, M.J., Roth, E.A., Shekelle, P.G., 2004. Interventions for the prevention of falls in older adults: systematic review and meta-analysis of randomised clinical trials. *BMJ* 328, 680.
- Chaytor, N., Schmitter-Edgecombe, M., 2003. The ecological validity of neuropsychological tests: a review of the literature on everyday cognitive skills. *Neuropsychol. Rev.* 13, 181–197.
- DerSimonian, R., Kacker, R., 2007. Random-effects model for meta-analysis of clinical trials: an update. *Contemp. Clin. Trials* 28, 105–114.
- Dubois, B., Pillon, B., 1996. Cognitive deficits in Parkinson's disease. *J. Neurol.* 244, 2–8.
- Eggenberger, P.S., Schumacher, V., Angst, M., Theill, N., de Bruin, E.D., 2015. Does multicomponent physical exercise with simultaneous cognitive training boost cognitive performance in older adults? A 6-month randomized controlled trial with a 1-year follow-up. *Clin. Interv. Ageing* 10, 1335–1349.
- Eggenberger, P., Wolf, M., Schumann, M., de Bruin, E.D., 2016. Exergame and balance training modulate prefrontal brain activity during walking and enhance executive function in older adults. *Front. Ageing Neurosci.* 8.
- Erickson, K.I., Voss, M.W., Prakash, R.S., Basak, C., Szabo, A., Chaddock, L., Kim, J.S., Heo, S., Alves, H., White, S.M., 2011. Exercise training increases size of hippocampus and improves memory. *Proc. Natl. Acad. Sci.* 108, 3017–3022.
- Fabel, K., Wolf, S., Ehninger, D., Babu, H., Galicia, P., Kempermann, G., 2009. Additive effects of physical exercise and environmental enrichment on adult hippocampal neurogenesis in mice. *Front. Neurosci.* 3, 2.
- Firth, J., Stubbs, B., Rosenbaum, S., Vancampfort, D., Malchow, B., Schuch, F., Elliott, R., Nuechterlein, K.H., Yung, A.R., 2016. Aerobic exercise improves cognitive functioning in people with schizophrenia: a systematic review and meta-analysis. *Schizophr. Bull.* sbw115.
- Green, M.F., Kern, R.S., Braff, D.L., Mintz, J., 2000. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the right stuff? *Schizophr. Bull.* 26 (1), 119–136.
- Grigsby, J., Kaye, K., Baxter, J., Shetterly, S.M., Hamman, R.F., 1998. Executive cognitive abilities and functional status among community-dwelling older persons in the San Luis Valley Health and Ageing Study. *J. Am. Geriatr. Soc.* 46, 590–596.
- Higgins, J.P., Altman, D.G., Gøtzsche, P.C., Jüni, P., Moher, D., Oxman, A.D., Savović, J., Schulz, K.F., Weeks, L., Sterne, J.A., 2011. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 343, d5928.
- Hill, N.T., Mowszowski, L., Naismith, S.L., Chadwick, V.L., Valenzuela, M., Lampit, A., 2017. Computerized cognitive training in older adults with mild cognitive impairment or dementia: a systematic review and Meta-Analysis. *Am. J. Psychiatry* 174 (9), 329–334 (appiajp201616030360).
- Hirschfeld, L.A., Gelman, S.A., 1994. *Mapping the Mind: Domain Specificity in Cognition and Culture*. Cambridge University Press.
- Hughes, T.F., Flatt, J.D., Fu, B., Butters, M.A., Chang, C.C.H., Ganguli, M., 2014. Interactive video gaming compared with health education in older adults with mild cognitive impairment: a feasibility study. *Int. J. Geriatr. Psychiatry* 29, 890–898.
- Hunter, J.E., 1986. Cognitive ability, cognitive aptitudes, job knowledge, and job performance. *J. Vocat. Behav.* 29, 340–362.
- Kempermann, G., Fabel, K., Ehninger, D., Babu, H., Leal-Galicia, P., Garthe, A., Wolf, S., 2010. Why and how physical activity promotes experience-induced brain plasticity. *Front. Neurosci.* 4, 189.
- Kimhy, D., Vakhrusheva, J., Bartels, M.N., Armstrong, H.F., Ballon, J.S., Khan, S., Chang, R.W., Hansen, M.C., Ayanruoh, L., Lister, A., Castren, E., Smith, E.E., Sloan, R.P., 2015. The impact of aerobic exercise on brain-derived neurotrophic factor and neurocognition in individuals with schizophrenia A single-blind, randomized clinical trial. *Schizophr. Bull.* 41, 859–868.
- Knols, R.H., Vanderhenst, T., Verra, M.L., de Bruin, E.D., 2016. Exergames for patients in acute care settings: systematic review of the reporting of methodological quality, FITT components, and program intervention details. *Games Health J.* 5, 224–235.
- Kodama, S., Tanaka, S., Heianza, Y., Fujihara, K., Horikawa, C., Shimano, H., Saito, K., Yamada, N., Ohashi, Y., Sone, H., 2013. Association between physical activity and risk of all-cause mortality and cardiovascular disease in patients with diabetes. *Diabetes Care* 36, 471–479.
- Kooiman, B.J., Sheehan, D.P., 2015. Interacting with the past, present, and future of exergames: at the beginning of a new life cycle of video games? *Soc. Leisure* 38, 55–73.
- Li, J., Theng, Y.-L., Foo, S., 2016. Effect of exergames on depression: a systematic review and meta-analysis. *Cyberpsychol. Behav. Soc. Networking* 19, 34–42.
- Maillot, P., Perrot, A., Hartley, A., 2012. Effects of interactive physical-activity videogame training on physical and cognitive function in older adults. *Psychol. Ageing* 27, 589–600.
- Marshall, G.A., Rentz, D.M., Frey, M.T., Locascio, J.J., Johnson, K.A., Sperling, R.A., Initiative, A.S.D.N., 2011. Executive function and instrumental activities of daily living in mild cognitive impairment and Alzheimer's disease. *Alzheimer's Dement.* 7, 300–308.
- Mathuranath, P., Nestor, P., Berrios, G., Rakowicz, W., Hodges, J., 2000. A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology* 55, 1613–1620.
- Melby-Lervåg, M., Hulme, C., 2013. Is working memory training effective? A meta-analytic review. *Dev. Psychol.* 49, 270.
- Mirelman, A., Rochester, L., Maidan, I., Del Din, S., Alcock, L., Nieuwhof, F., Rikkert, M.O., Bloem, B.R., Pelosin, E., Avanzino, L., Abbruzzese, G., Dockx, K., Bekkers, E., Giladi, N., Nieuwboer, A., Hausdorff, J.M., 2016. Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial. *Lancet* 388, 1170–1182.
- Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 6, pe1000097.
- Nuechterlein, K.H., Barch, D.M., Gold, J.M., Goldberg, T.E., Green, M.F., Heaton, R.K., 2004. Identification of separable cognitive factors in schizophrenia. *Schizophr. Res.* 72, 29–39.
- Oh, Y., Yang, S., 2010. Defining exergames and exergaming. *Proceedings of Meaningful Play* 1–17.
- Orwin, R.G., 1983. A fail-safe N for effect size in meta-analysis. *J. Educ. Stat.* 157–159.
- Park, J., Yim, J.E., 2016. A new approach to improve cognition, muscle strength, and postural balance in community-dwelling elderly with a 3-D virtual reality Kayak program. *Tohoku J. Exp. Med.* 238, 1–8.
- Pompeu, J., Mendes, F., Silva, K., Mondenes, A., Oliveira, T., Peterson, A., Piemonte, M.E.P., 2011. Balance improvement in patients with parkinson's disease after motor and cognitive training. *Physiotherapy (United Kingdom)* 97, eS1012–eS1013.
- Schattin, A., Arner, R., Gennaro, F., de Bruin, E.D., 2016. Adaptations of prefrontal brain activity, executive functions, and gait in healthy elderly following exergame and balance training: a randomized-controlled study. *Front. Ageing Neurosci.* 8 (Nov) (no pagination).
- Schoene, D., Lord, S.R., Delbaere, K., Severino, C., Davies, T.A., Smith, S.T., 2013. A randomized controlled pilot study of home-based step training in older people using videogame technology. *PLoS One* 8, e57734.
- Shatil, E., 2013. Does combined cognitive training and physical activity training enhance cognitive abilities more than either alone? A four-condition randomized controlled trial among healthy older adults. *Front. Ageing Neurosci.* 5, 8.
- Şimşek, T.T., Çekok, K., 2016. The effects of Nintendo Wii™-based balance and upper extremity training on activities of daily living and quality of life in patients with subacute stroke: a randomized controlled study. *Int. J. Neurosci.* 126, 1061–1070.
- Sinclair, J., Hingston, P., Masek, M., 2007. Considerations for the design of exergames. In: *Proceedings of the 5th international conference on Computer graphics and interactive techniques in Australia and Southeast Asia*. ACM, pp. 289–295.
- Smith, P.J., Blumenthal, J.A., Hoffman, B.M., Cooper, H., Strauman, T.A., Welsh-Bohmer, K., Brownndyke, J.N., Sherwood, A., 2010. Aerobic exercise and neurocognitive performance: a meta-analytic review of randomized controlled trials. *Psychosom. Med.* 72, 239.

- Staiano, A.E., Abraham, A.A., Calvert, S.L., 2012. Competitive versus cooperative exergame play for African American adolescents' executive function skills: short-term effects in a long-term training intervention. *Dev. Psychol.* 48, 337–342.
- Stewart, A.L., Hays, R.D., Wells, K.B., Rogers, W.H., Spritzer, K.L., Greenfield, S., 1994. Long-term functioning and well-being outcomes associated with physical activity and exercise in patients with chronic conditions in the Medical Outcomes Study. *J. Clin. Epidemiol.* 47, 719–730.
- Strauss, E., Sherman, E.M., Spreen, O., 2006. A compendium of neuropsychological tests: Administration, norms, and commentary. *Am. Chem. Soc.*
- Van Hooren, S., Valentijn, A., Bosma, H., Ponds, R., Van Boxtel, M., Jolles, J., 2007. Cognitive functioning in healthy older adults aged 64–81: a cohort study into the effects of age, sex, and education. *Ageing Neuropsychol. Cogn.* 14, 40–54.
- Vaynman, S., Ying, Z., Gomez-Pinilla, F., 2004. Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition. *Eur. J. Neurosci.* 20, 2580–2590.
- Warburton, D.E., Nicol, C.W., Bredin, S.S., 2006. Health benefits of physical activity: the evidence. *Can. Med. Assoc. J.* 174, 801–809.
- Zheng, G., Xia, R., Zhou, W., Tao, J., Chen, L., 2016. Aerobic exercise ameliorates cognitive function in older adults with mild cognitive impairment: a systematic review and meta-analysis of randomised controlled trials. *Br. J. Sports Med.* 50, 1443–1450.
- Zimmermann, R., Gschwandtner, U., Benz, N., Hatz, F., Schindler, C., Taub, E., Fuhr, P., 2014. Cognitive training in Parkinson disease: cognition-specific vs nonspecific computer training. *Neurology* 82, 1219–1226.
- van't Riet, J., Crutzen, R., Lu, A.S., 2014. How effective are active videogames among the young and the old? Adding meta-analyses to two recent systematic reviews. *Games Health: Res. Dev. Clin. Appl.* 3, 311–318.