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REVIEW

Exergames for balance dysfunction in neurological disability: a meta-analysis with meta-regression

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Abstract

Objective To evaluate systematically the efficacy of exergames for balance dysfunction in neurological conditions and to identify factors of exergaming protocols that may influence their effects.

Methods We searched electronic databases for randomized clinical trials investigating the effect of commercial exergames versus alternative interventions on balance dysfunction as assessed by standard clinical scales in adults with acquired neurological disabilities. Standardized mean differences (Hedge's g) were calculated with random-effects models. Subgroup analyses and meta-regression were run to explore potential modifiers of effect size.

Results Out of 106 screened articles, 41 fulfilled criteria for meta-analysis, with a total of 1223 patients included. Diseases under investigation were stroke, Parkinson's disease, multiple sclerosis, mild cognitive impairment or early Alzheimer's disease, traumatic brain injury, and myelopathy. The pooled effect size of exergames on balance was moderate ($g=0.43$, $p<0.001$), with higher frequency (number of sessions per week) associated with larger effect ($\beta=0.24$, $p=0.01$). There was no effect mediated by the overall duration of the intervention and intensity of a single session. The beneficial effect of exergames could be maintained for at least 4 weeks after discontinuation, but their retention effect was specifically explored in only 11 studies, thus requiring future investigation. Mild to moderate adverse events were reported in a minority of studies. We estimated a low risk of bias, mainly attributable to the lack of double-blindness and not reporting intention-to-treat analysis.

Conclusions The pooled evidence suggests that exergames improve balance dysfunction and are safe in several neurological conditions. The findings of high-frequency interventions associated with larger effect size, together with a possible sustained effect of exergaming, may guide treatment decisions and inform future research.

Keywords Exergames · Balance · Rehabilitation · Disability · Meta-analysis

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Introduction

Falls are a major public health problem worldwide, not only because they represent one of the commonest reasons for unintentional injury death, but also because more than 30 million non-fatal falls require medical care every year (https://www.who.int/news-room/fact-sheets/detail/falls). Together with advanced age, many neurological conditions are associated with an increased risk of accidental falls that contribute to further worsening of neurological disability [1]. Falls occurring in the context of neurological diseases are about twice as frequent as in the general population, especially due to disease-related mechanisms affecting balance and gait [2]. This is expected given that the postural control of human balance requires the integration of central and peripheral components that result in complex behaviors based on the interaction of dynamic sensorimotor processes.

All the neural components that ensure the correct postural and balance control can be damaged at different levels by various neurological diseases [3]. While there is little evidence that pharmacological interventions can improve balance only in a limited number of conditions (e.g., Parkinson's disease [4]), some medications that are largely prescribed in the neurological setting may even worsen balance, especially when multiple drugs are administered [2]. Therefore, successful strategies aimed at improving balance and reducing the risk of falls are mainly based on non-pharmacological multidisciplinary interventions, among which stands out the physiotherapy approach [1]. However, common barriers make the access to standard rehabilitation services difficult for all the patients [5]. For this reason, alternative interventions that can reach most of the patients, such as video game-based training, can offer an easier, accessible and possibly more cost-effective approach than standard physiotherapy.

Playing exergames (the portmanteau word for "exercise" and "games") is a form of whole-body physical exercise delivered by commercial video games [6] with the aim of improving fitness and promoting an active lifestyle. The use of commercial devices for neurorehabilitation purposes is considered an example of non-immersive virtual reality-based sensorimotor training that can improve balance control and gait [7]. However, accumulating studies investigating the efficacy of exergames on balance have yielded mixed results, possibly due to the heterogeneity of intervention protocols, small sample sizes and low statistical power. Thus, the effort of integrating and arranging these findings is warranted to estimate more accurately the effects of exergaming on balance dysfunction in neurological conditions.

The objectives of this meta-analysis were (1) to evaluate systematically the efficacy of exergame-based interventions compared to conventional physiotherapy for balance dysfunction in neurological conditions from randomized clinical trials (RCTs), and (2) to identify factors of exergaming protocols that may influence their effects.

Methods

Study design and registration

Our meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [8] and the review protocol was registered in the PROSPERO database (Registration Number: CRD42020161568).

Search strategy

To identify studies to include in this meta-analysis, we searched PubMed/Medline, Scopus, Physiotherapy Evidence Database (PEDro), and Google Scholar, using combinations of free-text and MeSH terms for articles published until December 31, 2019 as follows:

("neurological diseases"[MeSH] OR "nervous system diseases"[MeSH] OR "Neurodevelopmental diseases"[MeSH] OR "multiple sclerosis"[MeSH] OR "Parkins*"[MeSH] OR "Stroke"[MeSH] OR "brain injur*"[MeSH] OR "Trauma"[MeSH] OR "Alzheimer*"[MeSH] OR "Dementia"[MeSH] OR "intellectual disability"[MeSH] OR"chorea"[MeSH] OR "Cerebral Palsy"[MeSH]) AND ("exergam*"[All Fields] OR "video gam*"[All Fields] OR "Wii"[All Fields] OR "Kinect"[All Fields] OR "Nintendo"[All Fields] OR "Balance board"[All Fields] OR "Computer*"[All Fields] OR "Sony"[All Fields] OR "Dance Dance Revolution"[All Fields] OR EyeToy[All Fields] OR "Microsoft"[All Fields]) AND ("balance"[MeSH] OR "posture"[MeSH] OR "postur*"[MeSH]).

We restricted the search to the following article types: "clinical studies", "clinical trials", "multicenter studies", and "randomized clinical trials". To avoid the risk of missing relevant articles, we searched for additional papers through the bibliography of previous published reviews; we also performed a generic web search. One reviewing author (LP) ran the search strategy and screened the initial titles after removing duplicates. Two authors (LP and LC) independently examined each potential relevant article, using the following criteria as defined by the PICO model [9]: (1) population: adult persons (aged ≥ 18 years) affected by acquired neurological disabilities; (2) intervention: "off-the-shelf" exergames (i.e. exergaming-based interventions delivered by commercial devices); (3) comparison: conventional treatments or other rehabilitation interventions or no intervention (i.e. waiting-list control group) (4): outcomes: clinical scales whose area of assessment includes "balance (non-vestibular)" according to the Rehabilitation Measure Database (https://www.sralab.org/rehabilitation-measures). The most frequently reported clinical scale was selected from studies exploring multiple balance outcomes. We decided not to include studies where the balance outcomes were assessed only by instrumented measurements (e.g. static and dynamic posturography) to limit heterogeneity [10].

Additional inclusion criteria were based on study design (parallel or crossover RCTs) and language (articles written in English only). We excluded conference papers, or unpublished materials, as well as articles reporting findings of both non-experimental studies and studies where exergames were delivered by non-commercial video games.

Data extraction

Two authors (LP and LC) independently performed data extraction, with disagreement resolved by a third author (DC). Extracted data included first author name, journal, year of publication, sample size, numbers of men and women, mean age of participants, disease under investigation, eligibility criteria, mean and standard deviation of the outcome of interest, timing of outcome measurement, type of intervention in control group, intervention protocol including type of commercial device, setting (supervised or home-based), administration modality (exclusive or add-on intervention), duration (overall length in weeks), frequency (number of sessions per week) and intensity (minutes spent in a single session) of intervention. Data on adverse events related with exergames were also collected.

If a study had multiple assessments from the same group (e.g. immediate post-intervention and long-term follow-up data), we meta-analysed only the immediate post-intervention data and examined the long-term effect of exergames in a separate analysis. If a study had more than two groups, we meta-analysed only the exergaming group versus the alternative intervention group rather than the no intervention group.

When reported data were insufficient for the analysis, we contacted the study author to request access to additional data.

An Excel spreadsheet containing all data of included studies is available as supplemental file (appendix.xlxs).

Statistical analysis

We estimated the pooled effect size of exergame interventions by the bias-corrected Hedges' g with its relative 95% confidence intervals (CIs). This is equivalent to a Cohen's d with an additional correction factor for small samples, thus providing more conservative results. A random-effects model weighted by inverse variance was used to calculate the pooled effect size. Positive effect sizes indicated greater improvement in balance with exergames than alternative interventions. Effect sizes were graded as small ($g = 0.20$), medium ($g = 0.50$) and large ($g = 0.80$) [11]. To account for the expected heterogeneity between studies and outcome measures of balance, we carried out a random-effects model by entering only post-intervention scores [12].

Subgroup analyses were conducted to compare effect sizes between categorical moderators. Meta-regression was run to identify which factors or covariates were associated with a greater effect size of exergames, by using the Hedge's g from each study as dependent variable.

Heterogeneity was assessed by the I^2 index, considering an $I^2 \leq 40\%$ as marginal, 30–60% moderate and 50–90% substantial heterogeneity, respectively. Risk of publication bias was assessed by visual inspection of funnel plot and the Egger test of asymmetry. We also computed the Orwin fail-safe N test to estimate the number of missing studies that we would need to retrieve and incorporate in our meta-analysis to make the summary effect become trivial, on the assumption that studies demonstrating a lack of benefit might not have been published or submitted for publication. Each single study included in this meta-analysis was handled as a statistical unit. Two-tailed p values < 0.05 were considered as significant. Data were analysed by using the OpenMeta(analyst) software (http://www.cebm.brown.edu/openmeta/).

Quality assessment in individual studies and across studies

The methodological quality of each included study was assessed by the PEDro scale [13], by downloading the available scores on the website (https://www.pedro.org.au); if a trial had not been rated in the PEDro archive, two authors (LP and AT) independently assessed the rates. Disagreements between authors were resolved by consensus and, if necessary, a third author was consulted (DC). The total score on PEDro scale ranges through the following scores: 9–10 'low' risk of bias; 6–8 'moderate' risk of bias, while RCTs with a score < 6 were considered as carrying 'high' risk of bias. The overall risk of bias was assessed by the Cochrane risk of bias assessment tool [12].

The Grading of Recommendation, Assessment, Development and Evaluation (GRADE) system was employed to score the overall quality of evidence [14]. An initially assumed high level of evidence was downgraded according to the following pre-defined criteria [15]: risk of bias (> 50% of included studies scored ≤ 6 on the PEDro scale); inconsistency (significant between-study heterogeneity and $I^2 \geq 40\%$); indirectness (> 50% of the participants were outside the target population); imprecision (< 400 participants); publication/selection bias (asymmetry of funnel plot). Consequently, the evidence could be ranked into four levels: very low, low, moderate and high.

Results

Search findings

Our initial search of databases retrieved 276 studies, including 24 additional titles that were identified from the bibliography of selected papers and previous published reviews. After removing duplicates and screening from title and abstract, we assessed 106 full-text articles for eligibility. Of these, 41 studies met the eligibility criteria for this meta-analysis (Fig. 1) [16–56].

Participants

Forty-one eligible studies randomized 1381 participants. Post-intervention data were available for 1223 (88.6%), 621 in the exergaming group and 602 in the control group.

Table 1 shows the demographic and clinical characteristics of participants across the included studies. The age distribution and men:women ratio varied according the diseases under investigation, that were stroke ($n=18$) [16, 17, 19–21, 24, 27–31, 33, 34, 37, 42, 48, 54, 55], Parkinson's disease ($n=8$) [25, 35, 43, 45–47, 49, 53], multiple sclerosis ($n=7$) [18, 36, 38, 39, 44, 52, 56], mild cognitive impairment or early Alzheimer's disease ($n=3$) [32, 40, 41], traumatic brain injury ($n=2$) [22, 50], and myelopathy ($n=2$) including tropical spastic paraparesis [23] and traumatic spinal injuries [51]; one study included a mixed population of patients affected by stroke, traumatic brain injury, and benign cerebral neoplasm [26].

The overall disability level of participants was moderate, with almost all the studies requiring adequate visual acuity and hearing function, ability to walk independently or at least to stand upright without assistance. Only one study enrolling patients with severe spinal cord injury required the ability to sit independently [51]. Four studies did not report an explicit recruitment criterion for independence in standing or walking [31, 32, 48, 54]. A severe cognitive impairment was an explicit exclusion criteria in 35 articles, but screening through specific batteries was performed in 24 studies with the Mini-Mental State Examination ($n=23$) [19–21, 25, 26, 28, 30, 34, 35, 37, 39–43, 45–49, 53, 55], Montreal Cognitive Assessment ($n=1$) [33], and Levels of Cognitive Functioning ($n=1$) [50].

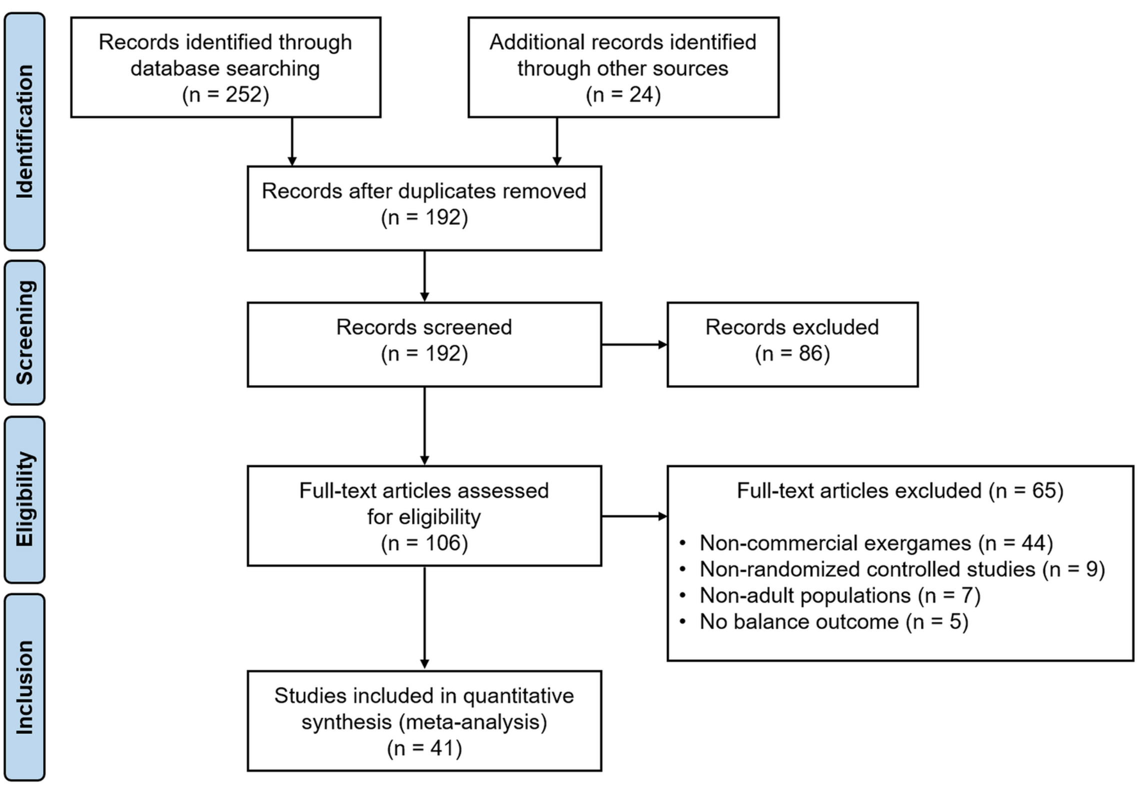

Fig. 1 PRISMA flowchart for study selection

Table 1 Characteristics of participants in the included studies ($n=41$)

Study [reference]	Sample size	Men:women ratio	Age	Condition	Clinical scale	Mean baseline score
Barcala (2013) [16]	20	1.2:1	64	Stroke	BBS	38.4
Bower (2014) [17]	21	1.3:1	64	Stroke	TUG	31.1 s
Brichetto (2013) [18]	36	0.6:1	42	MS	BBS	49.1
Cho (2012) [19]	22	0.7:1	64	Stroke	BBS	40.1
Choi (2017) [20]	24	1.4:1	62	Stroke	TUG	15.3 s
Choi (2018) [21]	28	1.5:1	50	Stroke	BBS	48.7
Cuthbert (2014) [22]	20	1.9:1	31	TBI	BBS	47.4
de Oliveira Arnaut (2014) [23]	9	0.5:1	58	MP	BBS	33.4
Fritz (2013) [24]	28	N/A	67	Stroke	BBS	46.6
Gandolfi (2017) [25]	76	2:1	68	PD	BBS	47.1
Gil-Gomez (2011) [26]	17	1.8:1	47	Mixed	BBS	43.3
Golla (2018) [27]	11	1.8:1	74	Stroke	BBS	48.5
Hung (2014) [28]	30	1.8:1	54	Stroke	TUG	27.7 s
Hung (2017) [29]	24	2.4:1	56	Stroke	BBS	48.0
Kannan (2019) [30]	20	1.2:1	59	Stroke	BBS	44.4
Karasu (2018) [31]	23	0.8:1	63	Stroke	BBS	38.9
Lee (2016) [32]	30	1.5:1	64	MCI	BBS	39.8
Lee (2017) [33]	50	2.6:1	57	Stroke	BBS	43.4
Lee (2018) [34]	30	1.5:1	61	Stroke	FRT	8.8 cm
Laio (2014) [35]	24	0.9:1	65	PD	TUG	12.3 s
Lozano-Quilis (2014) [36]	11	1.8:1	45	MS	BBS	49.7
Morone (2014) [37]	47	2.3:1	60	Stroke	BBS	42.1
Nilsagard (2012) [38]	80	0.3:1	50	MS	TUG	11.8 s
Ortiz-Gutierrez (2013) [39]	47	0.7:1	41	MS	BBS	46.0
Padala (2012) [40]	22	0.4:1	80	AD	BBS	42.3
Padala (2017) [41]	30	1.7:1	73	AD	BBS	46.1
Park (2017) [42]	20	1:1	63	Stroke	BBS	36.5
Pompeu (2012) [43]	32	1.1:1	67	PD	BBS	52.4
Prosperini (2013) [44]	36	0.4:1	36	MS	FSST	17.4 s
Ribas (2017) [45]	20	0.7:1	61	PD	BBS	49.6
Santos (2020) [46]	27	2.2:1	64	PD	BBS	42.0
Shih (2016) [47]	20	4:1	68	PD	BBS	50.6
Song (2015) [48]	40	1.2:1	51	Stroke	TUG	18.9 s
Song (2017) [49]	53	0.7:1	66	PD	TUG	9.5 s
Straudi (2017) [50]	21	4.3:1	36	TBI	TUG	16.3 s
Tak (2015) [51]	26	3.3:1	46	MP	FRT	16.7 cm
Thomas (2017) [52]	29	0.1:1	49	MS	TUG	10.9 s
Tollar (2019) [53]	50	N/A	70	PD	BBS	24.2
Yang (2014) [54]	12	3:1	60	Stroke	BBS	12.5
Yatar (2015) [55]	30	1.3:1	63	Stroke	BBS	42.6
Yazgan (2019) [56]	27	0.2:1	43	MS	BBS	44.8

AD Alzheimer's disease, *BBS* Berg Balance Scale, *FRT* Functional Reach test, *FSST* Four-Step Square Test, *MCI* mild cognitive impairment, *MP* myelopathy, *MS* multiple sclerosis, *N/A* not available, *PD* Parkinson's Disease, *TBI* traumatic brain injury, *TUG* timed up-and-go test

Study characteristics

Most of the studies were designed as parallel-group trials ($n=39$) [16–43, 45–51, 53–56], while a crossover design and a mixed method was adopted in the remaining two studies [44, 52]. Randomization of participants in three groups was made in five studies also including a no intervention group ($n=4$) [21, 35, 53, 56] and two groups that underwent either balance re-training or non-commercial video games ($n=1$) [29]. The Berg balance scale was the most frequently investigated balance outcome ($n=29$) [16, 18, 19, 21–28, 30–33, 36, 37, 39–43, 45–47, 53–56], followed by the timed up-and-go test ($n=9$) [17, 20, 28, 35, 38, 48–50, 52], functional reach test ($n=2$) [34, 51], and four-step square test ($n=1$) [44]. A post-intervention follow-up assessment was planned in 11 studies after a median time of 8 (range 4–24) weeks following the intervention completion [24, 25, 28, 29, 31, 37, 41, 43–45, 52, 55].

Interventions

The main characteristics of the interventions are described in Table 2.

Exergames were delivered through the Wii Balance Board, Nintendo® ($n=32$) [16–23, 25–32, 34, 35, 37, 38, 40, 41, 43–47, 51, 52, 54–56], Kinect, Microsoft® ($n=7$) [25, 33, 36, 39, 42, 48, 50], or Dance Dance Revolution, Sony® ($n=1$) [49]; a mixed intervention based on Wii Balance Board plus Play Station 2, Sony® was administered in one study [24]. The intervention with exergames was carried out in a supervised outpatient ($n=34$) [16–24, 26, 28–38, 40, 42, 43, 45–48, 50, 51, 53–56] or home setting ($n=7$) [25, 27, 39, 41, 44, 49, 52], as exclusive intervention ($n=24$) [17, 18, 24–28, 30, 35, 36, 38–41, 44, 45, 47–50, 52–54, 56] or in addition to other type of rehabilitation ($n=17$) [16, 19–23, 29, 31–34, 37, 42, 43, 46, 51, 55].

The control group consisted of standard physical therapy ($n=23$) [16, 18–20, 22–24, 26–28, 30, 31, 33–37, 39, 42, 43, 45, 46, 51], different types of balance training ($n=6$) [21, 25, 29, 47, 50, 55, 56], waiting list ($n=4$) [38, 44, 49, 52], stationary bicycling ($n=2$) [48, 53], alternative types of video games ($n=2$) [17, 29], walking activity ($n=2$) [40, 41], mirror visual feedback training ($n=1$) [54] and traditional cognitive rehabilitation ($n=1$) [32].

The median duration of the intervention was 6 (range 3–24) weeks; the median frequency was three (range 1–5) sessions per week; the median intensity was 30 (range 15–90) min.

Effect size of exergaming

The overall effect size of exergames on balance was moderate ($g=0.43$; 95% CIs 0.24–0.62, $p<0.001$), indicating an almost medium effect size favouring exergames over alternative interventions. This finding did not change after removing the four studies where the waiting-list group served as comparator ($g=0.48$; 95% CIs 0.28–0.67, $p<0.001$) and after limiting the analysis to studies with Berg balance scale as outcome ($g=0.54$; 95% CIs 0.31–0.78, $p<0.001$).

Forest plot summarizing the main finding of this meta-analysis is shown in Fig. 2.

There was a moderate heterogeneity between the included studies ($Q_{40}=97.7$, $p<0.001$, $I^2=60\%$). The Egger test did not reveal significant asymmetry across the included studies ($\text{intercept}_{39}=0.92$; t value $=0.88$; $p=0.38$), but the visual inspection of funnel plot revealed that three studies overestimated the effect size in favour of exergames and one study overestimated the effect size in favour of the control group (Fig. 3). The Orwin fail-safe N analysis showed that 145 studies with a mean effect size of 0 would be required to alter the significant difference between the exergames and the alternative interventions, i.e. to bring the effect size under a trivial value of <0.1.

Subgroup analyses

The effect sizes estimated in stroke ($g=0.26$; 95% CIs 0.02–0.51, $p=0.038$), Parkinson's disease ($g=0.62$; 95% CIs 0.19–0.99, $p=0.005$), mild cognitive impairment or Alzheimer's disease ($g=0.93$, 95% CIs 0.37–1.49, $p=0.001$), and myelopathies ($g=0.78$, 95% CIs 0.09–1.46, $p=0.027$) were significant. The effect size estimated in multiple sclerosis ($g=0.44$; 95% CIs −0.03 to 0.91, $p=0.065$) and traumatic brain injuries ($g=0.05$, 95% CIs −0.61 to 0.62, $p=0.98$) were not significant. Exergames delivered through Wii balance board had a significant effect size ($g=0.49$; 95% CIs 0.29–0.70, $p<0.001$), whereas effect size was not significant with other devices ($g=0.18$; 95% CIs −0.25 to 0.61, $p=0.41$). The effect sizes of exergames were significant in both supervised ($g=0.41$; 95% CIs 0.21–0.60, $p<0.001$) and home-based setting ($g=0.52$; 95% CIs 0.01–0.95, $p=0.048$), and regardless of being an add-on intervention ($g=0.43$; 95% CIs 0.21–0.65, $p<0.001$) or not ($g=0.44$; 95% CIs 0.15–0.72, $p=0.003$).

Meta-regression

The effect size of exergames was not influenced by the men:women ratio ($\beta=-0.128$, $p=0.18$) or age of participants ($\beta=0.009$, $p=0.29$), and did not relate to the intensity of a single session ($\beta=-0.003$, $p=0.56$) or to the overall duration of the intervention ($\beta=-0.008$, $p=0.75$). We found a direct relationship between the effect size of exergames and the frequency of weekly sessions, approaching to statistical significance ($\beta=0.16$, $p=0.057$) in the univariate analysis (Fig. 4); this effect became significant in a multivariable analysis including all variables collected for this meta-analysis ($\beta=0.24$, $p=0.01$).

Long-term retention

The retention, defined as the consolidation of balance improvement beyond the intervention completion, was investigated in 11 studies [24, 25, 28, 29, 31, 37, 41, 43–45, 55] (see also Table 3) where patients were assessed after a median time frame of 8 (range 4–12) weeks following the

Table 2 Interventions under investigation in the included studies ($n=41$)

Study [reference]	Device	Setting	Strategy	Alternative intervention	Duration, weeks	Frequency, sessions per week	Intensity, min per session
Barcala (2013) [16]	Wii-BB	SV	Add-on	Standard physical therapy	5	2	30
Bower (2014) [17]	Wii-BB	SV	Exclusive	Upper limb video games	4	3	45
Brichetto (2013) [18]	Wii-BB	SV	Exclusive	Standard physical therapy	4	3	60
Cho (2012) [19]	Wii-BB	SV	Add-on	Standard physical therapy	6	3	30
Choi (2017) [20]	Wii-BB	SV	Add-on	Standard physical therapy	4	3	30
Choi (2018) [21]	Wii-BB	SV	Add-on	Balance re-training or waiting list	6	3	30
Cuthbert (2014) [22]	Wii-BB	SV	Add-on	Standard physical therapy	4	4	15
de Oliveira Arnaut (2014) [23]	Wii-BB	SV	Add-on	Standard physical therapy	8	2	30
Fritz (2013) [24]	Mixed	SV	Exclusive	Standard physical therapy	5	4	50
Gandolfi (2017) [25]	Wii-BB	HB	Exclusive	Balance re-training	7	3	50
Gil-Gomez (2011) [26]	Wii-BB	SV	Exclusive	Standard physical therapy	5	3	60
Golla (2018) [27]	Wii-BB	HB	Exclusive	Standard physical therapy	6	3	30
Hung (2014) [28]	Wii-BB	SV	Exclusive	Standard physical therapy	12	2	30
Hung (2017) [29]	Wii-BB	SV	Add-on	Balance re-training or non-commercial video games	12	2	30
Kannan (2019) [30]	Wii-BB	SV	Exclusive	Standard physical therapy	6	3	90
Karasu (2018) [31]	Wii-BB	SV	Add-on	Standard physical therapy	4	5	20
Lee (2016) [32]	Wii-BB	SV	Add-on	Cognitive rehabilitation	12	3	40
Lee (2017) [33]	Kinect	SV	Add-on	Standard physical therapy	6	2	90
Lee (2018) [34]	Wii-BB	SV	Add-on	Standard physical therapy	5	3	30
Laio (2014) [35]	Wii-BB	SV	Exclusive	Standard physical therapy or waiting list	6	2	45
Lozano-Quilis (2014) [36]	Kinect	SV	Exclusive	Standard physical therapy	10	1	60
Morone (2014) [37]	Wii-BB	SV	Add-on	Standard physical therapy	4	3	20
Nilsagard (2012) [38]	Wii-BB	SV	Exclusive	Waiting -list	6	2	30
Ortiz-Gutierrez (2013) [39]	Kinect	HB	Exclusive	Standard physical therapy	10	4	20
Padala (2012) [40]	Wii-BB	SV	Exclusive	Walking activity	8	5	30
Padala (2017) [41]	Wii-BB	HB	Exclusive	Walking activity	8	5	30
Park (2017) [42]	Kinect	SV	Add-on	Standard physical therapy	6	5	30
Pompeu (2012) [43]	Wii-BB	SV	Add-on	Standard physical therapy	7	2	30
Prosperini (2013) [44]	Wii-BB	HB	Exclusive	Waiting list	12	4	30
Ribas (2017) [45]	Wii-BB	SV	Exclusive	Standard physical therapy	12	2	30
Santos (2020) [46]	Wii-BB	SV	Add-on	Standard physical therapy	8	2	50
Shih (2016) [47]	Wii-BB	SV	Exclusive	Balance re-training	8	2	30
Song (2015) [48]	Kinect	SV	Exclusive	Stationary bicycling	8	5	30
Song (2017) [49]	DDR	HB	Exclusive	Waiting list	12	3	15
Straudi (2017) [50]	Kinect	SV	Exclusive	Balance platform therapy	6	3	60
Tak (2015) [51]	Wii-BB	SV	Add-on	Standard physical therapy	6	3	30
Thomas (2017) [52]	Wii-BB	HB	Exclusive	Waiting list	24	2	30
Tollar (2019) [53]	Kinect	SV	Exclusive	Stationary bicycling or waiting list	5	5	60
Yang (2014) [54]	Wii-BB	SV	Exclusive	Mirror visual feedback training	3	3	20
Yatar (2015) [55]	Wii-BB	SV	Add-on	Balance re-training	4	3	30
Yazgan (2019) [56]	Wii-BB	SV	Exclusive	Balance re-training or waiting list	8	2	60

DDR Dance Dance Revolution, *HB* home-based, *SV* supervised, *Wii-BB* Wii balance board

last session of rehabilitation (henceforth defined as long-term assessment). The effect size of exergames at long-term assessment was moderate ($g=0.61$, 95% CIs 0.21–0.99, $p=0.002$) and did not overcome the effect size observed at the immediate post-intervention assessment ($g=0.65$, 95% CIs 0.35–0.94, $p<0.001$).

The retention effect of exergames appeared to be mediated by the weeks elapsed between intervention

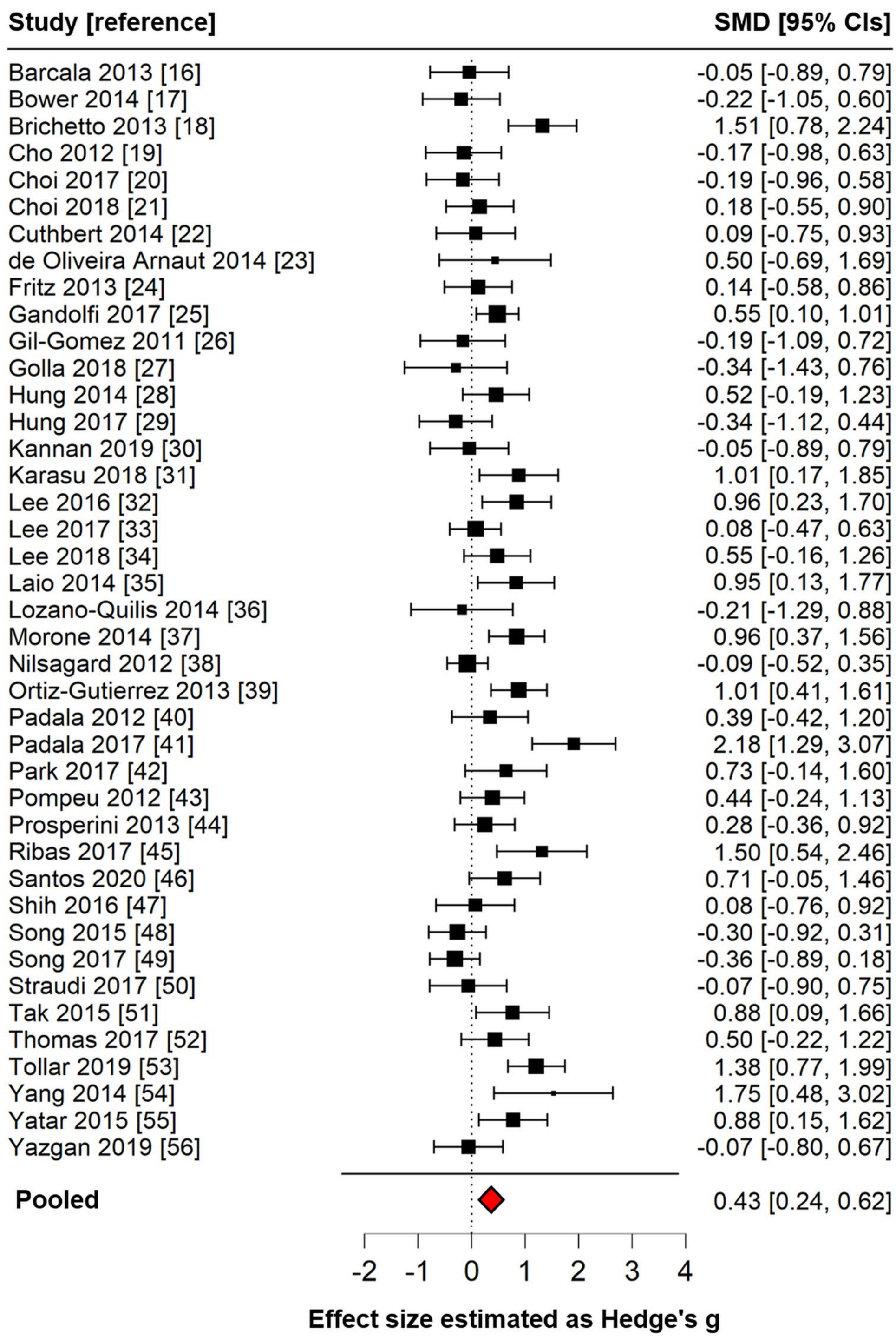

Fig. 2 Forest plot showing the effect size of included studies ($n=41$) and their pooled effect size (diamond), estimated by an inverse variance random-effects model as standardized mean difference (SMD) and 95% confidence intervals (CI). Positive Hedge's g values indicate a better outcome for exergames

completion and long-term assessment ($\beta = -0.12$, 95% CIs -0.22 to -0.03, $p = 0.008$). However, this indirect association between the retention effect of exergames and the duration of the post-intervention phase became barely not significant after adjusting for the immediate post-intervention effect size ($\beta = -0.07$, 95% CIs -0.16 to 0.01, $p = 0.08$).

Adverse events

Data on exergaming-related adverse events is available in 23 articles [17, 22, 25, 26, 28, 33, 35, 36, 38, 40–47, 49, 52–54, 56], of which 17 reported that no adverse event occurred during the studies. In the remaining six articles, adverse events were always graded as mild or moderate and occurred

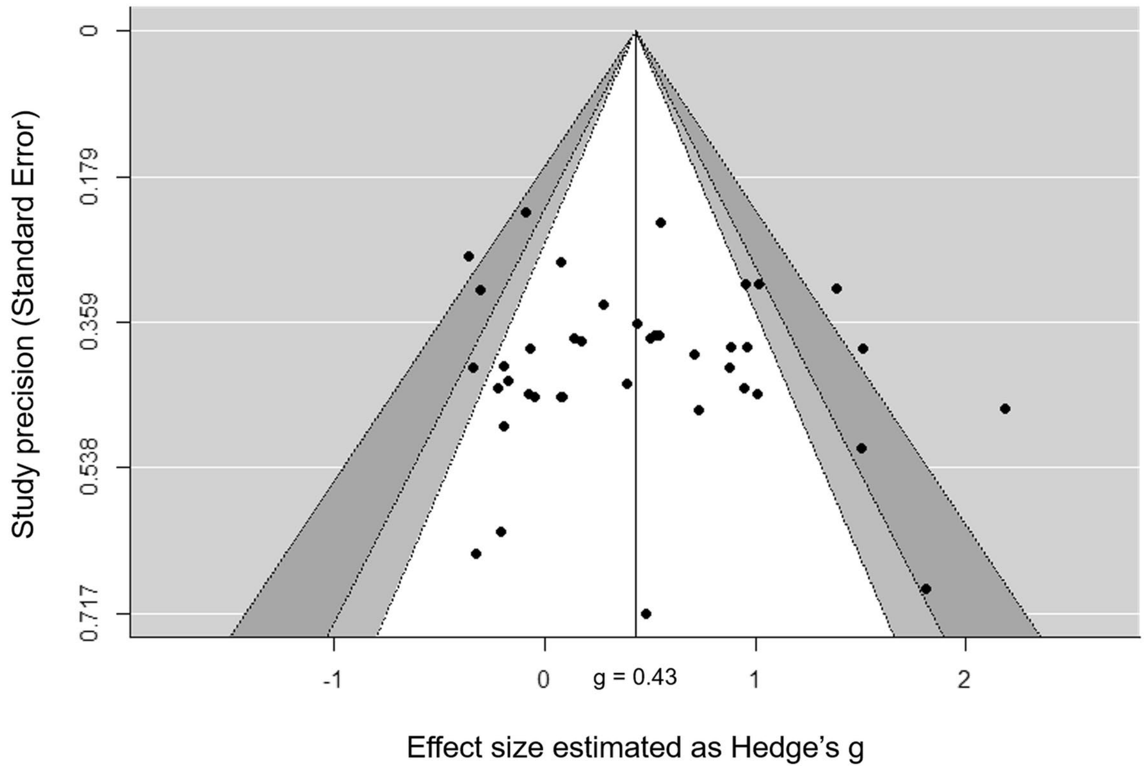

Fig. 3 Funnel's plot of included studies ($n = 41$) revealed the existence of publication bias in four studies, in the absence of asymmetry (low risk of reporting bias)

in 10–38% out of randomized subjects) who reported musculoskeletal disorders ($n = 5$) such as knee, leg or back pain; accidental falls while playing exergames ($n = 3$); increased spasticity ($n = 2$); dizziness ($n = 1$). There was no serious adverse event reported.

Risk of bias assessment

Quality assessment of the included study by the PEDro scale is shown in Table 4. Approximately, 75% of included studies ($n = 31$) were of high quality (rating $\geq 6/10$ on the PEDro scale), nine studies were of fair quality (rating 4–5/10 on the PEDro scale), and only one study was of poor quality (rating 3/10 on the PEDro scale). Removing those studies ($n = 10$) of fair or poor quality did not affect the main meta-analysis finding ($g = 0.49$, 95% CIs 0.29–0.69, $p < 0.001$). The most frequent methodological weaknesses of included studies were the lack of double-blindness and the fact that less than 25% of studies reported an intention-to-treat analysis. The assessment of risk of bias for all included studies is summarized in Fig. 5.

According to the GRADE criteria, an initially assumed high level of evidence was downgraded once, because of the presence of inconsistency due to significant between-study heterogeneity and $I^2 \geq 40\%$). Despite inconsistency, our meta-analysis exhibited directness (all participants were affected by balance dysfunction due to neurological diseases), precision (more than 1000 participants) and was free from publication/selection bias across included studies. Consequently, the quality of evidence presented is moderate.

Discussion

In this meta-analysis, we explored to what extent exergaming was superior to physiotherapy or other forms of rehabilitation in improving balance dysfunction due to neurological conditions. We found a significant medium effect size favouring exergames over alternative interventions or waiting list.

Further general considerations can be drawn based on the findings of the present meta-analysis.

Firstly, the most robust evidence of a beneficial effect of exergames on balance exists for studies in stroke, Parkinson's disease and, although to a lesser extent, for multiple sclerosis; it is not possible to draw robust conclusions on other conditions, such as mild cognitive impairment or Alzheimer's disease, traumatic brain injuries and myelopathies, mainly due to the smaller numbers of included studies.

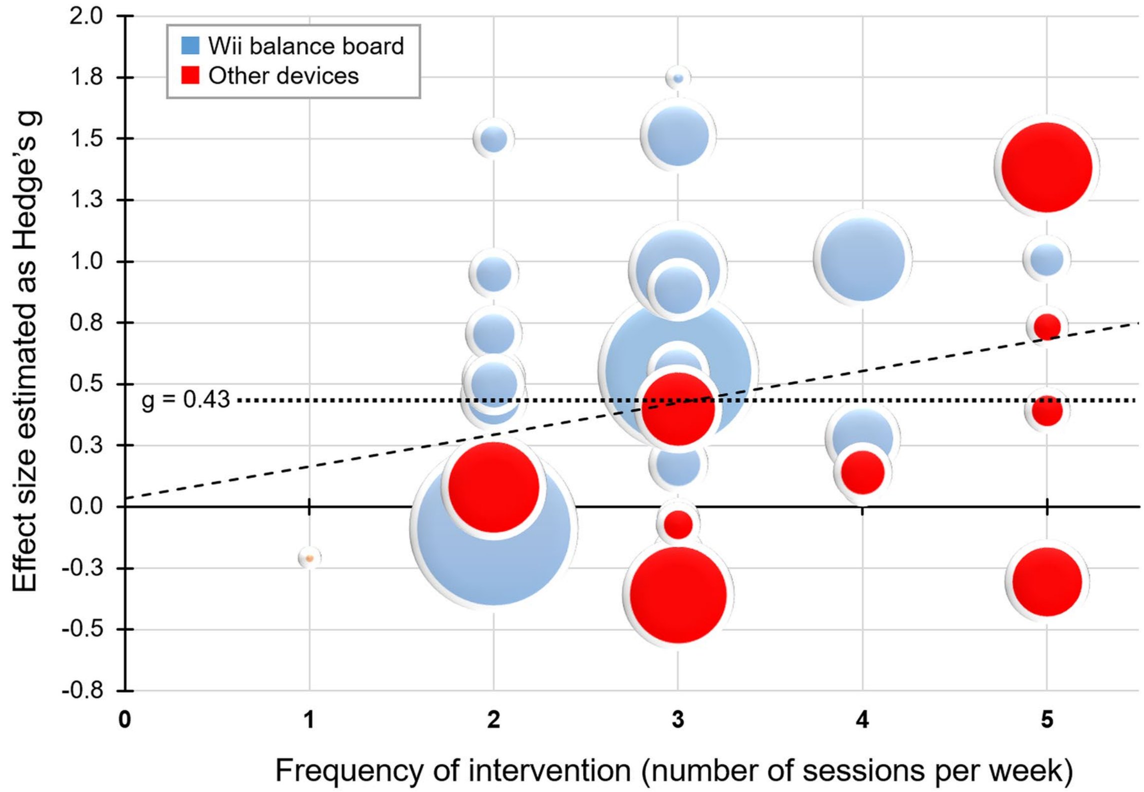

Fig. 4 Meta-regression revealed a direct association between the effect size of exergames on balance and frequency of the intervention (number of sessions per week); each circle represents a study, with the circle area proportional to the sample size of that study

Table 3 Studies investigating the retention effect of exergames on balance ($n = 11$)

Study [references]	Condition	Immediate post-intervention effect size (Hedge's *g*)	Long-term follow-up effect size (Hedge's *g*)	Difference in effect size (%)	Off-intervention duration (weeks)
Gandolfi (2017) [25]	PD	0.55 (0.23)	0.37 (0.36)	− 33	4
Karasu (2018) [31]	Stroke	1.01 (0.43)	1.72 (0.30)	70	4
Morone (2014) [37]	Stroke	0.96 (0.30)	1.11 (0.45)	16	4
Yatar (2015) [55]	Stroke	0.88 (0.37)	0.95 (0.23)	8	4
Padala (2017) [41]	AD	1.4 (0.40)	1.67 (0.35)	19	8
Pompeu (2012) [43]	PD	0.44 (0.35)	0.35 (0.33)	− 20	8
Ribas (2017) [45]	PD	1.50 (0.49)	0.20 (0.37)	− 87	8
Fritz (2013) [24]	Stroke	0.14 (0.37)	0.07 (0.23)	− 50	12
Hung (2014) [28]	Stroke	0.52 (0.36)	0.22 (0.40)	− 58	12
Hung (2017) [29]	Stroke	− 0.23 (0.40)	− 0.35 (0.43)	− 52	12
Prosperini (2013) [44]	MS	0.28 (0.33)	0.24 (0.49)	− 14	12
Pooled effect	–	0.65 (0.15)	0.61 (0.20)	− 6	–

AD Alzheimer's disease, *MS* multiple sclerosis, *PD* Parkinson's disease, *SE* standard error

Secondly, the beneficial effect of exergames on balance was independent of the setting (supervised or home-based) and strategy (exclusive or add-on) of intervention. We observed a between-device difference on effect size, with the Wii balance board-based intervention giving a larger benefit when compared to other commercial devices.

Thirdly, the weekly frequency of sessions, rather than the duration of a single session and the overall duration of the intervention, significantly affected the effect size of exergames on balance.

Fourthly, there were some indications of a retention effect of exergames on balance of at least 4 weeks since

Table 4 Assessment of the methodological quality of individual studies included in the meta-analysis ($n=41$) by the PEDro scale

Study [references]	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	Score
Barcala (2013) [16]	×	×	×	×			×	×		×	×	7
Bower (2014) [17]	×	×	×	×	×		×	×		×	×	8
Brichetto (2013) [18]	×	×		×			×			×	×	5
Cho (2012) [19]		×		×			×	×		×	×	5
Choi (2017) [20]	×	×		×	×			×	×	×	×	6
Choi (2018) [21]	×	×	×	×			×	×	×	×	×	8
Cuthbert (2014) [22]	×	×		×			×	×		×	×	6
de Oliveira Arnaut (2014) [23]	×	×	×	×						×	×	5
Fritz (2013) [24]	×	×	×	×			×	×	×	×	×	8
Gandolfi (2017) [25]	×	×		×			×	×		×	×	6
Gil-Gomez (2011) [26]		×		×			×	×		×	×	6
Golla (2018) [27]	×	×		×			×	×			×	5
Hung (2014) [28]	×	×	×	×			×	×		×	×	7
Hung (2017) [29]	×	×	×	×			×	×		×	×	7
Kannan (2019) [30]		×		×						×	×	4
Karasu (2018) [31]	×	×	×	×			×	×		×	×	7
Lee (2016) [32]	×	×		×			×	×		×	×	6
Lee (2017) [33]	×	×		×			×	×		×	×	6
Lee (2018) [34]	×	×		×			×	×		×	×	6
Laio (2014) [35]	×	×	×	×			×	×		×	×	7
Lozano-Quilis (2014) [36]	×	×		×				×		×	×	5
Morone (2014) [37]	×	×	×	×			×	×		×	×	7
Nilsagard (2012) [38]	×	×	×	×			×	×		×	×	7
Ortiz-Gutierrez (2013) [39]	×	×	×	×				×		×	×	5
Padala (2012) [40]	×	×		×					×	×	×	5
Padala (2017) [41]	×	×	×	×				×	×	×		6
Park (2017) [42]	×	×	×	×			×			×	×	6
Pompeu (2012) [43]		×		×			×			×	×	5
Prosperini (2013) [44]	×	×	×	×				×		×	×	6
Ribas (2017) [45]	×	×	×	×			×	×		×	×	7
Santos (2020) [46]	×	×		×			×	×	×	×	×	7
Shih (2016) [47]	×	×	×	×				×		×	×	6
Song (2015) [48]	×	×								×	×	3
Song (2017) [49]	×	×	×	×			×	×	×	×	×	8
Straudi (2017) [50]	×	×		×				×		×	×	6
Tak (2015) [51]	×	×		×			×	×	×	×	×	7
Thomas (2017) [52]	×	×	×	×				×	×	×	×	7
Tollar (2019) [53]	×	×		×			×	×		×	×	6
Yang (2014) [54]		×	×	×			×	×		×	×	7
Yatar (2015) [55]	×	×	×					×	×	×	×	6
Yazgan (2019) [56]	×	×		×				×		×	×	5

#1: eligibility criteria (not contributing to total score); #2: random allocation; #3. concealed allocation; #4: baseline comparability; #5: blind subjects; #6: blind therapists; #7: blind assessors; #8: adequate follow-up; #9: intention-to-treat analysis; #10: between-group comparisons; #11: point estimates and variability

the intervention completion, suggesting a sustained, but relatively short-lasting consolidation of their beneficial effect, unless exergames are continued over time. However, this latter point should be interpreted with great caution, because the retention effect was influenced also by the magnitude of the effect size estimated in the immediate post-intervention phase.

Lastly, exergaming appears to be safe, with only mild to moderate musculoskeletal adverse events reported in a

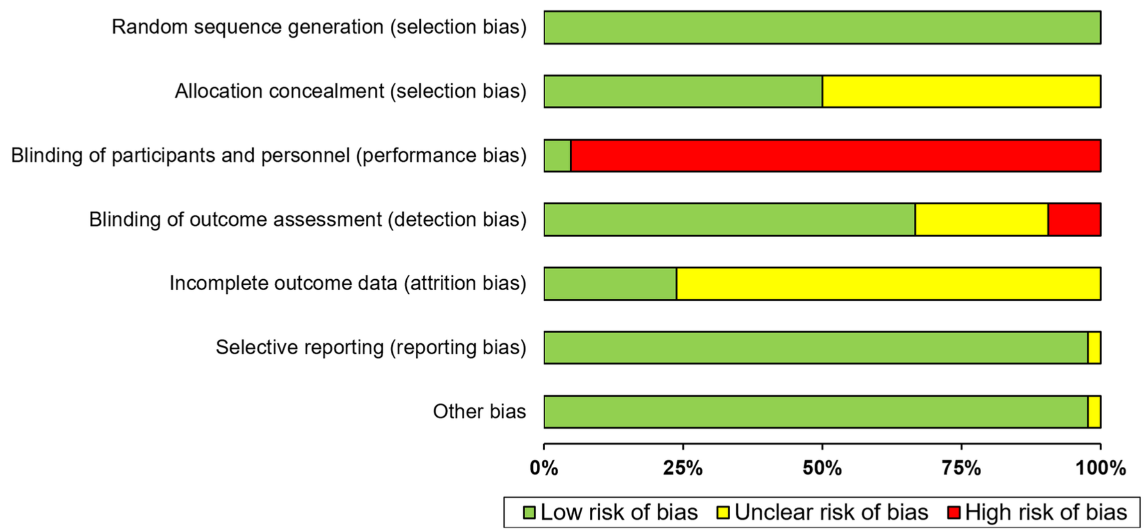

Fig. 5 Risk of bias assessment across all included studies ($n = 41$) according to the Cochrane Collaboration

minority of patients, with no significant increased risk of falls [57].

Our results in the context of existing literature

Our findings are consistent with previously published meta-analyses and systematic reviews supporting the efficacy of exergames in the neurological setting [58–61]. Meta-analyses investigating the effect of exergames for improving balance already exist, but they are either focused on specific neurological diseases [62–65] or incorporate commercial exergames into the wider category of virtual reality-based interventions [58, 65]. To our best knowledge, this is the first attempt to establish what is the optimal use of commercial exergames, in terms of device, setting, strategy, intensity, frequency and duration, to obtain the larger effect on balance. We choose to include only commercial exergames to explore if the lowest cost and easiest accessible solution can be encompassed in the therapeutic *armamentarium* for the management of balance problems due to neurological conditions. Although this approach cannot replace physiotherapy, on the basis of our findings, we suggest that exergames promote fitness and healthy behaviour in patients with mild to moderate disability (e.g. home-based training adaptable to work and family) and can be used to carry over, in the medium term, the effects of physiotherapy in the community setting (e.g. in case of pre-planned or unexpected interruption of rehabilitation). This latter indication comes from the indication of a maintained beneficial effect on balance of at least 4 weeks from exergaming discontinuation, a suggestion that encourages the adoption of a rehabilitation strategy based on "pulsed" exergaming cycles.

Exergames are not free from criticisms for several reasons: (1) given their commercial nature, game devices have roughly a 5-year life cycle before being replaced with novel hardware, implying that some types of exergames may be no longer available when their application in neurological setting is determined; (2) the possibility of a tailored balance re-training is very limited, thereby representing a "blockbuster" rather than a "personalized" intervention [63, 66, 67]; (3) being originally designed as a recreational activity, their applicability for the recovery of sensorimotor function is still debated and consequently the development of custom-written game software has been advocated [66].

Putative mode(s) of action of exergames

The improvement of balance control observed through exergames can result from three (not mutually exclusive) mechanisms: (1) muscle reinforcement; (2) re-training of sensorimotor strategies aimed to restore the axial control and anticipatory postural adjustments; (3) engagement of mirror neuron system mediated by the avatar (i.e. the graphical representation of the user in the virtual environment).

Like other forms of bodily exercise, playing exergames increases heart rate, oxygen consumption and energy expenditure to the same extent as a moderate-intensity physical activity [68]. However, the presumed mechanisms of action of exergames go beyond the merely increase in fitness. By requiring simultaneous physical and cognitive effort, exergames promote muscle reinforcement, as well as increasing efficiency of executive and attentional brain networks. As an intervention, exergaming encompasses most of the principles underlying experience-dependent neural plasticity [69], such as high-intensity repetition of task-oriented exercises, incrementally increase of task difficulty, real-time feedback, salience, motivation and reward. It is worth noting that the frequency of sessions, rather than intensity and overall duration, was associated with larger effect size. This finding suggests that higher frequency of exergaming may affect consolidation of motor memories through the influence of in-between sessions sleep on synaptic plasticity [70, 71].

Exergames applied to recovery of balance dysfunction have been also associated with structural and functional brain changes in cerebellar areas subserving postural control and in vestibular cortical network implicated in high-order multimodal integration and cognitive functions, including peri-personal space and self-referential processing [72, 73]. Their exploitation of complex brain networks makes them also potentially relevant tools to access cognitive domains of otherwise difficult accessibility that are subserved by the same neural circuits or hubs [74].

A multicenter RCT is ongoing to test the hypothesis that exergames (delivered by the Wii balance board) are not inferior to cognitive rehabilitation (delivered by a custom-written software application for mobile devices and tablets) and that both interventions are superior to a placebo-analogue cognitive intervention in improving cognitive function and reducing cognitive–motor interference due to multiple sclerosis (ClinicalTrials.gov Identifier: NCT04169750).

Conclusion

Despite the clinical and statistical heterogeneity of included RCTs, our findings provide a moderate evidence supporting the use of high-frequency commercial exergames delivered by Wii balance board as either supervised or unsupervised (namely home-based) rehabilitation tool, in addition or not with other interventions, to improve balance dysfunction due to neurological diseases. While the evidence is robust for stroke survivors and people with Parkinson's disease, future investigation is needed to extend recommendation to other neurological conditions and to better determine how long the beneficial effect of exergames lasts after their discontinuation.

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Compliance with ethical standards

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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