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REVIEW

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Effect of virtual reality on motor coordination in children with cerebral palsy: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Background: Improving motor coordination is an important prerequisite for the functional development of children with cerebral palsy (CP). Virtual reality (VR) may be efficient, interactive, adjustable and motivating physiotherapy choice for children with deficient coordination. This review aimed to identify, evaluate and formulate all the evidence concerning the efficacy of VR on motor coordination in children with CP and to compare the Physiotherapy Evidence Database (PEDro) with Cochrane Risk of Bias (RoB).

Main text: Five databases (PubMed, Cochrane Central Register of Controlled Trials, Web of Science, Science Direct and google scholar) were systemically searched from inception up to 1st January 2019. Studies included VR intervention for children with cerebral palsy with motor incoordination. Studies methodological quality was assessed by Cochrane RoB and PEDro scale. Nineteen studies met the prespecified eligibility criteria. There was a large effect size (SMD 0.75) on fine motor coordination. However, there was a non-significant, small beneficial effect (SMD 0.15) on gross motor coordination. The association between the overall Cochrane RoB and PEDro scores was fair ($r=0.28$, P value 0.248). There was a slight agreement between overall and moderate categories PEDro scores and Cochrane RoB ($\kappa=0.02$) and $\kappa=0.10$), respectively. However, high and low categories were moderately agreed with Cochrane RoB ($\kappa=0.43$) and ($\kappa=0.46$).

Conclusion: VR seems to be effective for improving fine motor coordination with questionable effect on gross motor coordination. PEDro scale is fairly correlated with Cochrane RoB, so development and validation of a more compatible quality assessment tools specific to physiotherapy trials are needed.

Keywords: Cerebral palsy, Virtual reality, Motor coordination, Systematic review, Meta-analysis, Randomized controlled trials

Background

Cerebral palsy (CP) is characterized by damage of the neonatal or infantile brain which affects the motor system and as a result, the child has poor coordination, poor balance or abnormal movement patterns or a combination of these characteristics [1].

Coordination is defined as the ability of the body to integrate the action of the muscles of the body to accomplish a specific movement or a series of movements in the most efficient manner [2]. Motor coordination is normally classified into two major categories, gross motor and fine motor [3]. Gross motor coordination refers to motor behaviors related to posture and locomotion, from early developmental milestones to finely tuned balance. Fine motor

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coordination involves motor behavior such as discrete finger movement, manipulations and eye-hand coordination [4]. An important term—dexterity—is often associated with motor coordination which is defined as the manual skill requiring rapid coordination of fine and gross movements [5, 6]. Two main types of dexterity exist: manual and finger dexterities [6]. Both gross and fine motor coordination are essential for performing functional tasks with the upper extremities (UEs) to succeed in daily activities and participate in school, leisure and social activities [7–9]. Gross motor coordination provides a stable postural base needed for the acquisition of both gross and fine motor skills. It is essential for the development of fine manual dexterity [10]. Fine motor coordination is important for the performance of activities of daily living such as eating, drinking, body care and fine object manipulation and of special importance for children in school-age because they spend a large proportion of their day coloring and writing which require a high degree of eye-hand coordination [11–13].

Impairment of motor coordination not only impacts the motor domain, but also encounters educational, behavioral and socio-emotional domains of the child development [11, 14]. Lack of gross motor coordination forces additional challenge for the child to cope with peers during team sports so he/she feels less physically competent, frustrated and anxious, loses his interest in participating in team and become less socially interactive [15, 16]. Lack of fine motor coordination restricts the performance of self-care activities and the academic achievement and hence diminishes the child's ability to develop independent and good quality of life [11, 17].

Over the past decades, new trends have been developed to improve sensory motor learning in children with CP [16–18]. One of these is virtual reality (VR) which has grown dramatically and represents a hopeful approach in pediatric rehabilitation [19].

VR is an interactive computer-simulated environment which creates the sense of being present in the real world by generating sensory experiences, which include artificial taste, sight, smell, sound and touch [20]. Virtual environment can be classified into two broad categories; immersive and non-immersive; with the immersive being the one by which the user is fully immersed into an artificially generated world as if he stepped into it, while the non-immersive or low-cost environments, the user becomes in contact with the virtual world "not within" [21].

The objective of this systematic review was to identify, evaluate and formulate the evidence- extracted from randomized controlled trials (RCTs) only-concerning the effectiveness of VR in rehabilitation of motor coordination in children with CP and to determine how far the sum scores of Cochrane RoB and PEDro scales are correlated and the degree of agreement between them.

Main text

Methodology

This systematic review was performed according to principles of Preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [22].

Search strategy

Five electronic databases were searched systematically and comprehensively from inception to 1st January 2019. They included the following English databases: PubMed, Cochrane database of systematic reviews, Web of Science, Science Direct and google scholar.

Medical subject heading (MeSH) terms and key words are of four groups: "virtual reality," "coordination," "cerebral palsy" and "children."

Study selection

Selection of Selection of the studies to be relevant to our review passed by two stages:

Stage 1 (filtration by title and abstract) Initially, two independent reviewers screened each title and abstract of the yielded search results to determine their eligibility for inclusion. Studies lack any of the eligibility criteria were instantly excluded. Only abstracts met the inclusion criteria or required full text review to confirm that they met all eligibility criteria (i.e., abstracts carrying information that supposed the study potentially relevant to our review) were kept for full-text review.

Stage 2 (full-text filtration) Then, full-text of the retained abstracts was retrieved and assessed by both reviewers for adherence to inclusion criteria to select the studies to be finally included in the review. Only full-text randomized controlled trials were included. Study reviews, commentaries or reports were used to identify the original article only, otherwise they were excluded. Whenever full-text manuscript or any further details were not available, a contact with the investigator was made by an e-mail. Any conflict about inclusion of the relevant studies was solved by discussion and a third reviewer was consulted if persisted.

Eligibility criteria

Using a PICOS format for questioning (Population, Intervention, Comparison/control, Outcome and study design), we set the eligibility criteria.

Inclusion criteria

- Studies had to fulfill the following criteria to be included in this systematic review:
- Study design was randomized controlled trial.
- 100% of the participants were pediatric patients diagnosed with any form of cerebral palsy aging from 3 up to 18 years.
- Intervention was virtual reality therapy alone or combined with other intervention or within the setup of any other modality against no, placebo or routine physiotherapy treatment.
- Outcome measure was motor coordination.

Exclusion criteria Studies were excluded if:

- Many publications of the same study reporting the same results.
- Participants are adults or suffering from any disability rather than cerebral palsy.
- Virtual reality is not the intervention of choice.
- Virtual reality used as an evaluative tool not a therapeutic modality.
- Robots are used as an orthosis only and not as VR component.
- Single session intervention is used.
- Not published in English due to shortage of translation resources.

Assessment of risk of bias and strength of evidence

Two quality assessment tools were used to critically appraise the methodological quality of the selected studies; the Cochrane Risk of Bias (RoB) tool as described in the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0) [23] and Physiotherapy Evidence Database (PEDro) scale [24–26]. Cochrane RoB tool has seven areas to assess the methodology of RCTs, whereas PEDro is an eleven criteria-based tool forming possible scoring of any study from 0 to 10. After assessing the idividual studies for their methodological quality using Cochrane RoB, they were rated according to the Agency for Healthcare Research and Quality standard of "good," "fair," and "poor" quality designations using conversion thresholds [27].

A PEDro score of 7 or greater was considered of 'high quality,' studies with a score of 5 or 6 were judged of 'moderate quality' and those with a score of 4 or less were deemed of 'poor quality' [28–30]. Two reviewers (S) and (N) independently rated the studies for quality assessment and then checked the scoring together. Any disagreement was solved by consensus.

Before scoring of the included studies and after studying of the Cochrane RoB tool well, we performed a pilot scoring of a previously published SR to make sure of our accurate use and estimation.

The level of evidence which each study add to the literature was evaluated by modified Sackett scale which adapted to rank studies according to their PEDro scores [31].

Data extraction

The data of the included studies were extracted by one reviewer (N) and checked by a second reviewer (S) using a data extraction form adapted from Cochrane's guidelines [23]. Then, the extracted data were tabulated, summarized narratively, statistically analyzed for calculating the ES together with the confidence interval and scores of the quality assessment were also reported.Information was collected on the basis of participants' demographic data (Table 1), studies' methodology (Table 2) and studies outcomes (Table 3).

Participant characteristics included age (mean, SD), gender, participant characteristics, the total sample size and the number of patients in each group. Study design, treatments received for both the experimental and the control groups, dosing (duration, frequency, length, and follow-up), VR equipment and its type (immersive vs non-immersive) were collected as methodological characteristics. Study outcomes include the outcome measures, their classification according to the International Classification of Functioning, Disability and Health (ICF), the results and the quality appraisal scores. Also, the author name and year of publication were reported. Any disagreement was solved by a consensus method.

Categorization of each outcome measure of the selected studies into ICF dimension was based upon a published literature. ICF domains are divided into two clusters (1) body structure and functions; and (2) activities and participation [50]. Activities were separated from participation because we wanted to illuminate whether or not participation outcomes were being examined. Investigators were contacted via emails if important data were unclear or unavailable.

Data synthesis

Estimation of the treatment effect This meta-analysis combined data at the study level. The outcome variables were fine motor coordination and gross motor coordination. To allow comparison of data from different scales, pooled statistics were calculated using standardized mean differences (SMDs) with 95% confidence intervals (CIs), which were computed using Comprehensive Meta-Analysis program (CMA, version 3.3.070). Means and SDs at

Table 1 Participants demographic data

Study, Year, Country	Mean age ± SD		Gender (male%)		Participant characteristics	Number (Exp./Cono.)
	Exp	Con	Exp	Con		
Chen et al. [32] 2012 Taiwan	8.7 y ± 2.1 y	8.5y ± 2.2 y	9 69.23%	10 66.67%	Spastic di. and Hemiplegic	30 (14/16)
Ramstrand and Lygnegård [33] 2012 Sweden	8–17		Not specified for each group		Hemiplegic diplegia	18
Rostami et al. [34] 2012 Iran	Mean 92 m 77–110) (range 100 m Range (74–124 m) 98 m Range (87–128 m)	96 m Range (74–140 m)	4 4 4	4	Spastic Hemiparetic	32 (24/8)
Druzibicki et al. [35] 2013 Poland		10.1 (10.5)*	11.0 (11.0)*	19 54	Spastic diplegia	52 (26/26)
Chiu et al. [36] 2014 Taiwan	9.4 y ± 1.9 y	9.5 y ± 1.9 y	15 47%	13 43%	Spastic Hemiplegic	62 (32/30)
Gilliaux et al. [37] 2015 Belgium	10.8 y ± 4.6 y	11 y ± 3.5 y	Not specified		Quadri-/di-/hemiplegic	16 (8/8)
James et al. [38] 2015 Australia	11 y 8 m ± 2 y 4 m	11 y 10 m ± 2 y 5 m	26 51%	25 50%	Spastic UCP	102 (51/51)
Greeco et al. [39] 2015 Brazil	8.2 (1.6)	8.8 (1.1)	6 60	5 50	Spastic diparetic	20 (10/10)
Zoccolillo et al. [40] 2015 Italy	6.89 y ± 1.91 y	Not specified		Not specified		22 (11/11)
Cho et al. [41] 2016 Korea	10.2 y ± 3.4 y	9.4 y ± 3.8 y	Not specified		Spastic C.P	18 (9/9)
Acar et al. [42] 2016 Turkey	9.53 y ± 3.04 y	9.73 y ± 2.86 y	8 53.33%	6 40%	Spastic Hemiplegic	30 (15/15)
Ürgen et al. [43] 2016 Turkey	11.07 ± 2.37 years	11.33 ± 2.19 years	7 46.67	7 46.67	Hemiplegic spastic CP	33 (17/16)
Bedair et al. [44] 2016 Egypt	7.05 y ± .0.99 y	7.25 y ± 0.96 y	12 60%	11 55%	Spastic Hemiplegic	40 (20/20)
Uysal and Baltaci [45] 2016 Turkey	9.13 y (2.57)	10.11 y (2.62)	8 66.7%	2 16.7%	Spastic hemiplegic	24 (12/12)
Tarakci et al. [34] 2016 Turkey	10.46 y (2.69)	10.53 y (2.79)	Not specified		Diplegia hemiplegia dyskinetic	38` (19/19)
Wallard et al. [46] 2017 France	8.3 ± 1.2	9.6 ± 1.7	8 57.14	7 43.75	Spastic diplegia	30 (14/16)
Lazzari et al. [47] 2017 Brazil	7.6 y ± 2.2 y	7.4 y ± 2 y	7 70%	7 70%	Not Specified	22 (11/11)

Table 1 (continued)

Study, Year, Country	Mean age ± SD		Gender (male%)		Participant characteristics	Number (Exp./Cono.)
	Exp	Con	Exp	Con		
Gatica Rojas et al. [48] 2017 Chile	10.2 y (3.1)	11.2 y (3.6)	10 62.5%	9 56.25%	Congenital Spastic hemiplegic Spastic diplegic	32 (16/16)
Sajan et al. [49] 2017 India	10.6 y ± 3.78 y	12.4 y ± 4.93y	6 55%	5 50%	Spastic di-/tri-/quadriplegic	20 (10/10)

SD standard deviation, *Exp*. experimental group, *Con*. control group, *no* number, *Y* years, *m.* months, *UCP* unilateral cerebral palsy

the end of the treatment for the treatment and control groups (when relevant) were used to compute SMDs. If appropriate, estimated effect size was calculated if the outcome variable was reported in ≥ 2 studies.

Since all the outcomes were continuous, they were pooled across studies and analyzed using a random-effects model for data collected from all eligible acute studies obtained from review and data collected from all eligible intervention studies obtained from review. A random-effects model was used because it involves the assumption of statistical heterogeneity across studies.

The effect estimate was classified as described by Cohen's three levels for the size of the between-group effects (i.e., SMD of less than 0.5 was considered to indicate a small beneficial effect, SMD from 0.5 to less than 0.8 medium or SMD ≥ 0.8 carry a large effect) [51].

Unit of analysis

Crossover studies Crossover studies were included only when outcome data for the first period of intervention were available or could be obtained upon request from the study authors.

Studies with multiple treatment groups: In case the study had multiple treatment groups, only the data for relevant treatment groups were included to create a single pair-wise comparison.

Assessment of heterogeneity Heterogeneity was assessed between studies using the I^2 statistic to quantify the proportion of the total outcome attributed to variability among studies. The following values were used: $I^2 = 0–30\%$ (no heterogeneity); $I^2 = 30–49\%$ (moderate heterogeneity); $I^2 = 50–74\%$ (substantial heterogeneity); and $I^2 = 75–100\%$ (considerable heterogeneity) [52]. The statistical analysis was conducted by using Comprehensive Meta-Analysis program for windows (CMA, version 3.3.070, Biostat, Inc. USA).

Correlation and agreement between study quality assessments with both tools To examine the degree of association between PEDro which is the best physiotherapy quality assessment tool and Cochrane which is the gold standard medical quality assessment tool, the yielded studies were further classified as adequate quality if generation of random sequence, concealment of allocation and blinding of outcome assessors were emphasized [53]. Because of the nature of the physiotherapy intervention modalities—in most situations can't not permit complete blinding of therapist and participant—performance bias was not included as a criteria in such judgment. So studies met three, two, one criteria were good, fair and poor quality, respectively. The statistical analysis for correlation between the scores obtained with the RoB and PEDro scales was assessed by using the statistical SPSS Package program version 24 for Windows (SPSS, Inc., Chicago, IL) by the nonparametric Spearman rank correlation coefficient because normal distribution could not be ascertained for all the parameters studied.

Spearman coefficient values were interpreted as an excellent relationship ≥ 0.91; good, 0.90 to 0.71; moderate, 0.70 to 0.51; fair, 0.50 to 0.31; and little or none, ≤ 0.3 [54].

Also, the strength of agreement between the scores of the 2 scales was measured by Cohen *k* coefficient categorical data (95% CI) for the overall grades and, with $k < 0.20$ indicates slight agreement; 0.21–0.40 fair agreement; 0.41–0.60 moderate agreement; 0.61–0.80 substantial agreement; and 0.81–1.0 almost perfect agreement [55]. Significance was set at $p < 0.05$.

Results

Systematic search results

The flow of different search stages and reasons for exclusion were outlined using a PRISMA diagram flow as shown in (Fig. 1). A total of potentially relevant 2347 citations were yielded, 968 from Pubmed, 571 from Web of Science, 105 from the Cochrane Library, 524 from Google Scholar and 179 from Science Direct. The identified citations were exported to Mendeley software which initially removed 383 duplicates. Then, the full-text of 271 citations was retrieved after the screening of the

Table 2 Studies methodology

Study, Year	Design	Intervention	Session duration and frequency	VR equipment	VR type	Control	Session frequency and duration	Length	Follow-up
Chen et al. [32] 2012 Taiwan	RCT	VR	VR: 40 min/day 3d/w	ElotonSimCycle Virtual Cycling System	Commercially available	General physical activity at home	-–	12w	
Ramstrand and Lygnegård [33] 2012 Sweden	Crossover RCT	VR	30 min. 5d/w	Wii Nintendo	Commercially available	No intervention	–	5w	–
Rostami et al. [34] 2012 Iran	SB-RCT	VR + CT	VR: 90 min. 3d/w CT: 30 min. 2d/w	E-Link Evaluation and Exercise System	Engineer-build	CT	30 min. 2d/w	4w	3 m
		CIMT + CT	CIMT: 90 min. 3d/w CT: 30 min. 2d/w						
		VR + CIMT + CT	VR: 90 min. 3d/w CIMT: 90 min. 3d/w CT: 30 min. 2d/w						
Druzibicki et al.* [35] 2013 Poland	RCT	Robotic-assisted gait training	45 min 20 sessions	Lokomat	Engineer-built	Individual exercises	20 sessions	4 w	–
		Individual exercises	20 sessions						
Chiu et al. [36] 2014 Taiwan	Prospective SB-RCT	VR + CT	VR: 40 min. 3d/w CT: – 3d/w	Home-based Wii Sports Resort	Commercially available	CT	– 3d/w	6w	12w
Gilliaux et al. [37] 2015 Belgium	SB-RCT	VR + CT	VR: 45 min. 2d/w CT: 45 min. 3d/w	REA Plan	Engineer-build	CT	45 min. 3d/w	8w	–
James et al. [38] 2015 Australia	RCT	VR + Standard Care	20–30 min. 6d/w	Internet-connected Computer	Commercially available	Standard Care	–	20w	–
Greeco et al. [39] 2015 Brazil	DB-RCT	Gait training with VR combined with anodal tDCS	20 min 5 s/w 2 w 10 sessions	Kinect program (Xbox 360)	Commercially available	Gait training with VR combined with sham tDCS	20 min. 5 s/w 2 w 10 sessions	3 w	7 w
Zoccolillo et al. [40] 2015 Italy	Crossover RCT	VR	30 min. 2d/w	Xbox with Kinect device	Commercially available	CT	30 min. 2d/w	8w	–
Cho et al. [41] 2016 Korea	RCT	VR Treadmill training	30 min. 3d/w	Wii Nintendo	Commercially available	Treadmill training	30 min. 3d/w	8w	–
		General P.T	30 min. 3d/w			General P.T	30 min. 3d/w		
Acar et al. [42] 2016 Turkey	RCT	VR + NDT	VR: 15 min. 2d/w CT: 30 min. 2d/w	Wii Nintendo	Commercially available	CT	45 min. 2d/w	6w	–

Table 2 (continued)

Study, Year	Design	Intervention	Session duration and frequency	VR equipment	VR type	Control	Session frequency and duration	Length	Follow-up
Bedair et al. [44] 2016 Egypt	RCT	VR + CT	VR: 30 min. 3d/w CT: 60 min. 3d/w	Xbox	Commercially available	CT	60 min –	4 m	–
Ürgen et al. [43] 2016 Turkey	RCT	VR Routine P.T	45 min. 2d/w 2d/ w	Nintendo Wii-Fit	Commercially available	Routine P.T	2d/ w	9 W	–
Uysal and Baltaci [45] 2016 Turkey	SB-RCT	VR Routine P.T	30 min. 2d/w 45 min. 2d/w	Wii Nintendo	Commercially available	Routine P.T	45 min. 2d/w	12w	–
Tarakci et al. [34] 2016 Turkey	RCT	VR	20 min. 2d/w	Wii-Fit Gaming console	Commercially available	NDT + conventional balance training	20 min. 2d/w 30 min. 2d/w	12w	–
Wallard et al. [46] 2017 France	RCT	Robotic-assisted gait training	40 min. 5 s/w	Lokomat®Pediatric	Engineer-built	P.T	40 min daily	4 w	–
Lazzari et al. [47] 2017 Brazil	DB-RCT	VR combined with active tDCs	20 min. 5d/w	Xbox 360 console with the kinetic movement sensor	Commercially available	VR combined with sham tDCs	20 min. 5d/w	2w	1 month
Gatica Rojas et al.* [48] 2017 Chile	Matched Pairs RCT	VR	30 min. 3d/w	Wii-Fit Plus with Nitnendo Wii-Balance Board	Commercially available	Standard P.T	40 min. 3d/w	6w	8th w 10th w
Sajan et al. [49] 2017 India	Pilot, Parallel group RCT	VR + Rehab	VR: 45 min. 6d/w CT: 5 h 15 min. 6d/w	Wii Nintendo	Commercially available	Rehab	6 h. 6d/w	3w	–

RCT randomized controlled trial, *SB-RCT* single-blinded randomized controlled trial, *VR* virtual reality, *CT* conventional therapy which includes physiotherapy and occupational therapy, *min* minutes, *d* day, *w* weeks, *CIMT* constraint-induced movement therapy, *DB-RCT* double-blinded randomized controlled trial, *tDCS* transcranial direct current stimulation, *P.T.* physiotherapy, *Rehab* rehabilitation, *h* hour

*Included by contact the authors

titles and abstracts of the remaining identified citation. Finally, a total of 19 studies were included in our review based upon full-text examination.

Characteristics the included studies

A detailed information about the study populations, study interventions strategy and outcomes measured is shown in Tables 1, 2 and 3.

Studies participants

A total of 645 participants were recruited with a 570 were who continued to the post-intervention assessments. Sample size ranged from 16 to 102 participants. The majority of the recruited participants were males 299 (54.56%) from a total of 548 participants in 15 studies which specify the participants sex with 6 of them removed the withdrawn participant (dropped-out) from the personal characteristics [32, 35, 38, 43, 47, 56], while 3 studies did not specify the gender of the both groups [37, 40, 41]. The mean age was ranging from 7.05 to 11.67 years in the experimental group and from 7.25 to 12.4 in the control group with two study did not report the mean for each group [40, 41]. Participants in seven of the selected trials were hemiplegic [34, 36, 38, 42–45] with mixed topographical distribution in five [32, 37, 48, 49, 56], diplegic in four [35, 39, 42, 46], whereas three did not clarify the distribution of CP [40, 41, 47]. At least 55.56% (355) of the patients

Table 3 Studies outcomes

Study, Year	Outcome measure	ICF B	ICF A	ICF P	Results	Cochrane	Pedro	Level of evidence	Setting
Chen et al. [32] 2012 Taiwan	BOTMP	√	√		Gross motor function did not improved, however, muscle strength- especially knee flexors at different angular velocities- improved	Poor quality	5 (moderate)	2a (limited)	Home
	Isokinetic Dynamometer	√							
Ramstrand and Lygnegåd [33] 2012 Sweden	Modified sensory organization test	√			No significant difference was observed between testing occasions for any of the balance measures investigated	Poor quality	2 (low)	2b (limited)	Home
	Reactive balance	√							
	Rhythmic weight shift		√						
Rostami et al. [34] 2012 Iran	PMAL		√	√	Improved quantity and quality of UE movements and speed and dexterity via CIMT in VR	Poor quality	6 (moderate)	1b (strong)	Laboratory
	BOTM (subset 8)	√	√						
Druzibicki et al. [35] 2013 Poland	3D Temporo-spatial and kinematic gait analysis	√			There was no a statically difference between the baseline and post-intervention assessment. At the end of intervention, there was a slight improvement in walking speed in both groups. Improvement in the mean walking speed was not significantly different between the groups. Range of motion decreased slightly in both groups, and the difference between mean amounts of change was not significant. There was significant improvement in maximal range of flexion in the hip joint in the study. It was shown that with a decrease in the mean value of adduction in hip joint, the mean walking speed increased	Poor quality	5 (moderate)	2a (limited)	
Chiu et al. [36] 2014 Taiwan	Joint Kinematics	√			Coordination, strength or hand function did not improve, however, hand function according to carers perception improved	Poor quality	7 (high)	1b (strong)	Home
	Dynamometer	√							
	Nine-hole peg test		√						
	JTTHF		√						
	Functional Use Survey			√					

Table 3 (continued)

Study, Year	Outcome measure	ICF B	ICF A	ICF P	Results	Cochrane	Pedro	Level of evidence	Setting
Gilliaux et al. [37] 2015 Belgium	UE Kinematics	√			Improved UE kinematics and manual dexterity but functional activities and social participation did not improved	Poor quality	5 (moderate)	2a (limited)	Rehabilitation department
	BBT		√						
	QUEST		√						
	Modified Ashworth Scale	√							
	Hand-Held dynamometer	√							
	Abilhand-Kids		√						
	PEDI		√	√					
	Life Habits			√					
James et al. [38] 2015 Australia	AMPS		√	√	Improvement in ADL motor and processing skills, occupation performance, goal attainment, visual processing and speed and dexterity of the dominant UE, however, impaired UE trended toward improvement	Poor quality	7 (high)	1b (strong)	Home
	AHA		√						
	JTTHF impaired UE		√						
	JTTHF dominant UE		√						
	MUUL	√	√						
	COPM			√					
	TVPS-3	√							
Greeco et al. [39] 2015 Brazil	3D Temporo-spatial and kinematic gait analysis	√			The experimental group had a better performance regarding gait velocity,cadence, gross motor function,independent mobility and motor evoked Potential	Poor quality	5 (moderate)	2a (limited)	Clinic
	GMFM		√						
	PEDI		√	√					
	Motor evoked potential	√							
Zoccolillo et al. [40] 2015 Italy	QUEST		√		QUEST scores significantly improved only after VR intervention, while the Abilhand-kids scores improved significantly after CT. Quantity of performed movements was three times higher in VGT than in CT. No significant changes in VMI scores occurred in both groups	Poor quality	4 (low)	2a (limited)	Clinic
	Abilhand-Kids		√						
	VMI	√							

Table 3 (continued)

Study, Year	Outcome measure		ICF B	ICF A	ICF P	Results	Cochrane	Pedro	Level of evidence	Setting
Cho et al. [41] 2016 Korea	Digital manual muscle tester		√			GMFM (standing) Gait and balance improved significantly in VR treatment training group compared to treadmill training group	Poor quality	6 (moderate)	1b (strong)	Clinic
	GMFM			√						
	PBS			√						
	Walking	10 MWT (speed)		√						
		2 MWT (endur)		√						
	Posturographic measures		√							
Acar et al. [42] 2016 Turkey	QUEST			√		Improved UE functions, speed, manual ability and independence level in ADL	Poor quality	6 (moderate)	1b (strong)	Clinic
	JTTHF			√						
	Abilhand-Kids			√						
	WeeFIM-self-care			√						
Ürgen et al. [43] 2016 Turkey	GMFM			√		Both groups had significant improvements in the GMFM and GMPM scores, durations of single leg and tandem standing, and PBS. The intervention group had more significant improvements in the mean duration of the TUG test and number of jumping than the control group. However, When the groups were compared post-intervention, the GMFM, the GMPM and PEDI scores were similar	Poor quality	8 (high)	1b (strong)	Clinic
	GMPM			√						
	Standing duration on flat and soft surfaces with eyes open and eyes closed		√							
	Single leg standing duration		√							
	Tandem standing duration		√							
	Number of jumping on single leg		√							
	TUG			√						
	PBS			√						
	Failing status									
	PEDI			√	√					
Bedair et al. [44] 2016 Egypt	PDMS-2			√		Improved hand skills and visual motor skills of UE	Poor quality	6 (moderate)	1b (strong)	Clinic
	Abilhand-Kids			√						

Table 3 (continued)

Study, Year	Outcome measure	ICF			Results	Cochrane	Pedro	Level of evidence	Setting
		B	A	P					
Uysal and Baltaci [45] 2016 Turkey	PEDI		√	√	Self-care, mobility, PEDI total, PBS and performance of COPM scores increased in the VR group after intervention. Self-care, mobility and total PEDI increased in the control group as well. However, there was no statistically significant difference found between the groups, except for PBS	Poor quality	5 (moderate)	2a (limited)	Clinic
	PBS		√						
	COPM			√					
Tarakci et al. [34] 2016 Turkey	FFRT		√		After the intervention, changes in balance scores and independence level in activities of daily living were significant in both groups. Statistically significant improvements were found in the Wii-based group compared with the control group in all balance tests and total WeeFIM score	Poor quality	4 (low)	2a (limited)	Rehabilitation unit
	FSRT		√						
	TGGT		√						
	STST	√							
	Wii Nintendo Fit Balance & Game Scores		√						
	10 mWT		√						
	10 sCT	√							
	WeeFIM		√						
Wallard et al. [46] 2017 France	3D full-body kinematic gait analysis	√			Between-group comparison shows significant differences for head, shoulder, elbow, knee and ankle kinematics and GMFM. However, parameters for the thorax, pelvis and hip angles show no significant differences No significant intragroup differences for the CG were shown in the terms of body kinematics and GMFM.On the other hand, significant differences are shown for intragroup comparison for TG for head, shoulder, elbow, knee and ankle and GMFM	Poor quality	6 (moderate)	1b (strong)	Laboratory
	GMFM		√						

Table 3 (continued)

Study, Year	Outcome measure		ICF B	ICF A	ICF P	Results	Cochrane	Pedro	Level of evidence	Setting
Lazzari et al. [47] 2017 Brazil	Static balance	Stabilometric evaluation COP "force plate"	√			Statically post-intervention & follow-up effects favoring the experimental group over the control group with regard to the PBS & TUGT & the area of oscillation of COP when standing on force plate	Poor quality	8 (high)	1b (strong)	Lab
	Functional balance	PBS		√						
		Timed up and Go test		√						
Gatica Rojas et al. [48] 2017 Chile	Posturographic measures including COP sway area, standard deviation and velocity of COP		√			Wii therapy significantly reduced the COP_{sway} and SD_{AP} in the eyes-open condition In Spastic hemiplegia, however, the effects wane after 2-4 h	Poor quality	6 (moderate)	1b (strong)	Rehabilitation unit
Sajan et al. [49] 2017 India	Static posturography		√			Improved postural control and balance, UE function, visual perceptual skills and functional mobility	Poor quality	7 (high)	1b (strong)	Clinic
	PBS			√						
	BBT			√						
	QUEST			√						
	TVPS-3		√							
	walking speed and distance			√						

BOTMP burininks osteretsky test of motor proficiency, *PMAL* pediatric motor activity log, *JTTHF* Jebsen Taylor test of hand function, *UE* upper extremity, *BBT* box and blocks test, *GMPM* growth motor, *QUEST* quality of performance measure, upper extremity skills test, *PEDI* pediatric evaluation of disability inventory, *AMPS* Assessment of Motor and Process Scale, *AHA* assisting hand assessment, *MUUL* melbourne assessment of unilateral upper limb function, *COMP* Canadian occupational performance measure, *TUG* timed up and go test, *FFRT* functional forward reach test, *FSRT* functional sideway reach test, *TGGT* timed get up and go test, *STST* sit-to-stand test, *10 mWT* 10 min walking test, *10s CT* 10 s climbing test, *GMFM* growth motor functional measure, *COP* center of pressure, *TVPS-2* test of visual and perceptual skills-2nd edition, *PDMS-2* Peabody Developmental Motor Scale-2, *WeeFIM-self-care* functional independence measure, *PBS* Pediatric Balance Scale

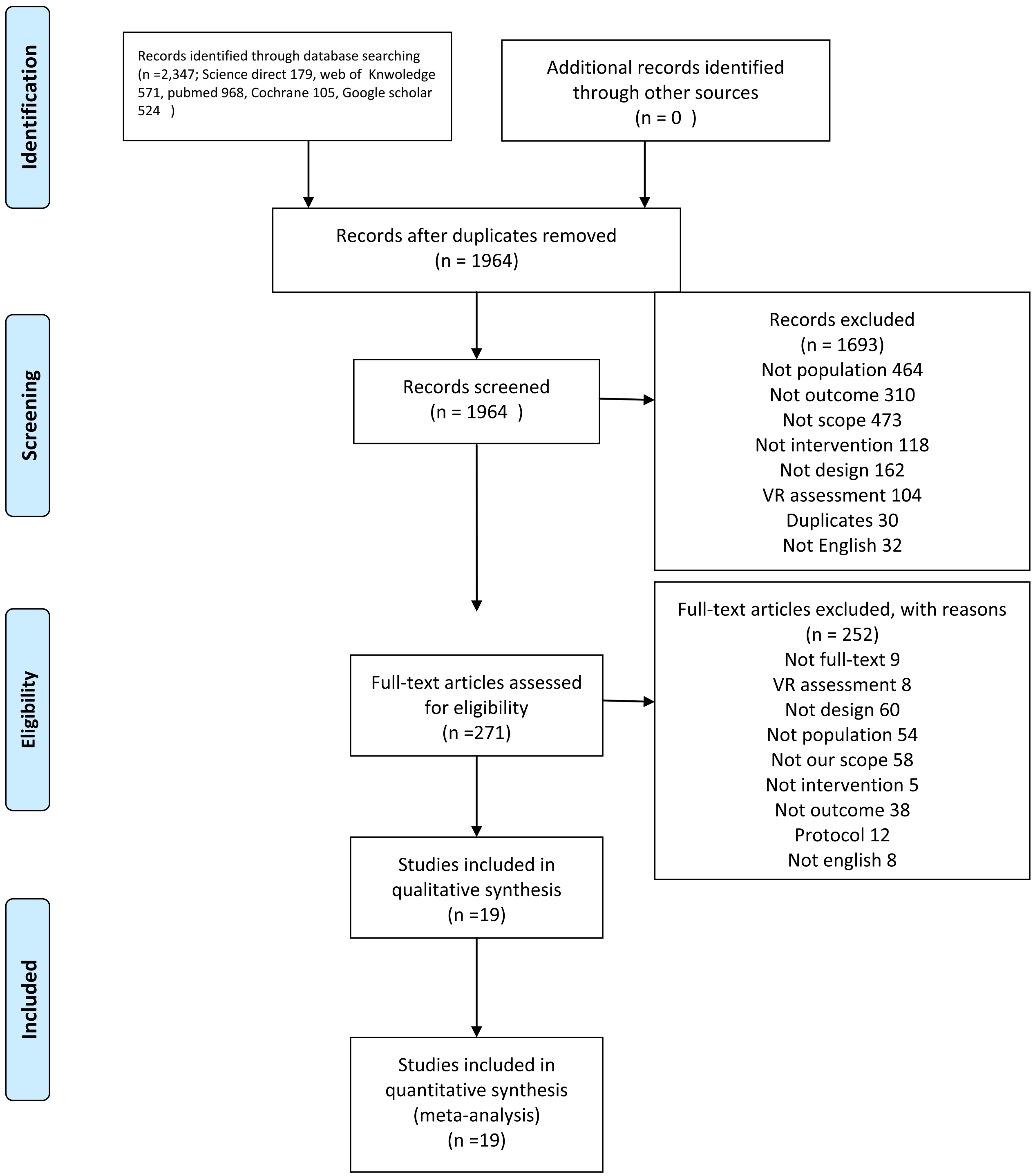

Fig. 1 PRISMA flow diagram

were affected by spastic hemiplegic, 128 (20.03%) with spastic diplegic CP, 10 (1.56%) with spastic quadriplegic, 5 (0.78%) with triplegic forms of CP.

Types of intervention

One of the included studies had a four comparison arms, comparing VR and rehabilitation to constraint-induced movement therapy (CIMT) and rehabilitation to VR,

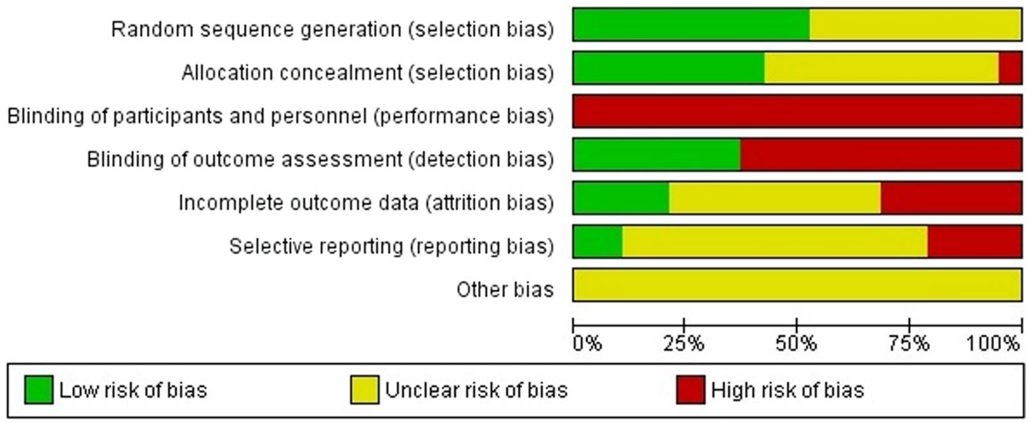

Fig. 2 Forest plot of the effect of VR on fine motor coodination in children with CP

CIMT and rehabilitation to rehabilitation alone [34]. Two groups (VR versus control group (CG)) were selected for inclusion in our review. However, all the other studies had two arms comparing either VR alone or when combined with usual care or VR training with transcranial direct current stimulation to usual care or no intervention or sham transcranial current direct stimulation. In the term of sophostication, fifteen studies utilized the commercially low-cost sets, whereas four used the engineer-built. Participants in fourteen studies received VR as an adjunctive therapy to conventional treatment, whereas others in another three studies received VR alone and in two studies, the participants received VR followed by a period of conventional treatment or no treatment or vice versa utilizing a crossover design. Location of VR therapy varied from laboratory, clinic or home-based. An overview of the characteristics of the eligible studies is presented in Table 2.

Types of outcome measures

A variety of assessment tools were used to evaluate different aspects of neuromotor status (e.g., coordination, strength, muscle tone) and functional performance.

The International Classification of Function (ICF) outlines two main domains of function for assessment: body function and structure domain and activity and participation domain (subdivided into activity subdomain and participation subdomain).

Through the use of ICF classification, we found that the majority of the outcome measures used in the included studies fit within the activity subdomain of the ICF model with lesser extent measures falling under the body function and structure domain while the participation domain having the least number of outcome measures. Table 3 represents different assessment scales used with their ICF classification.

Fine motor coordination

Under the body function and structures lies joint kinematics and Visual Motor integration (VMI) test, whereas Jebsen Taylor Test of Hand Function (JTTHF), Nine-hole Peg test and Peabody Developmental Motor Scale-2 PDMS-2 assess activity. BurininksOsteretsky Test of Motor Proficiency (BOTMP) "subset 8" lies under both categories.

JTTHF was used in three studies, joint kinematics, VMI test, PDMS-2 and Nine-hole Peg test are used once.

Gross motor coordination

Under the body function and structure lies Modified sensory organization test, reactive balance, Static Posturography, joint kinematics, 10 s climbing test (10s CT), standing durations, 3D temporo-spatial and full-body kinematic gait and motor evoked potential analysis, while Pediatric balance scale (PBS), Box and Blocks test (BBT), Rhythmic weight shift, Walking Speed and Distance, 10 min walking test (10m WT),sit-to-stand test(STST), Timed up and Go test, functional reaching tests, Wii Nintendo Fit Balance and Game Scores lie under the activity section of coordination. BOTMP-2 lies under both categories.

PBS was used in five studies, stabilometric evaluation center of pressure (COP) in 4, 3D temporo-spatial and full-body kinematic gait analysis, timed up and go (TUG) in 3, joint kinematics and BBT twice and Modified sensory organization test, reactive balance, Rhythmic weight shift, 10 sCT, STST, standing durations, Walking Speed & Distance, 10 m WT, functional reaching tests, Wii Nintendo Fit Balance & Game Scores and motor evoked potential were used once.

Intervention protocols

Studies used different treatment strategies with different durations from 3 up to 20 weeks, session duration

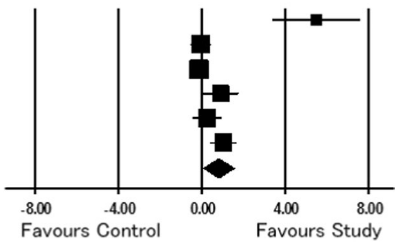

Fig. 3 Forest Plot ofthe effect of VR on gross motor coordination in children with CP

ranging from 15 to 90 min and frequency 2 to 6 sessions/week.

Effect of interventions

Fine motor coordination

Six studies provided post-intervention assessment of fine motor coordination on 255 participants [34, 36, 38, 40, 42, 44]. There was a low certainty level according to Cochrane RoB that VR a large beneficial effect than the controls immediately post-intervention (SMD 0.75, 95% CI 0.02–1.51) (Fig. 2). Between-study heterogeneity was considerable ($I^2 = 86\%$). On the other hand, when assessed by modified Sackett scale, the overall evidence for fine motor coordination was moderate that VR intervention is better than the control groups (83.3% $n = 5$ studies were scored as Ib).

Gross motor coordination

Fourteen studies on 363 children with CP were found to carry a low certainty level with respect to Cochrane RoB about the non-significant small beneficial effect on gross motor coordination brought out immediately following VR (SMD 0.15; 95% CI, 0.09 to 0.40) [32, 33, 35–37, 39, 41, 43, 45–49, 56] (Fig. 3). On modified Sackett's scale, 55.04% of studies have a moderate evidence. Between-study heterogeneity was negligible ($I^2 = 24\%$). Since only 55.04% of the studies carry a moderate evidence, pooling of individual evidence scoring for each study to reach the overall evidence outweighs a limited evidence.

Correlation of the total scores obtained with both quality scales

There was a non-significant difference between Cochrane RoB and PEDro scores (p value = 0.248) carrying a fair positive correlation ($r = 0.28$). The degree of overall agreement between the total scores of the two quality scales was slight ($\kappa = 0.02$; (95% CI −0.02 to 0.50) with non-significant difference (p value = 0.433).

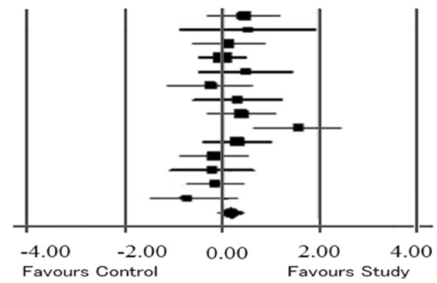

Fig. 4 Risk of bias: each risk of bias item presented as percentages across all included studies

High and low PEDro scores revealed moderate agreement with Cochrane RoB ($\kappa = 0.43$ (95% CI 0.36–0.49) and 0.46; (95% CI 0.40–0.51)), respectively, with a significant difference ($p = 0.0001$) for both. However, when compared with Cochrane RoB, moderate quality studies on PEDro exhibited slight agreement with no significant difference ($\kappa = 0.10$; (95% CI −0.09 to 0.29), $p = 0.404$).

Quality assessment

Figure 4 and Table 4 display a summary of the quality appraisal scores for each study by Cochrane RoB and PEDro, respectively. Scores were heterogeneous depending on the trial and the quality scale used. When assessed by Cochrane risk of bias assessment tools, all the included studies are considered to have a high risk of bias.

Whereas, when assessed by PEDro scale, more than half of the included studies (57.9%, $n = 11$) were of moderate quality [32, 34, 35, 37, 39, 41, 42, 44–46, 48], about the quarter of studies (26.13%, $n = 5$) of a high quality [36, 38, 43, 47, 49], whereas three studies (15.8%) were of a low quality [33, 40, 56].

Discussion

The objective of this systematic review was to synthesize the state of the evidence about the effect of virtual reality training on motor coordination in children with cerebral palsy. In order to achieve this aim, a list of strict eligibility criteria were set, nineteen RCTs matching the pre-defined inclusion criteria were evaluated for methodology and the reported results being analyzed statically.

This systematic review could not provide a firm conclusion about the superiority of VR therapy over usual care or no intervention for motor coordination in children with CP. The results revealed that there is a moderate evidence when assessed by modified Sackett scale in favor of VR for fine motor coordination. On the other hand, there was a conflicting evidence for gross motor coordination when assessed by modified Sackett scale moderate

Table 4 PEDro scores

Study	Eligibility criteria	Random allocation	Allocation concealment	Baseline similarity	Blind subject	Blind therapist	Blind assessor	Adequate follow-up	ITT	Between-group comparison	Point estimate
Chen et al. [32] 2012 Taiwan	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes
Ramstrand and Lygnegåd [33] 2012 Sweden	Yes	Yes	No	No	No	No	No	No	No	Yes	No
Rostami et al. [34] 2012 Iran	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes
Druzibicki et al. [35] 2013 Poland	No	Yes	No	Yes	No	No	Yes	No	No	Yes	Yes
Chiu et al. [36] 2014 Taiwan	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes
Gilliaux et al. [37] 2015 Belgium	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes
James et al. [38] 2015 Australia	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes
Greeco et al. [39] 2015 Brazil	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Zoccolillo et al. [40] 2015 Italy	Yes	Yes	No	No	No	No	Yes	No	No	Yes	Yes
Cho et al. [41] 2016 Korea	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes
Acar et al. [42] 2016 Turkey	No	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes

Table 4 (continued)

Study	Eligibility criteria	Random allocation	Allocation concealment	Baseline similarity	Blind subject	Blind therapist	Blind assessor	Adequate follow-up	ITT	Between-group comparison	Point estimate
Ürgen et al. [43] 2016 Turkey	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes
Bedair et al. [44] 2016 Egypt	Yes	Yes	Yes	No	No	No	No	No	No	Yes	Yes
Uysal and Baltaci [45] 2016 Turkey	Yes	Yes	Yes	No	No	No	No	Yes	No	Yes	Yes
Tarakci et al. [34] 2016 Korea	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes
Wallard et al. [46] 2017 France	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes	Yes
Lazzari et al. [47] 2017 Brazil	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes
Gatica Rojas et al. [48] 2017 Chile	Yes	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes
Sajan et al. [49] 2017 India	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes

to limited. Pooled results showed non-significant small effect of VR-based therapy for gross motor coordination.

Although Cochrane RoB and PEdro scales share the same scoring domains (PEDro has 71.4% of Cochrane scale), the quality of the included studies showed a great rating variations upon assessment by both. This variation is mainly due to different and more restrictive judgment criteria of Cochrane risk of bias than PEDro scale. All the included studies were rated as poor quality when assessed by Cochrane risk of bias; which is to a great extent due to incomplete blinding. Because of the nature of treatment using VR, this criteria could not be satisfied. Surprisingly, even if they were assessed again as having an adequate quality on Cochrane on the basis of generation of random sequence, concealment of allocation, and blinding of outcome assessors, the association and overall agreement between PEDro and Cochrane scores were only fair and slight, respectively. However, categorical agreement between PEDro and RoB was only moderate on the extreme categories (high and low) because the precise methods of randomization and concealment and blinding were accidently reported in many studies while the vast majority moderate ranks on PEDro (11 studies) were slightly agreed with RoB ranks which is logic because most of these studies ranked poor on RoB because the actual methods of randomization or concealment were not reported as required by RoB.

The improvement brought out through VR relies mainly on motor learning which requires many elements available in VR. This includes repetitions, feedback and motivation [57]. VR provides an opportunity for trial and error practice which requires a lot of repetitions together with feedback about performance success provided by the senses (e.g., vision, proprioception) can produce an incremental success and structural cortical changes [58]. But to practice movements more and more, participants must be motivated [58]. Unlike traditional exercise programs, VR not only allow repetitive practice but also engage the cognitive functions in problem solving for better motor learning [59]. Also, VR allows training in a real-world-simulated environment for better performance transfer.

The non-significant small treatment effect size of VR gross motor coordination may be attributed to incorporation of the commercially available VR devices which are not designed to be modified to meet the needs for children with physical impairments. Also, use of the immersive type of VR may improve the results as they enhance the sense of being present.

Adverse events

Only seven studies out of the nineteen studies clearly stated that there were no adverse effects of using VR occurred during their studies [32, 36–39, 48, 49], however, the remaining studies did not report the possible adverse events [33–35, 40–47, 56].

Limitations

The findings of this review are limited to non-immersive VR devices. So, we cannot generalize the effect of VR on motor coordination unless more studies including the immersive types of VR are performed. Several limitations of this review have been identified.

Although in-depth literature search was carried out, because resources were limited, we included only studies published in the English language, potentially excluding other important evidence. Four studies were published in a language other than English. However, the possibility of publication bias could not be excluded, as we did not attempt to retrieve unpublished studies. The potential effects of VR training dosage, game selection and case severity on the effectiveness of VR could not be ascertained because of large heterogeneity in reported data.

Research implications

A more rigorous well designed RCTs with larger sample sizes need to be conducted regarding the effect of virtual reality in children with CP impairing motor coordination with investigation of the optimal duration and frequency of virtual reality. Also, the more immersive types of VR should be recruited.

Conclusion

This systematic review yielded a moderate evidence about large effect of virtual reality on fine motor coordination in children with cerebral palsy when compared to other interventions and conflicting evidence that virtual reality could carry larger effect on gross motor coordination in the intervention group than the control group. Nevertheless, virtual reality could be used safely as a supplemental intervention for motivating children engaging in therapy. PEDro scale demonstrated a fair correlation when compared with Cochrane RoB, so development and validation of a more compatible quality assessment tools specific to physical therapy trials are needed.

Abbreviations
CP: Cerebral palsy; VR: Virtual reality; PEDro: Physiotherapy evidence database; RoB: Risk of bias; UEs: Upper extremities; RCTs: Randomized controlled trials; PRISMA: Preferred reporting items for systematic reviews and meta-analyses; MeSH: Medical subject heading; PICOS: Population, intervention, comparison/control, outcome and study design; ICF: International classification of functioning, disability and health; SMDs: Standardized mean differences; CIMT: Constraint-induced movement therapy; CG: Control group; JTTHF: Jebsen Taylor test of hand function; PDMS-2: Peabody Developmental Motor Scale-2; BOTMP: Burininks osteretsky test of motor proficiency; VMI: Visual motor integration; 10s CT: 10 Seconds climbing test; PBS: Pediatric balance scale; BBT: Box and blocks test; 10m WT: 10 Minutes walking test; COP: Center of pressure; TUG test: Timed up and go test.

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SE and NA contributed to systematic search and filtration. MA and SE contributed to data extraction. SE and NA contributed to quality assessment. MA and SE contributed to manuscript revision. All authors read and approved the final manuscript.

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Declarations

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Not applicable.

Consent for publication
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Competing interests
The authors have indicated they have no potential conflicts of interest to disclose.

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