Effectiveness of Virtual Reality in Children With Cerebral Palsy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Background. Researchers recently investigated the effectiveness of virtual reality (VR) in helping children with cerebral palsy (CP) to improve motor function. A systematic review of randomized controlled trials (RCTs) using a meta-analytic method to examine the effectiveness of VR in children with CP was thus needed.

Purpose. The purpose of this study was to update the current evidence about VR by systematically examining the research literature.

Data Sources. A systematic literature search of PubMed, CINAHL, Cochrane Central Register of Controlled Trials, ERIC, PsycINFO, and Web of Science up to December 2016 was conducted.

Study Selection. Studies with an RCT design, children with CP, comparisons of VR with other interventions, and movement-related outcomes were included.

Data Extraction. A template was created to systematically code the demographic, methodological, and miscellaneous variables of each RCT. The Physiotherapy Evidence Database (PEDro) scale was used to evaluate the study quality. Effect size was computed and combined using meta-analysis software. Moderator analyses were also used to explain the heterogeneity of the effect sizes in all RCTs.

Data Synthesis. The literature search yielded 19 RCT studies with fair to good methodological quality. Overall, VR provided a large effect size (d = 0.861) when compared with other interventions. A large effect of VR on arm function (d = 0.835) and postural control (d = 1.003) and a medium effect on ambulation (d = 0.755) were also found. Only the VR type affected the overall VR effect: an engineer-built system was more effective than a commercial system.

Limitations. The RCTs included in this study were of fair to good quality, had a high level of heterogeneity and small sample sizes, and used various intervention protocols.

Conclusions. When compared with other interventions, VR seems to be an effective intervention for improving motor function in children with CP.

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Cerebral palsy (CP) is the leading cause of childhood physical disabilities, affecting around 2 to 3 children per 1,000 live births.[1–3] CP is caused by damage to 1 or more areas of the developing brain which affect body movements, posture, and coordination.[4] The symptoms of CP vary, but all individuals with CP have problems in motor function and are often accompanied by disturbances of sensation, perception, cognition and communication.[3,4] The International Classification of Functioning, Disability and Health (ICF) model has been used extensively as a theoretical framework to understand the health-related outcomes of children with CP.[5–7] For example, a child with CP may have impaired "body structure and function" (eg, spasticity, range of motion limitations, muscle weakness, impaired sensation and impaired coordination), limited "activity" (eg, difficulty in maintaining and changing body positions, unstable walking and moving around, poor fine motor function, and unable to perform activities of daily living), and restricted "participation" (eg, difficulty in engaging in sports activities with peers in school or other life situations).[7] Moreover, environmental factors (eg, physical accessibility to a basketball court) that include accessibility, availability, opportunity, support, and attitudes of the settings where children live and personal factors (eg, age, motivation, priority and goals, CP type) are influential to the achievement of health and health-related outcomes (ie, body structure and function, activities, and participation) in children with CP.[6,7] Consequently, a plan of care for children with CP should not only consider improving their impaired body structure and function, limited activity, restricted participation, but also changing environmental and personal factors to have an optimal effectiveness.[6,7]

Virtual reality (VR) (eg, Xbox Kinect [Microsoft, Redmond, Washington], Wii [Nintendo, Kyoto, Japan]) has recently been explored as an intervention to improve motor function in children with CP. Virtual reality is defined as "the use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear to be and feel similar to real-world objects and events."[8] VR applications use interactive simulations that respond to a user's movement such that a child can interact within a virtual environment while performing functional activities.[9,10] Levac et al[11] summarized several "active ingredients" (ie, attributes) that VR can provide to help children improve in rehabilitation: VR system and games create an exercise environment in which children can increase duration, intensity, and frequency of practice. VR can provide an ecologically valid environment that is similar to the real world so children can perform task-specific practices.[11] In the virtual environment, task difficulty can be easily adjusted to provide sufficient challenge for a child while playing.[11] It can also provide immediate visual and auditory feedback that is related to task performance or results.[11] VR games can provide children opportunities for problem-solving through task-driven training to optimize motor learning, which can later lead to neuroplasticity changes.[11] Because of the game features and animation, VR can increase children's motivation and engagement during playing.[11] Moreover, VR offers social play opportunity for participating in play situation, and increases support from family members, peers, teachers, and therapists.[11] Therefore, through these attributes, VR can effectively improve the child's impaired body structure and function (eg, improved range of motion, increased muscle strength) and decrease limited activity (eg, improving reaching ability, grasping function, or ambulation ability) as well as influence the child's "personal factors" (eg, increased motivation and confidence).[12,13] Moreover, virtual environments can directly shape the "environmental factors" by decreasing the environmental barriers (eg, ease task difficulty by decreasing the required range of motion of finger flexion), increasing the roles of the supportive persons from family, siblings, or friends (eg, decreasing personal assistance).[11–13] The optimal goal of using VR intervention is to assist children in increasing their participation in the real-world environment by gradually overcoming and adapting all the possible environmental barriers via interaction in the virtual environment and transferring the learned skills to the real world.[13] However, whether the learning occurred in the virtual environment can successfully transfer to real world is still inconclusive and depends on the user characteristics and contextual factors.[13,14]

Studies investigating effectiveness of VR in children with CP have shown some effect on improving ambulation, postural control, and arm function.[15–19] In our previous meta-analysis,[16] which included 3 randomized controlled trials (RCTs) and 11 case series that examined the effect of VR on arm function in children with CP, we found VR overall provided a strong effect size (d = 1.00) when comparing between post-VR and pre-VR interventions. When the outcome variables were further broken down according to the ICF model, a large effect was reported in participation (d = 1.92), a small effect on activity (d = 0.46), and a medium effect on body structure and function (d = 0.70).[16] In addition, the subgroup analyses showed younger children receiving home or laboratory-based VR and using an engineer-built VR system had a better effect.[16] Dewar et al[18] examined the exercise interventions to improve postural control in children with CP and included 3 studies with level II and level III evidence[20] that used VR as the intervention. This study showed a conflicting result regarding whether VR could enhance postural control in children with CP: 2 studies showed improvement in standing balance and 1 showed no improvement in functional standing balance.[18] Bonnechère et al[19] included 31 studies (7 RCTs, 16 cohort studies, and 8 single-case studies) to examine the effect of "serious gaming" (defined as games whose primary focus is not pure entertainment) in pediatric rehabilitation. The authors concluded it was difficult to compare the different studies because of the lack of standardized rehabilitation strategies and different clinical assessment tools.[19] The latter 2 systematic reviews did not report the VR effect in different ICF components.

To the best of our knowledge, no systematic reviews using a meta-analytic method (ie, using statistical method to compute and combine data from multiple studies)[21,22] to examine the effectiveness of VR in children with CP have ever been published, except for our own work in arm function. All these published systematic reviews included very few RCTs (3–7 RCTs only). At least 20 studies using RCT design have been published since the databases were accessed by the authors of the most recently published systematic reviews. Therefore, the 4 aims of this review were to examine the effect of VR in children with CP using a systematic review and meta-analytic approach by adding more RCTs and quantifying effect sizes (Cohen *d*); to classify outcome measures based on the ICF model; to group studies based on the movements the outcome measures of each study intended to evaluate (ie, arm function, postural control, and ambulation); and to identify the association between the VR effect and key characteristics of the child (eg, CP type, age) as well as aspects of the intervention protocol (eg, intervention setting, intervention dosage).

Methods

Data Sources and Searches

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement to conduct this review.[23,24] Two authors (Y.C., H.D.F.) independently conducted systematic literature searches in December 2016, using the electronic databases: PubMed, CINAHL, Cochrane Central Register of Controlled Trials, ERIC, PsycINFO, and Web of Science, as well as a manual search of the reference lists of each article. Keywords or mesh terms (if applicable) used for the search included the following: virtual reality, virtual reality exposure therapy, virtual realities, virtual environment, computer game(s), Kinect, Wii, Playstation, videogame(s), active game(s), serious game(s); cerebral palsy, cerebral palsies, Little disease, infantile palsies, spastic diplegia(s), spastic diplegic, spastic hemiplegia(s), spastic hemiplegic, spastic quadriplegia(s), spastic quadriplegic; upper extremity, arm, upper limb, reach, grasp, grip, fine motor, gait, walking, leg, gross motor, ambulation, lower extremity, trunk, torso, posture, balance, postural control. An example of the search strategy used in PubMed is provided in the Appendix.

Study Selection

The 5 inclusion criteria for studies to be included in this systematic review/meta-analysis were as follows: participants in the study were children who had CP and were aged between birth and 21 years old; the study compared VR with a conventional therapy (eg, usual care) or control group (eg, no intervention); the outcome measures used in the study were related to motor function, such as arm function, walking, or postural control; the study design was an RCT or randomized cross-over design; and the study was written in English or Chinese. Studies were excluded if the study did not provide sufficient data to compute the effect size (eg, no standard deviations), or if the study was designed to compare the immediate response after being exposed to VR for a short period of time (eg, 60 minutes) without receiving a VR-related intervention in weeks.

Data Extraction and Quality Assessment

A meta-analysis coding template was created and used to code the demographic, methodological, and miscellaneous variables extracted from each RCT by following the methods suggested by Cooper and Hedges.[21] Demographic data included children's age, ethnicity, gender, diagnosis, severity, cognitive status, and other disabilities associated with the participants. Sample size, sampling method, type of movement investigated, VR type (eg, commercially available systems: Kinect, Wii), VR dosing (duration, intensity, length, total treatment duration), comparison therapy type, dosing in the comparison therapy, and instruments used to measure outcome variables were coded as methodological variables. Year of publication, name of the authors, country, and affiliation of the authors were included in the miscellaneous variables.

The quality of RCTs was evaluated using the Physiotherapy Evidence Database (PEDro scale).[25] The PEDro scale includes 11 items with 1 item assessing the external validity and 10 items assessing the internal validity (including random allocation, concealment of allocation, baseline equivalence, blinding procedure, intention to treat analysis, adequacy of follow-up, between-group analysis, and consideration of data variability). A total of 10 points could be yielded from evaluating the internal validity of each study, with scores of 9 to 10 representing "methodologically excellent," 6 to 8 representing "good," 4 to 5 representing "fair," and less than 4 representing "poor."[26]

Relevant information from the included studies was extracted and coded by the same author (Y.C.). A second reviewer (H.D.F.) checked all the extracted data. Any discrepancies were resolved by discussion in order to reach a consensus.

Data Synthesis and Analysis

The extracted outcome measures of each RCT were converted to a standard format by calculating the standardized mean difference (Cohen *d*), which is referred to as effect size (ES) throughout this review. The ES calculation was set up so that a positive ES indicated favoring VR efficacy. For studies in which means, standard deviations, and samples were reported, standardized mean differences were calculated using the pooled standard deviations as detailed by Borenstein et al.[22] If the study contained more than 1 outcome variable, which produced multiple effect sizes, standardized mean differences and variances were averaged to represent that study. After computing the effect size of each study, all the effect sizes were combined to form a common estimate of effect size. In addition, the outcome measures of each RCT were also classified using the ICF model as body structure and function, activity, and participation components. If each ICF component within 1 RCT study produced multiple ES, standardized mean differences and variances were also averaged to represent the specific ICF component of that study and then all ES from all RCTs of the same ICF component were combined to form a common estimate of effect size. Similar methods were applied

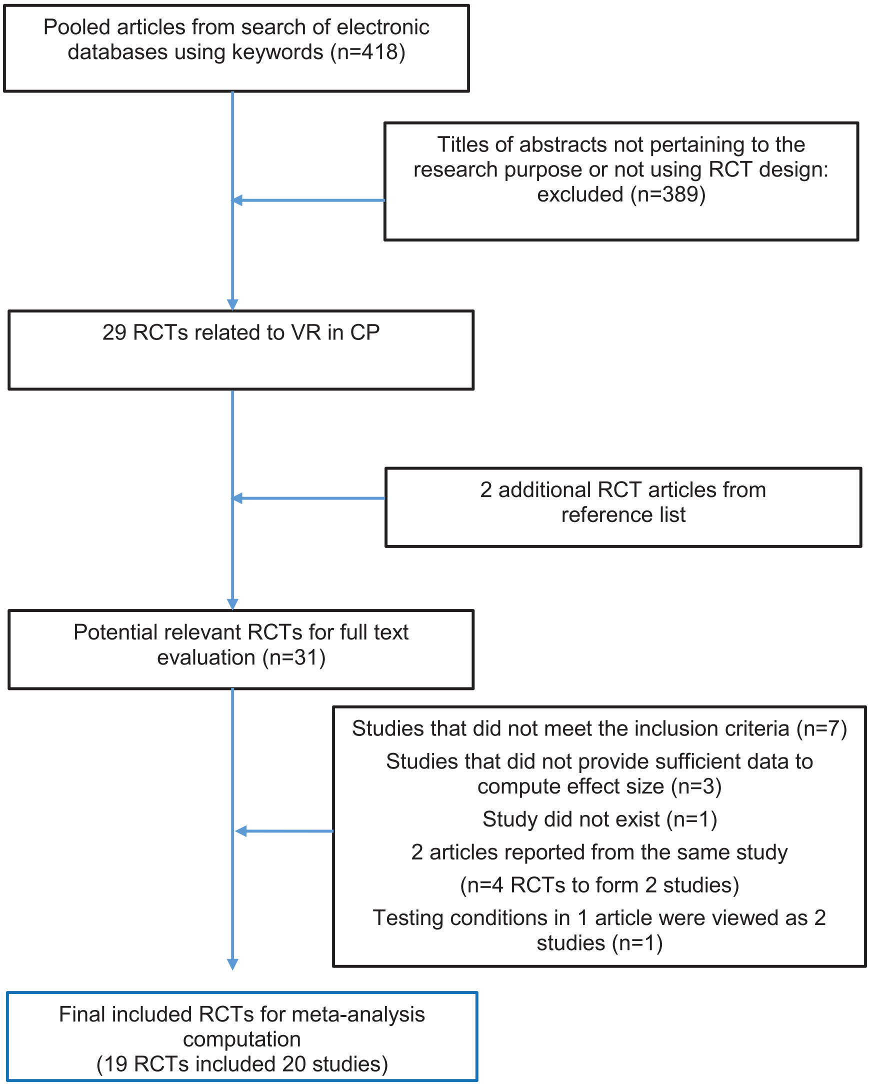

Figure 1.
Flow diagram of numbers of studies identified, excluded, and finally included in this meta-analysis. CP = cerebral palsy, RCT = randomized controlled trial, VR = virtual reality.

to obtain the common estimate of effect size when grouping the outcome measures based on different motor function (ie, arm function, ambulation, and postural control). Heterogeneity tests and *z* scores were also computed and reported. All these computations were calculated using Comprehensive Meta-Analysis software (version 2.2; Biostat Inc, Englewood, New Jersey). All effect sizes were interpreted with the Cohen convention of small (0.2), medium (0.5), and large (0.8).[27] Clinically, a medium effect size (d = 0.5) corresponds to an amount of change that is noticeable to a careful observer.[28–30] That is, a medium effect size that somewhat shows improvement after receiving VR could be perceived by the patients as beneficial and important.

Meta-analyses were run with a random-effects model that accounted for true interstudy variation in effects as well as for random error within studies. We then sought to determine the role of experimental factors in explaining the considerable inter-study variation observed in effect sizes. These experimental factors were treated as moderator variables in a meta-analysis. Meta-regression (using a method-of-moments model) for moderators with continuous values (eg, age) or subgroup meta-analyses for moderators with categorical values (eg, VR system) were used to examine the following 10 potential moderator variables: children's age, CP type, total VR intervention duration, VR daily dosage, VR treatment frequency per week, VR intervention duration in weeks, VR type, intervention setting, presence or not of a dose-equivalent comparison group, and PEDro score.[21,22] The effect of publication bias on the primary meta-analyses was addressed by combining a funnel plot assessment with the Duval-Tweedie trim and fill correction.[22] This is a preferred method for assessing the extent of publication bias as well as for making a correction to the overall effect size.

Results

A total of 418 nonoverlapping published articles were found from the database searches. After reviewing abstracts and titles, 29 RCTs related to VR in children with cerebral palsy were selected for full-text review. Two additional RCT were added after hand searching references in previously published reviews and articles. Thus, a total of 31 RCTs were retrieved for full evaluation (Fig. 1).

Among the 31 RCTs, 11 studies were excluded: 4 studies from the same research group compared VR with additional transcranial direct-current stimulation with VR alone[31–34]; participants in 2 studies were either children with developmental delay or children with an acquired brain injury, not cerebral palsy[35,36]; 1 study compared gait with or without a virtual environment, but did not test the intervention effect,[37] and 3 studies did not provide sufficient data to compute an effect size.[38–40] In addition, Chen et al[41,42] reported the same participants but different outcome measures; therefore, these 2 studies were combined as 1 single study. James et al[43] and Mitchell et al[44] also reported the same participants but different outcome measures; thus, these 2 studies were combined as 1 study. Soares et al[45] had the same citation as Sharan et al,[46] and we could locate only Sharan et al. Thus, Soares et al was excluded from this review. Rostami et al[47] randomly assigned children with CP in 4 different groups: VR alone, VR combined with constraint-induced movement therapy, constraint-induced movement therapy alone, and a control group. We treated this RCT as 2 separate studies: VR alone versus control (Rostami 2012_1) and VR combined with constraint-induced movement therapy versus constraint-induced movement therapy alone (Rostami 2012_2). Because we were interested in comparing VR with conventional therapy, we did not include VR alone versus constraint-induced movement therapy alone in this review. Therefore, a total of 19 studies (in 20 RCTs) that were published between 2002 and 2016 were included in this review.[41–44,46–61]

Description of Studies

The data extracted from the 19 studies are summarized in Tables 1 and 2. There were 504 participants in the 19 studies. The average age of participants ranged from 4.6 to 12.1 years. The VR types used in the studies included Nintendo Wii, PlayStation EyeToy (Sony, Tokyo, Japan), Xbox Kinect, GestureXtreme (GestureTek Health, Toronto, Ontario, Canada), web-based games, and other, engineer-built systems. The mostly commonly used VR system was Nintendo Wii (9/19 studies). VR intervention over the entire study ranged from 8 to 80 hours, and the daily dosage ranged from 20 minutes to 90 minutes. Intervention length ranged from 4 weeks to 20 weeks, and treatment frequency ranged from once per week to 7 d/wk. The focus of the outcome measures included arm function only (8 studies); postural control only (2 studies); combination of postural control and ambulation (4 studies); combination of postural control and arm function (1 study); combination of arm function and ambulation (1 study); and combination of arm function, postural control, and ambulation (4 studies). The PEDro quality scores for the studies ranged from 4 to 8 (4 studies with a score of 4, 4 studies with a score of 5, 3 studies with a score of 6, 3 studies with a score of 7, and 5 studies with a score of 8), indicating that the quality of the RCTs included in this meta-analysis was fair to good. Nine studies had a matched-dose comparison group, whereas 10 studies did not. Several outcome measures were used in these studies, including the Canadian Occupational Performance Measure, Pediatric Evaluation of Disability Inventory, the Quality of Upper Extremity Skills Test, the Jebsen-Taylor Hand Function Test, the Bruininks-Oseretsky Test of Motor Proficiency, Gross Motor Function Measure, Peabody Developmental Motor Scale—2nd edition, Pediatric Balance Scale, 10-m walk test, muscle strength, and coordination. When classifying outcome measures based on the ICF model (Tab. 2), the majority (9 studies) included outcome in the activity component only, 7 studies contained body structure and activity components, 2 studies contained activity and participation components, and 1 contained all components. VR intervention was offered mostly in clinics (9 studies), followed by in the laboratory (6 studies) and home (4 studies).

Overall Effect of VR Intervention

All of the studies but 4[51,55,57,58] showed at least 1 positive change in 1 outcome variable (Tab. 2) with VR intervention. Across all studies, there was a strong effect (d = 0.861; 95% CI = 0.51–1.22) of VR intervention in children with CP. The results from meta-analyses are illustrated in the forest plot in Figure 2. Not surprisingly, we also found large heterogeneity among the studies as the value of I^2 was 70% (Q = 60.36; P <.000001).

When further breaking down the effect size based on outcome variables classified by the ICF model, a medium effect was found when measured by the body structure and function component (8 studies; d = 0.672; 95% CI = 0.364–0.980), a large effect by the activity component (19 studies; d = 0.899; 95% CI = 0.530–1.267), and a small effect by the participation component (3 studies; d = 0.408; 95% CI = 0.078–0.738).

Publication bias was assessed by examining a funnel plot of standard error versus effect size. Minor asymmetry was noted in the plot, and the Duval-Tweedie trim and fill correction was used to correct the overall effect size. This correction shifted the overall effect size from 0.861 to 0.724. When excluding the 4 studies (Rostami 2012_1 and Rostami 2012_2,[47] Reid,[54] and Tarakci et al[59]) with ES larger than 2.000, the overall effect size shifted from 0.861 to 0.510.

Subgroups and Meta-Regression Analyses. Only "VR system" was a significant factor (P = .05): engineer-built VR systems seemed to be more effective than commercially available VR systems (d = 1.572 for engineer-built systems; d = 0.628 for commercially available systems).

In the next section, we classify studies based on the targeted function the study's outcome variables were intended to measure to further examine the up-to-date evidence of VR effectiveness on arm function, ambulation, and postural control.

Effectiveness of VR for Upper Extremity Function. There were 13 RCT studies that included outcome variables measuring arm function.[43,47–49,51,53,55–58,61] Across all studies, there was a strong effect (d = 0.835; 95% CI = 0.388–1.282) (Fig. 3a shows a forest plot). We found large heterogeneity among the studies, as the value of I^2 was 75% (Q = 47.82; P < .000001). Publication bias was also assessed, and minor asymmetry was noted. After using the Duval-Tweedie trim and fill correction, we found that the overall effect size shifted from 0.835 to 0.691.

For the subgroups and meta-regression analyses, VR system, children's age, and VR daily dosage were shown to be significant factors (P = .03 for VR system, P = .01 for children's age, and P = .04 for daily dosage). Studies using an engineer-built VR system had a larger effect size than studies using a commercially available VR system (d = 2.162 for engineer-built systems; d = 0.491 for commercially available VR systems). Meta-regression analyses also showed a statistically significant negative linear relationship between age and study effect size: the younger the children were, the larger the effect

Table 1.
Characteristics of Cerebral Palsy (CP) and Virtual Reality (VR) Studies that Met Inclusion Criteria of This Meta-Analysis[a]

Study	Total No. of Participants	Age Range ($\overline{X}$)	CP Type	VR Type	Dosage	Training Focus	Comparison Therapy (Matched Dosage)	Setting	Quality Score
Acar et al[48]	15 VR; 15 control	6–15 (9.6)	Hemiplegia	Nintendo Wii	45 min × 2 d × 6 wk	UE	NDT (yes)	Clinic	6/10
AlSaif et al[49]	20 VR; 20 control	6–10 (8.0)	Diplegia	Nintendo Wii Fit	20 min × 7 d × 12 wk	UE; postural control; LE	None (no)	Home	5/10
Chen et al[41,42]	13 VR; 14 control	6–12 (8.6)	Mixed	Eloton SimCycle[b]	40 min × 3 d × 12 wk	Postural control; LE	Usual physical activity (yes)	Home	7/10
Chiu et al[51]	32 VR; 28 control	6–13 (9.4)	Spastic hemiplegia	Nintendo Wii Sports	40 min × 3 d × 6 wk	UE	Usual care (no)	Home	8/10
Cho et al[52]	9 VR; 9 control	4–16 (9.8)	Mixed	Nintendo Wii	30 min × 3 d × 8 wk	Postural control; LE	Treadmill training (yes)	Clinic	7/10
Jannink et al[53]	5 VR; 5 control	7–16 (12.1)	Mixed	PlayStation EyeToy	30 min × 2 d × 6 wk	UE	Usual care (yes)	Clinic	6/10
James et al[43]; Mitchell et al[44]	47 VR; 43 control	8–17 (11.2)	Hemiplegia	Mitii	30 min × 6 d × 20 wk	LE	None; wait-list (no)	Home	8/10
Reid[54]	3 VR; 3 control	10–12 (10.5)	Mixed	GestureX-treme	90 min × 2 d × 4 wk	Postural control	Standard care (no)	Laboratory	4/10
Reid, Campbell[55]	19 VR; 12 control	8–10 (11.9)	Not specified	GestureX-treme	90 min × 1 d × 8 wk	UE	Standard care (no)	Laboratory	5/10
Ren et al[56]	19 VR; 16 control	3–6 (4.6)	Diplegia	Q4[c]	80 min × 5 d × 12 wk	UE; postural control; LE	Physical therapy (yes)	Clinic	6/10
Rostami et al_1[47]	8 VR; 8 control	6–12 (7.8)	Hemiplegia	E-link[c]	90 min × 3 d × 4 wk	UE	Regular routine (no)	Laboratory	8/10
Rostami et al_2[47]	8 VR + mCIMT; 8 mCIMT	6–12 (8.3)	Hemiplegia	E-link	90 min × 3 d × 4 wk	UE	mCIMT (yes)	Laboratory	8/10
Sajan et al[57]	9 VR + control; 9 control	5–20 (11.5)	Mixed	Nintendo Wii	45 min × 6 d × 3 wk	UE; postural control; LE	Conventional therapy (yes)	Clinic	8/10
Sharan et al[46]	8 VR; 8 control	Not specified (9.6)	Not specified	Nintendo Wii Fit and Sports	? min × 3 d × 3 wk	UE; postural control	Conventional therapy (no)	Clinic	4/10
Shin et al[58]	8 VR; 8 control	Not specified (8.7)	Diplegia	Nintendo Wii	45 min × 2 d × 8 wk	UE	Basic exercises (no)	Clinic	5/10
Tarakci et al[59]	15 VR; 15 control	5–18 (10.5)	Spastic; mixed	Nintendo Wii Fit	20 min × 2 d × 12 wk	Postural control; LE	Balance training (yes)	Clinic	5/10
Atasavun Uysal et al[50]	12 VR; 12 control	6–14 (9.6)	Hemiplegia	Nintendo Wii	30 min × 2 d × 12 wk	Postural control; LE	Routine physical therapy (no)	Laboratory	7/10
Wade, Porter[60]	6 VR first; 7 control first	7–16 (9.83)	Not specified	Engineer-built seat cushion	3 mo	Postural control	None (no)	Laboratory	4/10
Zoccolillo et al[61]	10 VR first; 8 NDT first	4–14 (6.9)	Not specified	Xbox Kinect	30 min × 2 d × 8 wk	UE	NDT (yes)	Clinic	4/10

[a]LE = lower extremity, mCIMT = modified constraint-induced movement therapy, Mitii = Move It To Improve It (Elass Fonden, Charlottenlund, Denmark) (web-based therapy), NDT = neurodevelopmental therapy, UE = upper extremity.
[b]Eloton Inc, Minden, Nevada.
[c]The authors did not provide manufacturer or other identifying information, and Chen et al were unable to locate any information.

Table 2.
Outcome Measurements for Each Study Included in This Meta-Analysis[a]

Study	International Classification of Functioning, Disability and Health		
	Body Structure and Function	**Activity**	**Participation**
Acar et al[48]		ABILHAND: (+) JTHFT: (+) QUEST: Dissociated movements: (+) Grasp: (+) Protective extension: (+) Weight bearing: (+) WeeFIM: (+)	
AlSaif et al[49]	Upper limb coordination (BOTMP5:6): (+)	mABC-2: Manual dexterity: (+) Balance: (+) Catching and aiming: (+) 1-min walk test: (+)	
Chen et al[41,42]	Muscle strength: Curl up: NS Knee extension strength: (+) Knee flexion strength: (+) Bone density: Femur bone density: NS Lumbar bone density: (+)	GMFM-66: NS BOTMP: NS Balance: NS Bilateral coordination: NS Running speed and agility: NS Strength: NS	
Chiu et al[51]	Grip strength: NS Tracking: Finger: NS Elbow: NS	Functional hand use: Quality: NS Quantity: NS JTTHF: NS Nine-Hole Peg Test: NS	
Cho et al[52]	Muscle strength: Right knee flexors: (+) Right knee extensors: (+) Left knee flexors: (+) Left knee extensors: (+)	10-m walk test: (+) 2-min walk test: (+) GMFM: Standing: (+) Walking, running, jumping: NS PBS: (+)	
Jannink et al[53]		Melbourne: (+)	
James et al[43]; Mitchell et al[44]	TVPS-3: (+)	6-min walk test: (+) Repetitions of sit-to-stand, lateral step up, half-kneel to standing: (+) Walking steps: NS Mobility questionnaire: NS AHA: NS JTTHF: (+) Melbourne: NS	LIFE-Habits: NS AMPS: (+) COPM: (+)
Reid[54]		SACND: (+)	
Reid, Campbell[55]		QUEST: NS	COPM: NS
Ren et al[56]	Modified Ashworth Scale: Ankle plantar flexor: (+)	GMFM-88: Standing: (+) Walking, running, jumping: (+) PDMS-2: Grasping: (+) Visual-motor integration: (+) BBS: (+)	
Rostami et al_1[47]		BOTMP: Speed and dexterity: (+) PMAL: Amount: (+) Quality: (+)	
Rostami et al_2[47]		BOTMP: Speed and dexterity: (+) PMAL: Amount: (+) Quality: (+)	

(Continue)

Table 2.
Continued

Study	International Classification of Functioning, Disability and Health		
	Body Structure and Function	**Activity**	**Participation**
Sajan et al[57]	Sway velocity with eyes open: NS Sway velocity with eyes closed: NS	Box and Block Test: NS QUEST: Dissociated: NS Grasping: NS Total: NS Pediatric Berg Balance Scale: NS TVPS: NS Walking: Distance: NS Speed: NS	
Sharan et al[46]	MACS: NS	PBS: (+)	
Shin et al[58]		KDTVP-2: Eye-hand coordination: NS Visual-motor speed: NS	
Tarakci et al[59]		10 Stairs Climbing Test: (+) 10-min walk test: (+) Functional reaching: (+) Sit to stand: (+) TUG: (+) Wii Balance: Walking a tightrope: (+) Balance: (+) WeeFIM: NS	
Atasavun Uysal et al[50]		PBS: (+)	COPM: Satisfaction: NS Performance: NS PEDI: Mobility: NS Self-care: NS Social: NS
Wade, Porter[60]		Chailey Levels of Ability: Shoulder girdle: (+) Spinal profile: (+) Other categories: NS SACND: Associated postural reaction: (+) Other categories: NS	
Zoccolillo et al[61]		ABILHAND: (+) QUEST: (+)	

[a] (+) = virtual reality statistically significantly improved this outcome variable, AHA = Assisting Hand Assessment, AMPS = Assessment of Motor and Process Skills, BBS = Berg Balance Scale, BOTMP = Bruininks-Oseretsky Test of Motor Proficiency, BOTMP5:6 = Bruininks-Oseretsky Test of Motor Proficiency Subtest 5, item 6, COPM = Canadian Occupational Performance Measure, GMFM = Gross Motor Function Measure, JTTHF = Jebsen-Taylor Test of Hand Function, KDTVP-2 = Korean Developmental Test of Visual Perception, LIFE-Habits = Assessment of Life Habits questionnaire, mABC-2 = Movement Assessment Battery for Children—2nd version, MACS = Manual Ability Classification System, Melbourne = Melbourne Assessment of Unilateral Upper Limb Function, NS = nonsignificant, PBS = Pediatric Balance Scale, PDMS-2 = Peabody Developmental Motor Scale—2nd edition, PEDI = Pediatric Evaluation of Disability Inventory, PMAL = Pediatric Motor Activity Log, QUEST = Quality of Upper Extremity Skills Test, SACND = Sitting Assessment for Children with Neuromotor Dysfunction, TUG = Timed "Up & Go" Test, TVPS = Test of Visual Perceptual Skills, TVPS-3 = Test of Visual Perceptual Skills (nonmotor)—3rd edition.

size was (slope = −0.1307). A statistically significant positive linear relationship was found between daily dosage and study effect size: the larger the daily dosage was, the larger the effect size was (slope = 0.01027).

Effectiveness of VR for Ambulation. There were 8 studies that included outcome variables that measured ambulation function.[41,42,44,49,50,52,56,57,59] The overall effect size was 0.755 (95% CI = 0.348–1.161), indicating a medium to large effect size (Fig. 3b). We found medium heterogeneity among the studies, as the value of I^2 was 59% (Q = 17.01; $P = .017$). Publication bias was found, and the Duval-Tweedie trim and fill correction was used. The effect size on ambulation shifted from 0.755 to 0.378.

For the subgroups and meta-regression analyses, CP type, children's age, and PEDro score were shown to be significant factors ($P = .02$ for CP type, $P = .037$ for children's age, and $P = .0002$ for PEDro score). Studies that included children with diplegia or mixed type seemed to have a better effect than studies that included only children with hemiplegia (d = 1.064

Study name	Std diff in means	Lower limit	Upper limit
	Statistics for each study		
Acar 2016	0.468	-0.269	1.205
AlSaif 2015	1.449	0.728	2.170
Chen 2012,2013	0.511	-0.263	1.285
Chiu 2014	0.317	-0.200	0.834
Cho 2016	0.714	-0.246	1.674
Jannink 2008	0.974	-0.337	2.285
James/ Mitchell 2015,2016	0.294	-0.125	0.713
Reid 2002	3.457	0.905	6.009
Reid 2006	0.419	-0.312	1.150
Ren 2016	1.094	0.371	1.817
Rostami 2012_1	5.576	3.379	7.773
Rostami 2012_2	2.647	1.301	3.993
Sajan 2017	0.351	-0.582	1.284
Sharan 2012	0.581	-0.421	1.583
Shin 2015	-0.261	-1.245	0.723
Tarakci 2016	2.282	1.339	3.225
Atasavun Uysal 2016	0.563	-0.262	1.388
Wade 2012	0.531	-0.257	1.319
Zoolillo 2015	0.272	-0.436	0.980
	0.861	0.506	1.215

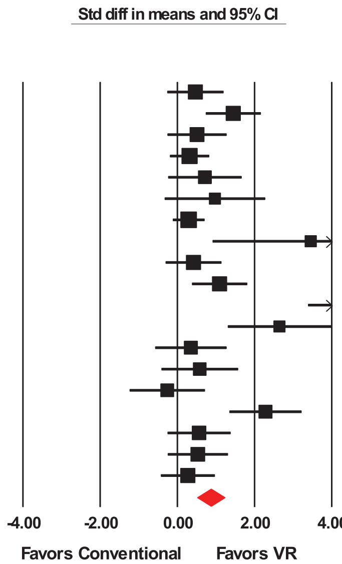

Figure 2.
Forest plot of effect size in all studies. Std diff = standard difference, VR = - virtual reality.

for diplegia, $d = 0.883$ for mixed type, and $d = 0.249$ for hemiplegia). Meta-regression analyses showed a statistically significant negative linear relationship between age and study effect size, and between PEDro score and study effect size: the younger the children's age was, the larger the effect size; and the lower the PEDro score was, the larger the effect size.

Effectiveness of VR for Postural Control. There were 10 studies that included outcome variables that measured postural control.[41,42,46,49,50,52,54,56,57,59,60] The overall effect size was 1.003 (95% CI = 0.503–1.502), indicating a large effect size (Fig. 3c). We found large heterogeneity among the studies as the value of I^2 was 67% (Q = 27.50; $P = .001$). There was no publication bias.

For the subgroups and meta-regression analyses, none of the moderators reached statistical significance.

Discussion

In general, when combining all outcome measures of all studies, virtual reality intervention showed a strong effect in improving motor function in children with CP when comparing with conventional therapy or controls ($d = 0.861$). The possible mechanism for why VR worked remained uncertain. Recently, Levac et al[11] in a scoping review suggested some possible reasons from VR therapy that help children with CP improve their motor skills including from the user's side (VR enhanced problem-solving and cognitive engagement during play and increased motivation and neuroplasticity changes); from the perspective of the VR system or game properties (VR created repetitive task-oriented and task-specific practices in an ecologically valid virtual environment that was similar to the real world and provided the flexibility of adjusting task difficulties, visual and/or auditory feedback, and the potential of social play and interaction); and from the personal support aspect (VR offered social support from parents, peers, or therapists). All these active elements from VR help to change personal and environmental barriers that a child with CP may face. By decreasing these barriers or enhancing the enablers, a child with CP may gradually decrease impairments of his/her body structure and function and activity limitations, and gradually improve participation in school, communities, and society.[11] From the motor learning perspectives, when children with CP learn a motor skill, it required hundreds of repetitions per day of a challenging functional task to lead to structural neurological change.[62,63] Learning would be optimized if learners not only repeat the tasks alone but also cognitively engage in problem solving the motor task.[12] Moreover, if motor learning occurred when the practice conditions are as similar as the contexts where the task would be performed, the learning will be promoted with better retention effect.[12–14] All these perspectives can be achieved via training in VR: the gaming features of the VR provide children the ability to repeatedly practice the same task with a greater number of repetitions without noticing. For example, when a child with CP played a PlayStation 2 Eye Toy game called Slap Stream, the child could repeat reaching movements at least 150 times in a 3-minute interval without notice.[15] The flexibility of many VR applications offers the opportunities to ensure that training is ecologically meaningful in an enriched environment, which provide the opportunity for children to cognitively engage in problem solving their motor task.[12,13] VR games usually have goals to attain that can be progressed and enhance children's attention in therapy.[11–13] For example, children will work hard to achieve a higher game score when receiving training in VR, which facilitate children's cognitive engagement in solving the motor task by 'thinking through' how to make their movements more efficiently and faster, which enhance their motor learning.[12] Also, the animated environment provided by VR can vividly provide a simulated environment for children to practice some skills that may not be feasible to do in the real world.[13] The more similar the VR is toward the real-world environment, the better transfer in motor skill.[13,14] The augmented feedback provided by the VR system such as seeing own movements during play can enhance motor learning, especially in children with CP whose intrinsic feedback from their sensory system might be impaired.[12,13] When children with CP played VR games in general, they did not pay attention to their own body movements, but instead, they paid

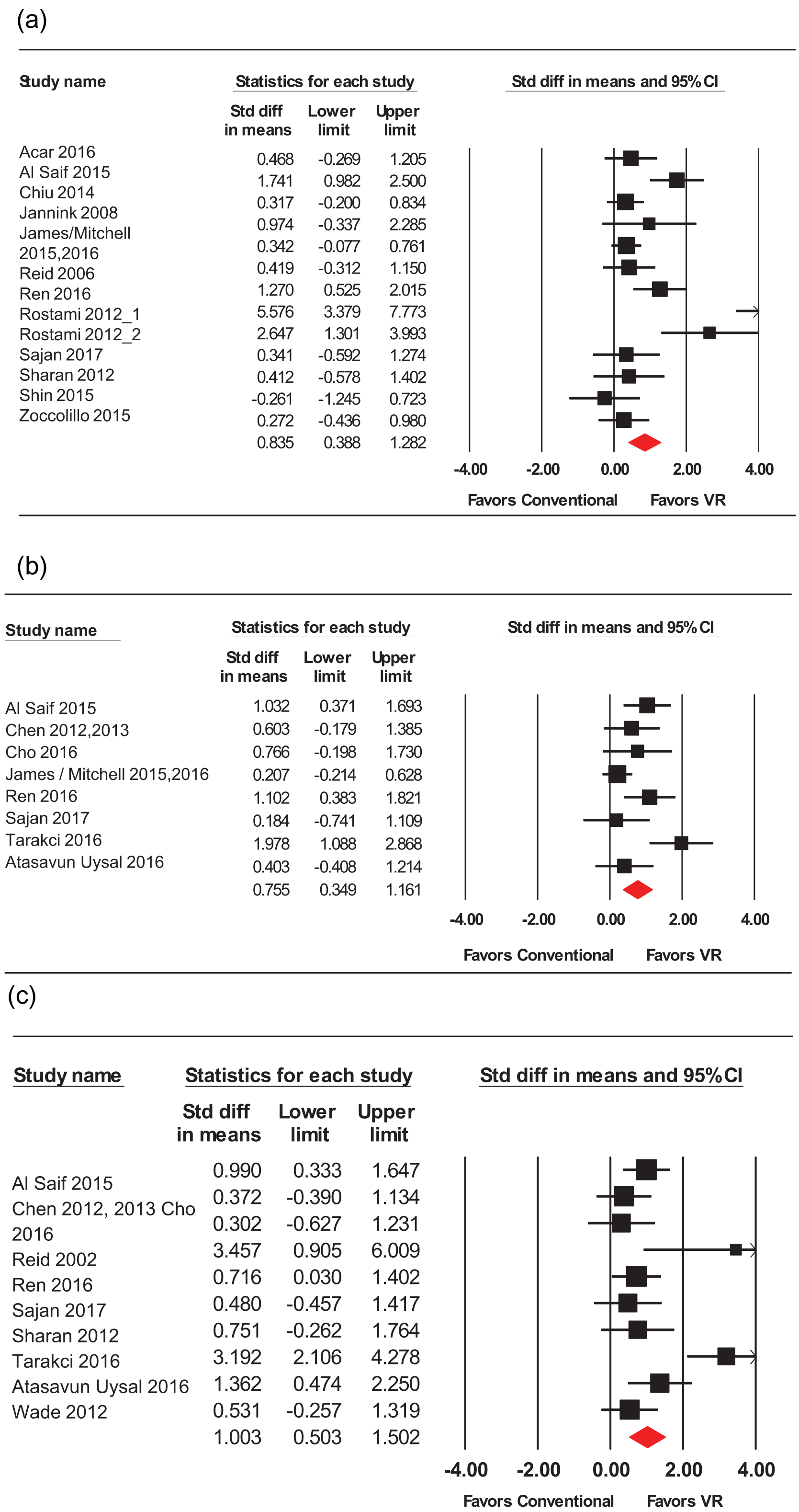

Figure 3.
Forest plots of effect sizes in different outcome measures. (a) Forest plot for studies including outcome variables that measured arm function. (b) Forest plot for studies including outcome variables that measured ambulation function. (c) Forest plot for studies including outcome variables that measured postural control. Std diff = standard difference, VR = - virtual reality.

attention to the games (ie, external attention cues, such as to hit as many enemies as possible or to move the avatar as quickly as possible). This was consistent with the proposal of Wulf and Lewthwaite[64]: when the instructions to learners prompted them to direct their attention to an external focus (eg, minimize movements of a balance platform) rather than to direct their attention to an internal focus (eg, try not to move your feet), learners in the external attention cue group learned faster and performed better.[65] Movement accuracy was also better with the external attention cues rather than with the internal attention cues.[66] Consequently, children with CP performed better with VR than with the conventional intervention in which therapists might focus more on internal attention cues by requesting the children to move their arms faster or to open their hands wider.

In addition, motivation has been recognized as an important reason in explaining why VR works.[11] Wulf and Lewthwaite[64] recently suggested supporting a learner's autonomy by providing choices and enhanced expectancies (eg, positive feedback, reduced perceived task difficulty) could optimize learning through increased motivation as autonomy and enhanced expectancies allow learners to feel "good" about themselves with more confidence in the tasks they are about to complete. Most of the VR system can provide more than 1 game with similar training goals and children with CP in these studies were encouraged to choose which games they wanted to play (or at least had the chance to discuss with their therapists which games to choose). This kind of game selection supports children's need for autonomy, enhances their motivation, increases task interest, and leads to a better learning as this grants learners control over their practice conditions. An advantage of using VR is how easy it is to adjust game difficulty. For example, in order for a child with CP to pick up a virtual object in the virtual environment, the child does not need to have a full range of finger flexion. Instead, a small range (eg, 5°) can easily allow the child to pick up an object in the virtual world, which reduces perceived task difficulty. This kind of accomplishment, picking up an object that the child cannot do in the real world, provides positive feedback to the child, enhances motivation and may optimize learning.

When outcome measures in our review were classified based on the ICF model, a medium effect size was found for the body structure and function component (d = 0.672), a large effect size was found for the activity component (d = 0.899), but a small effect size was found for the participation component (d = 0.408). When our findings were compared with those of a systematic review examining the effect of VR in adults with stroke,[67] there were small to medium effects for the body structure and function component, the activity component, and the participation component (Lohse et al[67] used Hedges g [G] instead of Cohen d: G = 0.48 for body structure and function; G = 0.58 for activity level; and G = 0.56 for participation level) for adults with stroke. Similarly, when we grouped studies based on the movement function that each study's outcome measures intended to measure (ie, arm function, ambulation function, and postural control), a large effect of using VR was shown in arm function and postural control (d = 0.835 for arm function; d = 1.003 for postural control), and a medium to large effect on ambulation (d = 0.755). The effect of using VR on arm function is quite consistent with our previous meta-analysis (d = 1.00 in Chen et al[16]), which included 3 RCTs and 11 case series. When compared with others' meta-analyses, a Cochrane systematic review by Laver et al indicated a small effect of using VR on arm function in adults with stroke (d = 0.28), a small effect on activity of daily living (d = 0.43), almost no effect on gait speed (d = 0.07), and almost no effect on global motor function (d = 0.14).[68] Interestingly, VR effect seemed to be more effective in children with CP than in patients with stroke. In the United States, around 84% of children between the ages of 2 and 17 are gamers and have stronger motivation and are more engaged in playing video games,[69] which might explain why children had a better effect of using VR as an intervention tool than adults with stroke.

Weiss et al[13] have proposed a model to explain VR-based rehabilitation within the context of terminology from the ICF model, which can help to explain why we found only small effect in participation level. In this model, there were 3 nested circles, the inner "interaction space," the intermediate "transfer phase," and the outer "real world." The virtual environment provided the user the ability to interact with the VR system in the interaction space: with the ease of adjusting task difficulty and the technology of simulation, the user could perform functional, task-specific tasks of varying levels of difficulty.[13] Since the goal in rehabilitation is to participate in daily activities in the real world, this requires transfer of the trained skill as well as environmental modifications from the interaction space through the transfer phase to the real world.[13] This will require overcoming, or minimizing the environmental barriers and gradually adapting to the real world. In this model, Weiss et al[13] recognize users' body structure and function, and personal factors combined with environmental factors to perform activities in the interaction space. However, the occupational performance in real world was recognized as participation in the real world, which was located in the outer space of Weiss' model.[13] VR training was mainly emphasized on the interaction space and would require some work (eg, gradually increase task difficulty, changing task demands and contexts) to transfer to real-world participation. This model might help to explain why our findings found a larger effect on body structure and function as well as activity, but not on participation.[13]

Our findings showed a trend that use of an engineer-built system was more effective than using a commercial system. As expected, an engineer-built system can meet the children's special needs through better adjustment of game difficulty and training goals. Commercial systems, on the other hand, are not designed to train children (eg, gradually increase task difficulty, changing task demands and contexts) with CP because these systems have more restrictions on their preset game difficulties and require some adaptations and careful game selections prior to use. The use of engineer-built system can provide optimal challenge of the skill difficulty to children with CP to obtain the optimal learning of the skill (challenge point theory).[70] Engineer-built system might also have the flexibility to provide a more task-specific training than the commercial systems.[70] For example, if a child is unable to reach outwards, an engineer-built system can be used to easily change the required movement direction without restrictions; whereas it is impossible to change the required movements in the commercial systems. However, the cost of purchasing an engineer-built VR system might be much higher than a commercially available system ($15,000 versus $150). When carefully examining the effect size in the commercial systems, they reached a medium effect size (d = 0.619) so such systems may be a good choice in clinics where there is a budget limitation, or they can be used as a good home exercise program for children with CP for maintaining therapeutic effects.

In our review, VR effect had a negative linear association with children's age in arm function and ambulation: the younger the children, the better the effect. This was consistent with the idea of early intervention as younger children may have more brain plasticity and adaptability to improve their motor function than children at older ages.[71,72]

Interestingly, the association between VR effect and treatment dosage was only significant in arm function: the larger the daily dosage, the larger the VR effect. When carefully examining the data, the daily dosage of James et al[43] and Zoccolillo et al[61] was 30 minutes, with small or almost no effect (d = 0.342 and d = 0.272, respectively), whereas the daily dosages of Ren et al[56] and Rostami et al[47] were 80 to 90 minutes, with a large effect (d ranged from 1.270 to 5.576). Our finding that intensive practice dosage in training upper extremity function in children with CP showed a better effect than low practice dosage was consistent with findings in the meta-analysis of Arpino et al.[73] When comparing more intensive interventions with nonintensive rehabilitation treatment for children with CP, a large effect size with intensive intervention (d = 1.32) compared with the nonintensive therapy. However, we did not find this similar trend in ambulation and postural control function. A possible reason was that only a handful of studies were included in ambulation and postural control function. The nonsignificant finding might simply be due to too few studies to show the association.

In addition, the majority of the studies used VR in training arm function and postural control. This may be due to the convenience of using a commercially available system to train UE and postural control. There is a need to develop a better VR system to help train ambulation function in children with CP.

Our current meta-analysis has improved the quality of evidence by only including research with RCT design. However, the quality of the research studies included in this review was fair to good with high heterogeneity among studies and various intervention protocols. The sample size in each RCT was relatively small. A large-scale RCT with multiple sites and with a more homogenous participant group of similar age and diagnosis is needed.

In conclusion, VR is a viable intervention to improve arm function, ambulation, and postural control in children with CP. Although using an engineer-built VR system may have a better effect, the use of a commercially available VR system may also be a good alternative choice as it provided a medium to large effect.

With regard to clinical implications, VR can motivate children to participate in the intervention. Human studies have shown that improving arm function requires hundreds of repetitions per day of a challenging functional task to lead to structural neurological change.[70] The required number of repetitions is very challenging to achieve in a single therapeutic session. Thus, therapeutic exercises should not only be performed in the clinical setting, but should be sustained in the home environment between clinical visits to maximize the effectiveness. It is suggested that using VR as a valid home exercise program can maximize the intervention.

Author Contributions

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Data analysis: Y. Chen, H.D. Fanchiang
Project management: Y. Chen
Providing facilities/equipment: Y. Chen, A. Howard
Providing institutional liaisons: Y. Chen
Clerical/secretarial support: Y. Chen, A. Howard
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Disclosure and Presentations

The authors completed the ICJME Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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Appendix.

Searching strategy, using PubMed as an example.

First round: using MeSH Terms

1. Virtual reality exposure therapy = 274 hits
2. Cerebral palsy = 17,487 hits
3. Movement = 448,825 hits
4. Arm = 28,562 hits
5. Upper extremity = 145,419 hits
6. Lower extremity = 146,357 hits
7. Leg = 60,286 hits
8. Torso = 169,731 hits
9. Posture = 65,971 hits
10. Postural balance = 17,612 hits
11. #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 = 904,812 hits
12. Combine #1 and #2 and #11 = 3 hits (all randomized controlled trials)

Second round: using keywords

13. Virtual reality or virtual realities or Kinect or Wii or Playstation or computer game or computer games or virtual environment or video game or video games or active game or active games or serious game or serious games or EyeToy = 15,601 hits
14. Cerebral palsy or cerebral palsies or spastic diplegia or spastic diplegic or spastic diplegias or spastic quadriplegia or spastic quadriplegias or spastic quadriplegic or spastic hemiplegia or spastic hemiplegias or spastic hemiplegic or Little disease or Little's disease or infantile palsy or infantile palsies = 126,688 hits
15. Arm or upper extremity or upper arm or reach or grasp or grip or fine motor or leg or lower extremity or lower leg or ambulation or walk or gait or gross motor or trunk or posture or postural control or balance = 1,148,647 hits
16. Combine #13 and #14 and #15 = 140 hits

Read through titles and abstracts of these 140 articles. Select 21 RCTs.