Virtual reality rehabilitation in children with brain injury: a randomized controlled trial

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ABBREVIATIONS

MA-2	Melbourne Assessment of Unilateral Upper Limb Function-2
MACS	Manual Ability Classification System
PEDI-CAT	Pediatric Evaluation of Disability Inventory Computer Adaptive Test
RCT	Randomized controlled trial
ROM	Range of motion
ULPRS	Upper Limb Physician's Rating Scale

AIM To investigate the efficacy of a virtual reality rehabilitation system of wearable multi-inertial sensors to improve upper-limb function in children with brain injury.

METHOD Eighty children (39 males, 41 females) with brain injury including cerebral palsy aged 3 to 16 years (mean age 5y 8mo, SD 2y 10mo) were assessed as part of a multicentre, single-blind, randomized controlled trial. The intervention group received a 30-minute virtual reality intervention and a 30-minute session of conventional occupational therapy while the control group received 60 minutes of conventional occupational therapy per session, with 20 sessions over 4 weeks. The virtual reality rehabilitation system consisted of games promoting wrist and forearm articular movements using wearable inertial sensors. The Melbourne Assessment of Unilateral Upper Limb Function-2 (MA-2), Upper Limb Physician's Rating Scale, Pediatric Evaluation of Disability Inventory Computer Adaptive Test, and computerized three-dimensional motion analysis were performed.

RESULTS Both groups (virtual reality, n=40; control, n=38) significantly improved after treatment compared to baseline; however, the virtual reality group showed more significant improvements in upper-limb dexterity functions (MA-2, virtual reality group: Δ=10.09±10.50; control: Δ=3.65±6.92), performance of activities of daily living, and forearm supination by kinematic analysis (p<0.05). In the virtual reality group, children with more severe motor impairment showed significant improvements compared to those with less severe impairment.

INTERPRETATION The virtual reality rehabilitation system used in this study, which consists of wearable inertial sensors and offers intensive, interactive, and repetitive motor training, is effective in children with brain injury.

Upper-limb dysfunction is a common neuromotor impairment in children with brain injury.[1] Impaired muscle activation and motor control have a negative impact on motor training of the upper limb for functional skills, which are related to performance of activities of daily living. This may restrict social participation and diminish quality of life.[2]

The principles of neurorehabilitation to elicit motor learning and brain plasticity include repetitive mass practice, practice dosage, task-oriented and goal-specific functional training, randomized variable practice, multisensory stimulation, and increasing difficulty.[3] Traditional conventional occupational therapy is effective in improving upper-limb function but is resource-intensive. To achieve significant improvements, longer duration and high repetitions are required;[4] however, sustaining engagement with repetitive task practice can be challenging for children.

Recent technological advances have allowed researchers and practitioners to use virtual reality as an alternative treatment modality.[5–7] Virtual reality-based motor rehabilitation offers repetitive intensive tasks with immediate sensory-motor feedback on performance, which is an important learning component. Additionally, using virtual reality games aimed at stimulating motivation and attention within an enjoyable and playful environment, as well as adjusting task difficulty according to the user, may be an attractive option for children,[5,8] allowing them to actively participate in rehabilitation.

Several studies demonstrated that using virtual reality has benefits for children with neurological impairments to improve upper-limb function.[6,7] However, in a recent

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systematic review, the role of virtual reality in improving hand function in children with cerebral palsy (CP) was unclear due to limited evidence; thus, virtual reality may be best used as an adjunct to other therapies.[9] To date, six randomized controlled trials (RCTs) investigating the effect of virtual reality training on upper-limb function in children with CP have been reported. Only two studies reported positive results, but the intervention groups performed virtual reality training as an add-on therapy, with more therapeutic doses compared to the control group.[10,11] Only one pilot study provided the same treatment intensity as an RCT design using a commercial virtual reality device; however, the sample size was too small for a statistical analysis to be conducted.[12] Therefore, high-quality RCTs with larger sample sizes are needed to determine the efficacy of using a virtual reality device in children with upper-limb dysfunction.

This study aimed to explore whether rehabilitation training using a virtual reality device would be more effective in improving upper-limb motor function than conventional occupational therapy alone in children with brain injury including CP. The device used in this study was developed for the purpose of upper-limb rehabilitation in children and was based on virtual reality technology. The device utilizes inertial measurement unit sensors for real-time feedback and outcome tracking of wrist and forearm articular movements; it also enables intensive, task-oriented, repetitive training using several engaging games and functional tasks.

What this paper adds

- Both virtual reality rehabilitation and conventional occupational therapy were effective for upper-limb training.
- Virtual reality training was superior in improving dexterity, performance of activities of daily living, and active forearm supination motion.
- The effect of virtual reality training was significant in children with more severe motor impairments.

METHOD

Study design

This international randomized controlled, single-blind, multicentre trial was conducted at four rehabilitation institutions in Korea and China. The internal review board of each participating hospital (Severance Hospital, Eulji Hospital, and Seoul Rehabilitation Hospital) approved the study and all parents and patients were informed about the purpose and protocol of the study before enrolment; written informed consent was obtained from all participants and/or their parents. The trial was registered at the Clinical Research Information Service (identifier no. KCT0002395).

After baseline assessment, participants were randomized into either intervention or control group via a centralized, web-based randomization system that assigned patients randomly to the intervention or control group using a 1:1 ratio (Fig. S1, online supporting information). The randomization sequence was generated at the start of the trial using R v3.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

Participants

The study included children with CP or other acquired brain injury at least 12 months after onset, aged 3 to 18 years. Children with upper-limb dysfunction who had active use of their arm according to Manual Ability Classification System (MACS) levels I to IV and House Functional Classification System levels 4 to 7 were included.

Children with severe intellectual disability who could not understand and perform the instructions, visual impairment, and a history of botulinum neurotoxin A injection in the upper limb within the last 6 months were excluded. Chemodenervation, constraint-induced movement therapy, surgery, or alternation of antiseizure medication regimen was not allowed for the study duration. Eighty children were enrolled (39 males, 41 females; mean age 5y 8mo, SD 2y 10mo). Seventy-four children had CP, five had paediatric stroke (age at onset: 3–5y), and one sustained traumatic brain injury at the age of 7 years.

Interventions

The intervention group received 30 minutes of treatment based on the virtual reality rehabilitation program, whereas the control group received conventional occupational therapy 5 days per week for 4 weeks. Furthermore, both groups received an additional 30 minutes per day of conventional occupational therapy for the affected upper limb. The amount of therapy for both groups was not different during the intervention period (1h/d, 5d/wk for 4 wks, 20h overall) but the content differed (intervention group: 30min virtual reality and 30min conventional occupational therapy; control group: two sessions of 30min conventional occupational therapy).

The control group (n=40) received two sessions of conventional occupational therapy per day in a one-to-one setting. Each conventional occupational therapy session consisted of 10 minutes of stretching, 10 minutes of strengthening, and 10 minutes of task-oriented training. Although stretching alone has shown limited evidence for improving upper-limb function, combined therapy may elicit functional benefits in children with CP.

The intervention group (n=40) participated in virtual reality training with the RAPAEL Smart Kids (Neofect Co., Ltd., Gyeonggi-do, Republic of Korea), which was developed for rehabilitation purposes. It consists of a band-like wrist attachment with two inertial measurement unit sensors on the dorsum of the hand and distal forearm and associated software (Fig. 1). The inertial measurement unit is an integrated sensor package consisting of accelerometers that measure linear acceleration, gyroscopes that measure angular velocity, and magnetometers that measure the amplitude and direction of movement in a three-dimensional space.[13] The sampling rate of the wearable device was 30Hz. When the child moves their upper limb while wearing the device, the avatar arm on

the computer screen moves simultaneously according to the child's active movements. The virtual reality rehabilitation program consists of several games and simulations including performance of activities of daily living and facilitating motions, such as wrist flexion/extension, forearm supination/pronation, and ulnar/radial deviation. At the beginning of training, upper-limb capability was assessed using the virtual reality device to determine the initial difficulty level. Then, the difficulty level of the training scenarios was adjusted based on performance parameters for each individual during each training session. Simultaneous feedback was provided on a computer screen with auditory and visual feedback during and after practice. During each session with the virtual reality system, the therapist helped the child to put the device on, motivated them, and stopped them from using the opposite limb during training. In 74 participants, the non-dominant and more involved side was selected as the training limb. However, the other six participants had bilateral-limb dysfunction, where function of the more involved side was equal to or less than House Functional Classification System level 3; thus, they received training for their dominant upper limb.

Outcome measures

Both functional and kinematic assessments were performed for all patients at baseline (within 72h before intervention), at the end of the 4-week intervention (within 1wk after intervention, posttest 1), and after the 8-week follow-up (8±1wk after intervention, posttest 2) to investigate how the effects were maintained. To avoid assessment bias, all assessments were completed by occupational therapists blinded to group assignment; all Korean children from the three institutions were evaluated by one common blinded assessor to reduce interrater bias.

Melbourne Assessment of Unilateral Upper Limb Function-2

The primary outcome measure was based on upper-limb motor function as assessed with the Melbourne Assessment of Unilateral Upper Limb Function-2 (MA-2) postintervention.[14] The MA-2 is a reliable and valid tool for measuring the unilateral quality of upper-limb movement based on activities such as reaching, grasping, releasing, and manipulation in children with CP.[14] Altogether, 14 video-recorded tasks were scored into the following four subscales: range of movement, target accuracy, dexterity, and fluency.[14] Scores assigned to each subscale were converted into percentage scores using the maximum possible score. The minimal clinically important difference for the MA-2 was estimated in a previous study as:[15] range of movement=2.35, target accuracy=2.09, dexterity=2.22, and fluency=3.20, indicating the minimum improvement scores that should be interpreted as both statistically significant and clinically important.

Upper Limb Physician's Rating Scale

The Upper Limb Physician's Rating Scale (ULPRS) is a semi-quantitative assessment designed to assess movement patterns, focusing on all three regions of the arm, including the palm, forearm, and elbow.[16] The ULPRS is a reliable and valid measure of quality of upper-limb movement in children with CP.[16] It determines whether there is an isolated functional impairment, such as restricted forearm supination, wrist in flexion and deviation, elbow flexed, or thumb-in-palm. A total score for unilateral limbs ranging from 0 to 25 was used for the analysis.

Pediatric Evaluation of Disability Inventory Computer Adaptive Test

The Pediatric Evaluation of Disability Inventory Computer Adaptive Test (PEDI-CAT) measures functional skills in

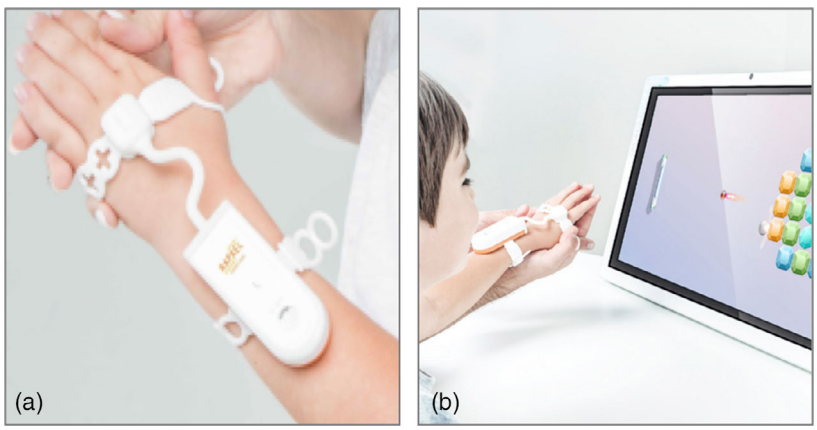

Figure 1: Component of the virtual reality device developed for upper-limb rehabilitation in children with disabilities. (a) Band-like wrist attachment device with two inertial measurement unit sensors on the hand dorsum and distal forearm. (b) Software in combination with a personal computer and a screen.

four domains, including performance of activities of daily living, mobility, social-cognitive, and responsibility.[17] The PEDI has been used as a comprehensive functional assessment designed to quantify function and measure change after interventions in children with CP. The newly developed PEDI-CAT utilizes a computer adaptive platform with 276 items based on parent or caregiver reporting, which demonstrates strong validity and reliability.[18] In our study, scaled scores of each domain ranging from 0 to 100 were used for analysis. The minimal clinically important difference for the PEDI-CAT has not yet been established.

Computerized three-dimensional motion analysis

The task of drinking from a glass while sitting, which is known to have the least variation in performance, was deemed suitable as a standardized task when assessing the impact of pathology on movement.[19] Participants were asked to reach and grasp a cup on the table at their own speed and repeat the task three times for the limb being evaluated. During this reach-and-grasp task, 17 surface markers were attached to trace the joint angles of the upper limb including forearm pronation/supination, wrist flexion/extension, and ulnar/radial deviation. We performed motion capture of the upper limb only at the Korean hospitals using computerized optoelectric motion analysis systems (VICON MX-T10 Motion Analysis System, Oxford Metrics, Oxford, UK [Severance Hospital]; Motion Analysis Corporation, Santa Rosa, CA, USA [Eulji University Hospital]; and Prime 13, OptiTrack, NaturalPoint, Inc., Corvallis, OR, USA [Seoul Rehabilitation Hospital]) to calculate the kinematic data (sampling frequency=100Hz).

Motion analysis data were segmented into four sequential phases (Fig. S2, online supporting information): phase 1, from baseline position to arm extension targeting the object; phase 2, flexing the arm and targeting self; phase 3, extending arm and targeting the table; and phase 4, retracting the arm.

Kinematic data consisted of the range of motion (ROM) of each joint during phases 1 to 4, whereas spatio-temporal data consisted of movement time and index of curvature during each phase.[20] Afterwards, data from all three trials were processed to calculate each parameter and the mean data were used for the analysis.

Statistical analysis

A sample size calculation using a two-tailed *t*-test for a randomized controlled design was performed. It indicated that a sample size of 64 was sufficient to detect a difference of 5.2 percentage points in the MA-2 score after a 4-week intervention, assuming an SD of 7.0 percentage points, a power of 90%, and a significance level of 5%. This number was increased to 80 to allow for a predicted dropout rate of approximately 20%.

Because of the repeated measurements in this design, a linear mixed model with an unstructured covariance matrix was used to analyse the impact of the type of intervention on functional outcomes, with a random effect for participants, fixed effects of time and group, and interactions between time and group.

A Mann–Whitney *U* test or independent *t*-test was used to compare the extent of improvement between the two treatment groups. All statistical analyses were carried out using SAS v9.4 (SAS Institute, Cary, NC, USA); $p \leq 0.05$ with Bonferroni adjustment for multiple comparisons was considered statistically significant.

RESULTS

Seventy-eight children (38 males, 40 females) aged 3 to 16 years (mean age 5y 11mo, SD 2y 10mo) in MACS levels I and IV (MACS levels I and II:III and IV ratio=29:49) completed the intervention. Two children in the control group dropped out of the trial due to consent withdrawal. Forty (51.3%) and thirty-eight (48.7%) participants were randomized to the virtual reality and control groups respectively. Demographic characteristics did not differ significantly (Table 1). No safety issues were reported and no children in the intervention group experienced any side effects during the virtual reality training.

Functional assessments

Regarding upper-limb dexterity measured using the MA-2, the virtual reality group showed significant improvements postintervention in terms of interaction effect by time, compared with the control group ($p<0.01$; linear mixed model). Regarding the mean change, there was a significant difference in the dexterity percentage score of the MA-2 immediately after training (virtual reality group: $\Delta=10.09\pm10.50$; control: $\Delta=3.65\pm6.92$; $p<0.01$). Additionally, all subscales of the MA-2, including ROM, accuracy, dexterity, and fluency domains, achieved minimal clinically important difference thresholds after the intervention in both groups, showing clinical and statistical significance

Table 1: Baseline characteristics of the study participants

Characteristic	Virtual reality group (*n*=40)	Control group (*n*=38)	*p*[a]
Age, y:mo (IQR)	4 (3–6:10)	6 (4–7)	0.219
Sex, *n* (%)			0.825
Male	19 (47)	19 (50)	
Female	21 (52.5)	19 (50)	
MACS, *n* (%)			0.380
Levels I and II	13 (32.5)	16 (42.1)	
Levels III and IV	27 (67.5)	22 (57.9)	
HFCS (study limb), *n* (%)			
4	19 (47.5)	12 (31.6)	0.183
5	11 (27.5)	9 (23.7)	
6	8 (20.0)	16 (42.1)	
7	2 (5.0)	1 (2.6)	
Involved side, *n* (%)			0.266
Unilateral	15 (37.5)	19 (50)	
Bilateral	25 (62.5)	19 (50)	

[a]*p*-values were calculated using a Mann–Whitney *U* test, χ^2 test, or Fisher's exact test. IQR, interquartile range; MACS, Manual Ability Classification System; HFCS, House Functional Classification System.

($p<0.01$). This improvement was maintained until the 8-week follow-up in both groups (Table 2 and Fig. S3, online supporting information).

According to the ULPRS, which assesses segmental movements in the affected limb, significant improvements were observed in both groups ($p<0.01$) without statistically significant differences.

According to the PEDI-CAT, the virtual reality group demonstrated significant improvements in the performance of activities of daily living domain compared with the control group ($p<0.01$). Additionally, the social-cognitive domain improved greatly in the virtual reality group immediately after the 4-week intervention, although it did not reach significance regarding group differences. The mobility and responsibility domains showed no statistically significant group differences.

Regarding the subgroup analysis of the intervention group, there were differences in the degree of improvement according to baseline manual ability. Children in MACS levels III and IV showed significant improvements in the ROM and accuracy domains in the MA-2, ULPRS total score, and performance of activities of daily living domain in the PEDI-CAT compared to children in MACS levels I and II (Table 3).

Computerized three-dimensional motion analysis

Computerized three-dimensional motion analysis was conducted only in the Korean hospitals. A total of 36 participants underwent motion analysis (virtual reality group, $n=19$; control group, $n=17$).

Forearm supination ROM during phase 1 was significantly improved in the virtual reality group ($p=0.02$) compared with the control group (Table S1, online supporting information). In the post hoc analysis, significant improvement in forearm supination ROM was noted between baseline and the 8-week follow-up. Additionally, wrist extension ROM during phase 1 was improved in the virtual reality group ($p=0.01$) postintervention, although it did not reach significance.

Regarding the spatio-temporal parameters, the index of curvature during phase 4 was significantly decreased only in the control group, indicating improvement. This parameter also did not reach significance.

DISCUSSION

We report on a large multicentre trial using a virtual reality training system developed to rehabilitate children with brain injury including CP. Functional parameters, as measured by the MA-2, ULPRS, and PEDI-CAT, showed statistically significant improvement in both groups. For the MA-2, the minimal clinically important difference thresholds were achieved after the intervention in all subscales for both groups, indicating clinically significant changes. Additionally, the virtual reality group showed significant improvement in unimanual dexterity, performance of activities of daily living, and forearm articular movement compared with the control group.

Virtual reality-based rehabilitation enhances motor learning processes by offering implicit learning, concrete tasks, and focused attention. In motor learning theory, two interdependent learning processes mediate the acquisition

Table 2: Functional outcome measures at baseline, postintervention, and at the 8-week follow-up

Variable	Group	Baseline ($n=78$)	Postintervention ($n=78$)	8-week follow-up ($n=78$)	*p*		
					Time	Group	Time × group
MA-2							
Range	Virtual reality	54.72 (4.02)	61.48[a] (3.62)	63.98[a] (3.36)	<0.01[b]	0.65	0.08
	Control	54.78 (4.13)	58.77[a] (3.72)	59.55[a] (3.45)	<0.01[b]		
Accuracy	Virtual reality	60.80 (4.63)	68.70[a] (4.08)	71.30[a,c] (3.98)	<0.01[b]	0.81	0.68
	Control	60.63 (4.75)	66.84[a] (4.19)	68.74[a] (4.08)	<0.01[b]		
Dexterity	Virtual reality	50.09 (3.75)	60.17[a] (3.53)	62.92[a] (3.51)	<0.01[b]	0.73	0.01[b]
	Control	52.08 (3.85)	55.72[a] (3.62)	60.07[a,c] (3.60)	<0.01[b]		
Fluency	Virtual reality	45.60 (3.77)	51.91[a] (3.53)	53.57[a] (3.30)	<0.01[b]	0.48	0.39
	Control	43.62 (3.86)	47.49[a] (3.62)	49.37[a,c] (3.39)	<0.01[b]		
ULPRS							
Total score	Virtual reality	13.05 (1.13)	14.67[a] (1.02)	15.50[a] (0.98)	<0.01[b]	0.99	0.47
	Control	13.29 (1.16)	14.66[a] (1.05)	15.24[a,c] (1.00)	<0.01[b]		
PEDI-CAT							
Performance of activities of daily living	Virtual reality	47.20 (0.71)	49.35[a] (0.53)	50.33[a,c] (0.56)	<0.01[b]	0.76	0.03[a]
	Control	48.05 (0.72)	48.84 (0.54)	49.26[c] (0.58)	0.02[b]		
Mobility	Virtual reality	55.80 (0.96)	56.70 (0.95)	57.30[a] (0.84)	0.02[b]	0.75	0.19
	Control	56.95 (0.98)	56.95 (0.98)	57.13 (0.86)	0.90		
Social-cognitive	Virtual reality	63.05 (0.51)	63.90[a] (0.48)	64.93[a,c] (0.49)	<0.01[b]	0.88	0.08
	Control	63.32 (0.53)	63.87 (0.49)	64.40[c] (0.51)	<0.01[b]		
Responsibility	Virtual reality	44.93 (0.82)	45.78 (0.69)	46.58[a] (0.63)	0.02[b]	0.94	0.86
	Control	44.92 (0.84)	45.53 (0.71)	46.61[a,c] (0.65)	0.01[b]		

Values are the least square mean (standard error of the mean). [a]$p<0.05$ by Bonferroni-adjusted post hoc analysis compared with baseline assessment. [b]$p<0.05$ by linear mixed model. [c]$p<0.05$ by Bonferroni-adjusted post hoc analysis compared with postintervention assessment. MA-2, Melbourne Assessment of Unilateral Upper Limb Function-2; ULPRS, Upper Limb Physician's Rating Scale; PEDI-CAT, Pediatric Evaluation of Disability Inventory Computer Adaptive Test.

Table 3: Extent of improvement in the virtual reality group according to MACS level

		MACS levels I and II			MACS levels III and IV			
		Baseline	Postintervention	Change	Baseline	Postintervention	Change	*p*
MA-2								
Range	Virtual reality	81.48 (13.18)	84.33 (11.63)	2.85 (4.58)	41.84 (20.44)	50.48 (17.94)	8.64 (6.25)	<0.01[a]
	Control	67.36 (21.86)	70.37 (21.60)	3.01 (5.10)	45.62 (22.79)	50.34 (20.91)	4.83 (5.63)	0.29
Accuracy	Virtual reality	87.08 (18.27)	89.54 (16.29)	2.46 (2.60)	48.15 (26.19)	58.67 (22.90)	10.81 (10.16)	<0.01[a]
	Control	70.75 (26.80)	76 (22.01)	5.25 (9.32)	53.27 (27.89)	60.18 (27.48)	6.96 (7.65)	0.29
Dexterity	Virtual reality	72.46 (14.94)	79.62 (11.79)	7.37 (8.91)	39.32 (20.67)	50.81 (20.15)	13.76 (17.82)	0.39
	Control	62.14 (18.48)	66.9 (18.92)	6.95 (11.22)	44.76 (23.36)	47.59 (21.23)	1.67 (6.94)	0.15
Fluency	Virtual reality	66.67 (20.11)	69.96 (16.54)	3.30 (7.11)	35.45 (20.77)	43.21 (18.72)	8.11 (9.23)	0.18
	Control	56.25 (19.69)	61.61 (19.63)	5.36 (8.32)	34.43 (19.82)	37.23 (19.36)	2.99 (5.51)	0.60
ULPRS								
Total score	Virtual reality	20.08 (3.01)	20.46 (3.48)	0.38 (1.04)	9.69 (6.07)	11.77 (5.52)	2.18 (2.04)	<0.01[a]
	Control	16.38 (6.71)	17.94 (5.84)	1.56 (1.86)	11.05 (6.67)	12.27 (6.14)	1.22 (1.62)	0.83
PEDI-CAT								
Daily activities	Virtual reality	50.23 (3.22)	50.54 (2.79)	0.31 (0.95)	45.74 (4.39)	48.78 (2.94)	3.04 (3.49)	<0.01[a]
	Control	50.13 (3.90)	50.5 (3.50)	0.38 (2.03)	46.55 (4.17)	47.64 (3.35)	1.22 (2.71)	0.30
Mobility	Virtual reality	56.77 (5.93)	57.92 (5.33)	1.15 (2.34)	55.33 (6.25)	56.11 (5.74)	0.78 (2.62)	0.91
	Control	59.06 (5.57)	58.06 (6.09)	−1.00 (3.16)	55.41 (5.89)	56.14 (6.72)	0.74 (2.96)	0.90
Social-cognitive	Virtual reality	64.92 (3.62)	65.31 (3.52)	0.38 (1.19)	62.15 (3.38)	63.22 (2.87)	1.07 (1.82)	0.28
	Control	63.31 (3.42)	64.06 (3.32)	0.75 (1.53)	63.32 (2.17)	63.73 (2.47)	0.35 (1.99)	0.66
Responsibility	Virtual reality	46.08 (3.66)	46.54 (3.46)	0.46 (2.07)	44.37 (4.76)	45.41 (4.33)	1.04 (2.80)	0.52
	Control	45.56 (5.25)	47.00 (4.73)	1.44 (2.61)	44.45 (6.34)	44.45 (4.45)	−0.44 (4.61)	0.07

Values are the mean change between baseline and first follow-up assessment (SD). [a]$p<0.05$ by Mann–Whitney *U* test to compare the extent of improvement between the Manual Ability Classification System (MACS) I and II and III and IV groups. MA-2, Melbourne Assessment of Unilateral Upper Limb Function-2; ULPRS, Upper Limb Physician's Rating Scale; PEDI-CAT, Pediatric Evaluation of Disability Inventory Computer Adaptive Test.

of functional skills, that is, explicit and implicit learning. Implicit learning is an unconscious learning process through exposure to play, for example, thus this is more suitable for children.[3,21] Virtual reality training can offer implicit learning by providing a range of enjoyable games. Additionally, virtual reality technology provides more concrete tasks and richer perceptual information to guide movement, for example turning over book pages (a training task in our virtual reality device), which are effective in motor learning compared to abstract tasks, such as a simple forearm pronation/supination motion.[22] Moreover, focusing the learner's attention to the results of their movements using sound, visual stimuli, or earning points, all possible in virtual reality games, is more effective than attending to the movement itself.[23] Moreover, a multisensory and multimodality approach has recently been recognized as an effective rehabilitation strategy.[24] Therefore, interactive technology, such as virtual reality, is useful to stimulate effective motor learning and drive actions.

Conventional occupational therapy is focused on meaningful activities and placing movements into context. Stimulating children's motivation and active participation can be challenging in some cases. However, when playing virtual reality games, children express greater fun and enjoyment, characterized by smiling, laughing, and screaming, compared to regular occupational therapy sessions. This not only enables more repetitions, but also intensifies the bioelectrical signals in the brain that are involved in neuroplasticity.[8]

The content of the games used for training in our study included activities such as performance of activities of daily living, including eating, pouring water, and cooking. Task-specific training that focuses on repeating specific functional tasks is a key principle in rehabilitation. The following strategies for task-specific training have been suggested: a task should be repetitive; relevant to the patient; randomly assigned; and reinforced with positive feedback.[25] Such therapeutic strategies of task-specific training can be realized using virtual reality rehabilitation. Therefore, improvement in upper-limb function could lead to enhanced participation in the activities of daily living as measured using the PEDI-CAT in our study.

Additionally, eye–hand coordination, improving movement accuracy, and visual perception were also included in the main tasks of the device used in our study. In an animal model, an enriched environment offered a combination of multisensory/cognitive stimulation and increased physical activity.[26,27] Thus, combining virtual reality and conventional occupational therapy can offer intensive, multisensory, and multimodality stimulation that could have profound positive effects on the human brain. In our study, the significant improvement in social-cognitive aspects and motor function measured by the PEDI-CAT can be related to these multimodal approaches.

However, previous studies of virtual reality training for rehabilitation purposes reported mixed results. The heterogeneity of the virtual reality treatment effect can be explained by the following factors: type of device used; purpose of the device and interacting interface; study design; therapeutic dose in an RCT design; participants' age and functional status; and outcome measurement.

While studies investigating the use of commercial gaming devices have shown modest results, these systems have

limitations when applied to rehabilitation.[12,28] Virtual reality training with a commercial gaming device would not be possible for patients with severe upper-limb impairments and it would be difficult to adjust the gaming level according to the child's abilities.[12] A virtual reality training system developed for rehabilitation purposes can promote the child's voluntary movement, enhance therapeutic effects more effectively than a commercial device, and can be applied to children with severe disabilities. In our study, effective training was possible even for children with severe impairments. Moreover, children with more severe motor impairments (MACS levels III and IV) showed significant improvements compared to children with fewer impairments (MACS levels I and II). Although a ceiling effect may be present that affects differences in score changes in children with greater manual ability (MACS levels I and II), this is an important clinical feature for children with limited residual function.

The level of interaction and immersion in virtual reality is another important issue. The interactive interface can vary from a simple joystick to a complex motion camera and the display can be adapted, for example with screen- and head-mounted displays. Thus, virtual reality rehabilitation can be categorized as immersive, semi-immersive, and non-immersive. The effectiveness of immersive and non-immersive virtual reality on upper-limb training for stroke rehabilitation has been studied and compared; however, the superiority of one type of virtual reality environment over another with regard to immersion level is still unclear.[27] Although our device is non-immersive, we still observed a significant improvement in participants' upper-limb function.

The total dose of the intervention is another important factor for determining efficacy. In a previous study, Rostami et al.[11] reported positive results when the total duration of the intensive intervention for the virtual reality group was 1080 minutes over 4 weeks. However, the study by Reid and Campbell[29] had a training duration of 720 minutes over 8 weeks and showed limited evidence regarding upper-limb function in children with CP. This suggests that an intensive virtual reality intervention may be more likely to result in improvement. In our study, 600 minutes of virtual reality and another 600 minutes of conventional occupational therapy for 4 weeks were enough to elicit functional improvements. Furthermore, most previous RCTs provided only add-on virtual reality therapy or provided no specific details about the control group; so the specific effects of virtual reality were unclear. However, our study provided the same therapeutic dose in both groups and the control group was strictly defined and controlled. Therefore, we can conclude that multimodal therapy including virtual reality can be more effective in some functional contexts than occupational therapy alone. Virtual reality may have synergistic effects with conventional occupational therapy through a multimodal approach.

Regarding participants, our study recruited children aged 3 years and older; thus, some children in our study group were younger than those in previous studies whose participants were aged 6 years and older. Early intervention is known to optimize motor and cognitive plasticity in children with brain injury.[30] Additionally, the virtual reality device in this study was relatively easy to fit in younger patients.

We quantified the effects of virtual reality training on body function of the upper limb using three-dimensional upper-limb kinematic evaluation, which is a reliable and precise tool that objectively measures changes in joint kinematics posttreatment. This is the first study that reported significant improvements in forearm supination and wrist extension using computerized kinematic analysis after virtual reality training. Furthermore, motion of the distal upper limb was assessed while executing standardized everyday tasks. Therefore, improvements in upper-limb function can be correlated with improvements in assessing performance of activities of daily living.

Study limitations

Our virtual reality system was not immersive since it did not provide the real experience of being in another reality. New developments, such as applying a head-mounted display, may add another dimension and increase the effects of motor training. Future studies should investigate whether a more immersive experience would make a difference. Additionally, virtual reality telerehabilitation strategies for patients to use at home, which could lessen travel burden and costs, deserve further examination. Moreover, computerized three-dimensional motion analysis was conducted in only 36 participants from the Korean hospitals. Two children were excluded from the motion analysis due to poor cooperation. Finally, variation in participant characteristics, such as unilateral or bilateral involvement, CP, or brain injuries acquired later, may represent further limitations.

CONCLUSIONS

The results of this RCT showed that virtual reality training was more effective than conventional occupational therapy in improving dexterity, performance of activities of daily living, and active forearm supination motion in children with chronic brain injury, especially those with severe motor impairments. A virtual reality rehabilitation system with wearable inertial measurement unit sensors was as effective as conventional occupational therapy for upper-limb training in children with brain injury including CP. This innovative therapeutic approach using virtual reality may effectively complement standard rehabilitation by providing motivation and enhancing motor learning in children with brain injury.

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SUPPORTING INFORMATION

The following additional material may be found online:

Figure S1: CONSORT diagram.

Figure S2: Segmentation of motion capture data of the reach-and-grasp task.

Figure S3: Melbourne Assessment 2 changes at baseline, postintervention, and 8-week follow-up.

Table S1: Motion analysis at baseline, postintervention, and at the 8-week follow-up

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