

Cortical reorganization induced by virtual reality therapy in a child with hemiparetic cerebral palsy

Sung H You* PT PhD, Assistant Professor, Physical Therapy Program, Hampton University, VA, USA.

Sung Ho Jang MD, Assistant Professor, Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University;

Yun-Hee Kim MD PhD, Professor, Department of Physical Medicine and Rehabilitation, College of Medicine, Sungkyunkwan University;

Yong-Hyun Kwon PT MS, Graduate student, Department of Physical Medicine and Rehabilitation, School of Medicine, Yeungnam University, Republic of Korea.

Irene Barrow PhD, Assistant Professor, Communicative Sciences and Disorders, Hampton University, VA;

Mark Hallett MD, Chief, National Institute of Neurological Disorders and Stroke (NINDS), Human Motor Control Section, Bethesda, MD, USA.

*Correspondence to first author at Hampton University, Phoenix Hall 219B, Hampton, VA 23668, USA.
E-mail: sung.you@hamptonu.edu

Virtual reality (VR) therapy is a new, neurorehabilitation intervention aimed at enhancing motor performance in children with hemiparetic cerebral palsy (CP). This case report investigated the effects of VR therapy on cortical reorganization and associated motor function in an 8-year-old male with hemiparetic CP. Cortical activation and associated motor development were measured before and after VR therapy using functional magnetic resonance imaging (fMRI) and standardized motor tests. Before VR therapy, the bilateral primary sensorimotor cortices (SMCs) and ipsilateral supplementary motor area (SMA) were predominantly activated during affected elbow movement. After VR therapy, the altered activations disappeared and the contralateral SMC was activated. This neuroplastic change was associated with enhanced functional motor skills including reaching, self-feeding, and dressing. These functions were not possible before the intervention. To our knowledge, this is the first fMRI study in the literature that provides evidence for neuroplasticity after VR therapy in a child with hemiparetic CP.

Hemiparetic cerebral palsy (CP) is a common neurological condition associated with sensorimotor function and development in children (Ashwal et al. 2004). It often leads to delay in motor development or deconditioning of the affected limbs because of the affected individual's tendency to compensate with the intact limbs rather than attempt to use the involved limbs (Held 2000). Non-intervention or intervention that emphasizes compensatory or a reflex inhibition mechanism contribute to never-learned-to-use (NLTU) or underutilization of the impaired limb (DeLuca et al. 2003) respectively. This may result in suppression of development of cortical representation of the affected limb and further inhibit its functional use (Cicinelli et al. 1997, Liepert et al. 2000).

To help children with hemiparetic CP overcome NLTU or underutilization, various neurorehabilitation therapies have been used including neurodevelopmental treatment (Butler and Darrah 2001), neuromuscular electrical stimulation and dynamic bracing (Schecker et al. 1999), and constraint-induced movement therapy (Liepert et al. 2000, Page et al. 2002), but outcomes have been variable (Butler and Darrah 2001, Page et al. 2002). Of these treatments, constraint-induced movement therapy was found to produce measurable functional motor improvement in a child with hemiparetic CP (DeLuca et al. 2003) and in adults with chronic hemiparesis (see Liepert et al. 2000, Page et al. 2002), but its cost-effectiveness, safety, and issues of compliance (Page et al. 2002) call into question its

See end of paper for list of abbreviations.

practicality in the clinical setting.

Virtual reality (VR) therapy is an interactive and enjoyable intervention which has recently been shown to improve upper extremity motor function in adults with chronic hemiparesis with greater compliance by the patient (Merians et al. 2002). VR therapy has the capability of creating a virtual rehabilitation scene where the intensity of practice and sensory feedback can be systematically manipulated to provide the most appropriate, individualized, play-based motor retraining in children (Reid 2002) or adults with neurological impairments (Holden and Dyar 2002, Merians et al. 2002). Despite the potential importance of VR therapy, no previous study has assessed the neuroplastic mechanisms supporting VR-induced motor development. Therefore, the purpose of this study was to examine VR-induced cortical reorganization and functional motor development in a child with hemiparetic CP. Our premise was that intensive VR therapy would promote practice-dependent plasticity, thereby enhancing functional motor development and helping to overcome NLTU.

Case report

HISTORY

The child in this report is an 8-year-old male, delivered by Cesarean section at 36 weeks' gestation. He was jaundiced, but required no mechanical ventilation. He spent three weeks in a neonatal intensive care unit and was discharged on caffeine-citrate after 40 days owing to bradycardia during feedings. Follow-up examination at 2 months post-gestational age was non-remarkable; however, at 6 months he showed asymmetrical posture with shoulder retraction on the right. Hemiparetic CP was diagnosed at 36 months; subsequently, brain magnetic resonance imaging (MRI) showed encephalomalacia on the left temporo-parietal lobe (Fig. 1). He was unable to control his head until 6 to 7 months or to stand until 12 months. He performed all functional reaching or grasping tasks using the left hand. Clinical and demographic characteristics are presented in Table I.

MEASUREMENTS

Ethical approval for the study was granted by the Institutional Review Board at Yeungnam University Medical Centre, Korea. The child's parents gave informed consent. The therapist who conducted the intervention did not know whether or not the child was being investigated for the study. Pre- and posttests included motor function tests and functional MRI (fMRI). Motor function tests included the Bruininks–Oseretsky Test of Motor Proficiency (BOTMP; Bruininks 1978), the modified Pediatric Motor Activity Log (PMAL) questionnaire (Taub and Wolf 1997, van der Lee et al. 2004), and the upper limb subtest

of the Fugl-Meyer assessment (FMA; Fugl-Meyer et al. 1975). The pretest was implemented before the 4-week VR intervention, followed by the posttest. Outcome measures were emphasized on the proximal muscle movement, such as elbow and shoulder, because VR therapy was designed to improve primarily shoulder and elbow movement control.

Motor function tests

Item 6 'touching a swinging ball with preferred hand' from subtest 5 of the BOTMP was used to measure upper limb coordination. The modified PMAL questionnaire was used to determine the amount of use and quality of movement of the child's affected upper limb during activities of daily living. The upper limb subtest of the FMA was used to examine sensation, range of motion, reflexes, synergy, muscle strength, and movement speed. The validity and reliability of the selected motor tests are well established (Fugl-Meyer et al. 1975, Bruininks 1978, Taub and Wolf, 1997, van der Lee et al. 2004).

Functional MRI

Imaging was performed on a 1.5T MR scanner (Vision; Siemens, Erlangen, Germany) using a block paradigm (15s control/stimulation) of the elbow flexion–extension movements (0.5Hz). Thirteen axial Echo Planar Imaging (EPI) blood oxygen level dependent (BOLD) images were acquired with the established parameters: TE (echo time), 25ms; TR (repetition time), 111ms; field of view (FOV), 210°×210°/mm; matrix, 64×64; thickness, 5mm. Acquired data were analyzed using SPM99 (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK). Statistical parametric maps were obtained using the criterion $p < 0.001$, corrected, minimum cluster size equal to 5. Regions of interest (ROIs) were drawn around the primary sensorimotor cortex (SMC), the premotor cortex (PMC), and the supplementary motor area (SMA), because these areas have been reported to have neuroplastic recovery potential (Cramer et al. 1997, Liepert et al. 2000, Carey et al. 2002). The laterality index was calculated to determine relative cortical activity because it was stable over repeated measures (Cramer et al. 1997; Liepert et al. 2000; Carey et al. 2002; Kim et al. 2003, 2004). Further details on the fMRI method are presented in Appendix I.

VR therapy

As shown in Figure 2a, the IREX VR therapy system requires a television monitor, a video camera, cyber gloves, virtual objects, and a large screen (Hedenberg and Ajemian 2003). The video camera is used to capture and track movement and immerse the patient inside the VR scene. The system offers an alternative to the problems existing in other VR systems

Table I: Clinical and demographic characteristics of patient

Age	School grade	Lesion (topography)	Diagnosis	Functional status
8y	2	Left temporo-parietal cortex and corona radiata	Right hemiparesis	Limited reaching and grasp No functional use of affected upper extremity Right visual perceptual impairment

Clinical examination revealed a tendency to neglect right upper extremity and an abnormal palmar grasp reflex. Head and trunk posture were asymmetrical, with slight anterior tilt of pelvis and shoulder retraction on right side. Relatively adequate protective extension and equilibrium reactions were demonstrated in standing to left, but delayed response to right. Right upper extremity function was limited to gross reaching, grasping, and hand manipulation.

because the patients do not require head-mounted displays (HMDs), data gloves, or other peripheral devices that connect to the computer. This enables them to move freely about in the real world while allowing manipulation of the virtual objects and navigation in the three-dimensional virtual world (Reid 2002, Hedenberg and Ajemian 2003). The bird-ball, conveyor, and soccer exercise games (Fig. 2b–d) were interfaced with

virtual environments to facilitate range of motion, mobility, and strength, which are important elements in developing reaching skill. Each game was played five times and, depending on the game, within each game there were three levels resulting in a range of 88 to 131 opportunities to perform the exercise per game. The intervention was given for 60 minutes a day, five times a week for 4 weeks. A detailed description of the VR therapy protocol is presented in Appendix II.

Table II: Bruininks–Oseretsky Test of Motor Proficiency (BOTMP), modified Pediatric Motor Activity Log (PMAL), and Fugl-Meyer assessment (FMA) scores for pre- and post-virtual reality (VR) therapy

	<i>BOTMP</i>	<i>PMAL</i>		<i>FMA</i>
	<i>Item 6</i>	<i>AOU</i>	<i>QOM</i>	<i>Upper limb</i>
Pre-VR therapy	1	0	0	39
Post-VR therapy	5	3	3	52
Difference (%)	80	100	100	25

Upper extremity motor function outcomes were determined by item 6 ('touching a swinging ball with preferred hand') from subtest 5 of the BOTMP (Bruininks 1978), the modified PMAL questionnaire (Taub and Wolf 1997, van der Lee et al. 2004), and the upper limb subtest of the FMA (Fugl-Meyer et al. 1975). The BOTMP item has reported good test–retest reliability and construct validity (Bruininks 1978). During the test, the child was asked to use the index finger of the affected hand to touch a ball as it swung in front of his face. The child was given one point for each trial (total five trials) in which he hit the ball once. Thus, the raw scores range from 0 to 5. The subset of the modified PMAL interview was used to examine the use of his affected upper limb in amount of use (AOU) and quality of movement (QOM) during activities of daily living. Scores range from 0 (never used) to 5 (normal). Validity was good, Pearson's correlation, $r=0.63$ and test–retest reliability was good, ranging from $r=-0.70$ to 0.85 and -0.61 to 0.71 for AOU and QOM respectively (Taub and Wolf 1997, van der Lee et al. 2004). The upper limb motor subset of FMA includes sensation, range of motion, reflexes, synergy, muscle strength, and movement speed. Scoring criteria range from 0 (cannot perform) to 2 (faultless motion). Possible scores range from 0 to 66. Reliability and validity were intraclass correlation coefficient, $ICC=0.97$ and $ICCs=0.73$ to 0.85 respectively (Fugl-Meyer et al. 1975).

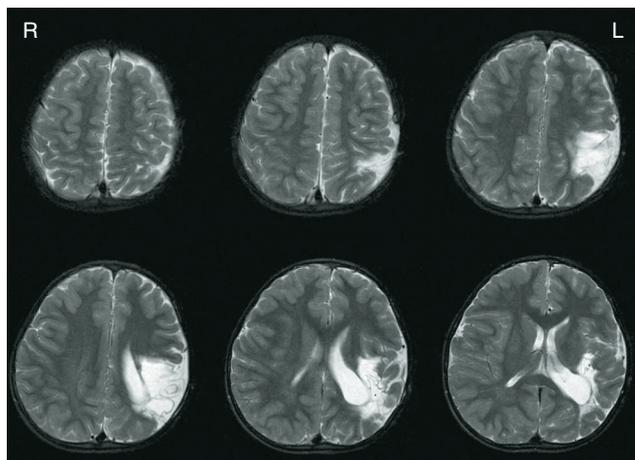


Figure 1: T_2 -weighted diagnostic brain magnetic resonance imaging. T_2 -weighted images (rostral six slices) showing cephalomacia in left temporo-parietal lobe.

Results

MOTOR FUNCTION

Descriptive statistics of functional motor scores pre- and postintervention are presented in Table II. Before VR therapy, the child had no functional use of the affected hand, which was evident in the PMAL test score. After VR therapy, the BOTMP item score improved from 1 to 5. The modified PMAL showed that the use of the affected limb improved from 0 to 3, suggesting increased amount of use and quality of movement of the affected hand during functional motor skills (i.e. holding a book or shirt, washing face, and carrying an object). FMA showed improvement in the performance score from 39 to 52, indicating enhanced active movement control, reflex activity, and coordination in the upper extremity motor performance. Specifically, the interval changes in the performance scores in the shoulder, elbow, and forearm items (43% increase) as well as in the wrist item (67% increase) were greater than in that of the digits (18.2% increase). These findings suggest that VR therapy enhanced functional motor skills and increased amount of use and quality of movement in the affected limb.

NEUROIMAGING

Cortical reorganization in the principal ROIs activated pre- and post-VR therapy during either affected right elbow movement or unaffected left elbow movement is presented in Tables II and III respectively. In movement of the affected elbow before VR therapy, the activated voxels were 121 for ipsilateral SMC and 207 for contralateral SMC, indicating bilateral activations, which constituted a laterality index of 0.26 (bilateral). After VR therapy, the activated voxels were 0 for ipsilateral SMC and 97 for contralateral SMC, which made up a laterality index of 1.0 (contralateral; Fig. 3a). Among the other ROIs, the bilateral primary motor cortex (M1) and primary sensorimotor cortex, (S1), SMC, and ipsilateral SMA were activated, but the PMC was not activated before VR therapy. However, after VR therapy these aberrant activations disappeared and the contralateral SMC, along with the contralateral M1 and S1, were predominantly activated. In movement of the unaffected elbow the cortical activations in the ROIs were primarily contralateral, which was similar to normal activation to begin with. Essentially, VR therapy did not influence any observable or meaningful change in the ROIs (Fig. 3a,b).

Discussion

Cortical activation during affected elbow movement was adaptively reorganized from the aberrant bilateral SMCs (Briellmann et al. 2002, Maegaki et al. 2002) along with the bilateral M1s and S1s, and the ipsilateral SMA (pre-VR therapy) to the contralateral SMC (post-VR therapy), which accounts for significant decreases in voxel volumes in the ipsilateral hemisphere. However, the activation pattern during unaffected movement was comparable to normal activation to begin with and, thus, was probably unaffected by the intervention. Our findings are

consistent with previous studies that showed a shift in SMC activation from ipsilateral or bilateral to contralateral after intensive use of the paretic limb in adults (Liepert et al. 2000, Carey et al. 2002). This finding seems to support two possible neural mechanisms: (1) a migration from contralateral to ipsilateral (or bilateral) activation; or (2) reversion (Jones and Schallert 1994, Carey et al. 2002). The former may involve cortical migration from the infarcted hemisphere to the intact hemisphere or neurons after diaschisis and during the course of natural recovery (Jones and Schallert 1994, Carey et al.

2002). The latter may result from intensive use or practice-dependent neuroplasticity which could generate effective synaptic potentiation (Liepert et al. 2000, Carey et al. 2002). Certainly, our neuroimaging findings suggest that VR therapy could improve neuroplasticity by facilitating the development of neural motor pathways that have never been utilized (DeLuca et al. 2003). This was clearly manifested in the development of motor skills in the child's affected limb.

Empirical evidence has suggested that VR therapy is effective in improving motor performance by means of a learning by

Table III: Number of significantly ($p < 0.001$) activated voxels and laterality index (LI) for each region of interest during either affected right elbow movement (ArEM) or unaffected left elbow movement (UIEM)

ArEM	M1			S1			SMC			PMC			SMA		
	C	I	LI	C	I	LI	C	I	LI	C	I	LI	C	I	LI
Pre-VR therapy	79	51	0.21	86	21	0.61	207	121	0.26	0	0	0	0	55	-1
Post-VR therapy	41	0	1	31	0	1	97	0	1	0	0	0	0	0	0
UIEM	M1			S1			SMC			PMC			SMA		
	C	I	LI	C	I	LI	C	I	LI	C	I	LI	C	I	LI
Pre-VR therapy	30	0	1	57	0	1	87	0	1	0	0	0	21	0	1
Post-VR therapy	23	0	1	11	0	1	59	0	1	0	0	0	0	0	0

M1, primary motor cortex; S1, primary sensory cortex; SMC, primary sensorimotor cortex; PMC, premotor cortex; SMA, supplementary motor area; C, contralaterally activated voxel count; I, ipsilaterally activated voxel count; VR, virtual reality.



Figure 2: (a) Virtual reality experimental set-up; (b) bird-ball; (c) conveyor; (d) soccer.

imitation mechanism (Holden and Dyar 2002). This mechanism is believed to facilitate the M1 via 'mirror' neuron circuits (Rizzolatti et al. 1999, Holden and Dyar 2002). These neurons may map a pictorial and kinematic sensory consequence of the observed target action and topographically internalize its motor representation in the PMC by using a resonance mechanism (Iacoboni et al. 1999, Holden and Dyar 2002). The present findings suggest that the pictorial sensory feedback received during VR therapy facilitated internalization of the motor representation of the target motor behavior (Iacoboni et al. 1999, Holden and Dyar 2002). This internalization may have helped to establish new motor networks or pathways reorganized primarily around the contralateral SMC. Consequently, this might result in the development of motor function and the ability to overcome NLTU. The child might not have had an opportunity to learn and develop age-appropriate motor skills because he had received no intervention. This phenomenon would be conceptually different from 'learned non-use', which may be the case in adults with stroke who have learned to use their limbs again, but lost the ability after a neurological insult (see Taub and Wolf 1997, Liepert et al. 2000, DeLuca et al. 2003).

Among the other ROIs, the contralateral M1 and SMA activations are believed to be responsible for distal and proximal muscle movement respectively (Briellmann et al. 2002). Before VR therapy, the bilateral M1s, SMCs, and ipsilateral SMA were activated during affected elbow movement. Such a marked signal increase in both bilateral M1s, SMCs, and ipsilateral SMA activations during affected elbow movement is never observed in normally developing brains, although a subtle signal increase

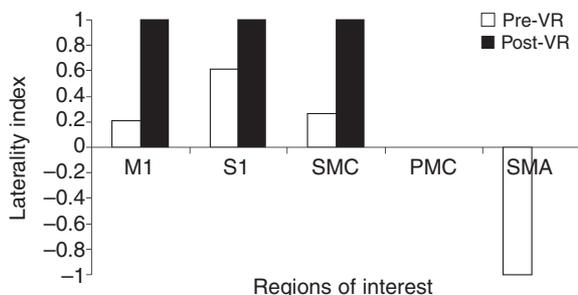


Figure 3a: Mean voxel numbers activated and laterality indexes for regions of interest (ROIs) pre- and post-virtual reality (VR) intervention during affected elbow movement. Before intervention, among ROIs, bilateral primary motor cortex (M1), primary sensory cortex (S1), primary sensorimotor cortex (SMC), and ipsilateral supplementary area (SMA) were activated, but pre-motor cortex (PMC) was not activated during affected elbow movement. However, post-VR therapy, contralateral SMC along with contralateral M1 and S1 were predominantly activated during affected right elbow movement. Cortical activations in ROIs during unaffected left elbow movement were contralateral and this was not affected by intervention, except in SMA.

may be noticed (Leinsinger et al. 1997). After VR therapy, the developmental change of cortical reorganization showed a similar pattern to that seen in normally developing children (Muller et al. 1997). Normally, the ipsilateral motor-evoked potentials (MEPs) after transcranial magnetic stimulation of the biceps brachii gradually decrease with increasing age; and ipsilateral MEPs are never evoked after the age of 10 years (Muller et al. 1997). The neural mechanism underlying hemiparetic CP was comparable with that of adults with stroke. The bilateral SMC activations were shown by fMRI in both child and adults with hemiparesis before the VR therapy. Thus, the present data combined with our previous findings in adults with hemiparesis (Kim et al. 2003, 2004) suggest that the ipsilateral corticospinal tract is accountable, in part, for the pathophysiology of such an altered bilateral cortical activation.

Conclusions

VR therapy produced measurable neuroplastic changes at the SMC and the changes seem to associate closely with enhancement of age-appropriate motor skills in the affected limb. The modified PMAL interview showed that the child was able to perform spontaneous reaching, self-feeding, and dressing, which were not possible before the intervention. Further development may reduce the cost of VR therapy and if so, additional, scrupulously designed experimental studies with larger sample sizes could be carried out to strengthen the generalizability of our findings (Merians et al. 2002). This study invites further investigations to compare whether the effectiveness and related neuroplastic changes after VR therapy are unique or comparable with those of other neurorehabilitations.

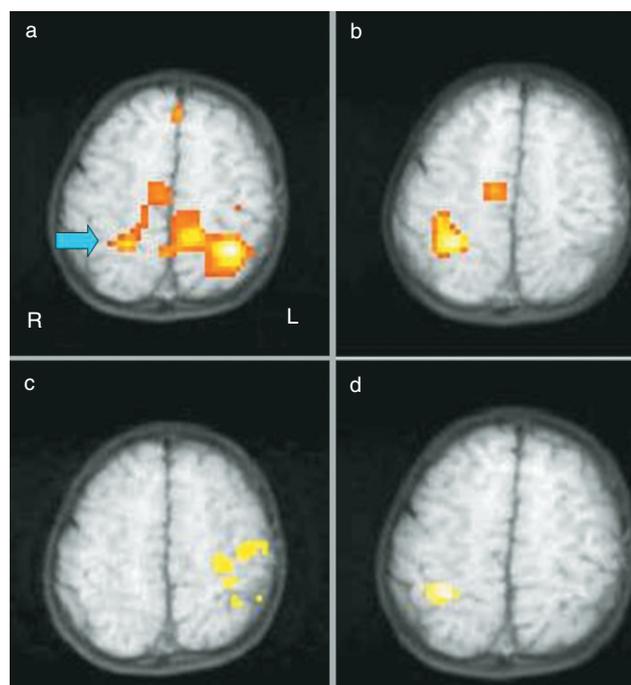


Figure 3b: Cortical reorganization (a,b) pre-VR therapy and (c,d) post-VR therapy during affected elbow movement and unaffected elbow movement. Functional magnetic resonance images (rostral four slices) for child performing elbow movement with paretic right arm before and after 12 sessions of VR therapy.

Accepted for publication 19th October 2004.

Sung H You, Sung Ho Jang, and Yun-Hee Kim contributed equally to this work.

Acknowledgments

We especially thank the IREX Corporation, a division of JesterTek, Inc, for supplying the hardware, software, and technical development expertise for this project. This research was supported by a Brain Research Center of the 21st Century Frontier Research Program grant (M103KV010014 03K2201 01430) from the Ministry of Science and Technology of the Republic of Korea.

References

- Ashwal S, Russman BS, Blasco PA, Miller G, Sandler A, Shevell M, Stevenson R. (2004) Practice parameter: diagnostic assessment of the child with cerebral palsy: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology* **62**: 851–863.
- Briellmann RS, Abbott DF, Caffisch U, Archer JS, Jackson GD. (2002) Brain reorganisation in cerebral palsy: a high-field functional MRI study. *Neuropediatrics* **33**: 162–166.
- Bruininks R. (1978) *Bruininks–Oseretsky Test of Motor Proficiency*. Minnesota: American Guidance Service.
- Butler C, Darrah J. (2001) AACPDM evidence report: effects of neurodevelopmental treatment (NDT) for cerebral palsy. *Dev Med Child Neurol* **43**: 778–790.
- Carey JR, Kimberley TJ, Lewis SM, Auerbach EJ, Dorsey L. (2002) Analysis of fMRI and finger tracking training in subjects with chronic stroke. *Brain* **125**: 773–788.
- Cicinelli P, Traversa R, Rossini PM. (1997) Post-stroke reorganization of brain motor output to the hand: a 2–4 month follow-up with focal magnetic transcranial stimulation. *Electroencephalogr Clin Neurophysiol* **105**: 438–450.
- Cobb SVG. (1999) Measurement of postural stability before and after immersion in a virtual environment. *Appl Ergon* **30**: 47–57.
- Cramer SC, Nelles G, Benson RR, Kaplan JD, Parker RA, Kwong KK, Kennedy DN, Finklestein SP, Rosen BR. (1997) A functional MRI study of subjects recovered from hemiparetic stroke. *Stroke* **28**: 2518–2527.
- DeLuca SC, Echols K, Ramey SL, Taub E. (2003) Pediatric constraint-induced movement therapy for a young child with cerebral palsy: two episodes of care. *Phys Ther* **83**: 1003–1013.
- Fugl-Meyer AR, Jaasko I, Leyman I, Olsson S, Steglind S. (1975) The post-stroke hemiplegic patient. A method for evaluation of physical performance. *Scand J Rehabil Med* **7**: 104–122.
- Hedenberg R, Ajemian S. (2003) *IREX 1.3 Clinical Manual*. New York: JesterTek.
- Held J. (2000) Recovery of function after brain damage: theoretical implications for therapeutic intervention. In: Carr JH, Shepherd RB, editors. *Movement Science. Foundations for Physical Therapy in Rehabilitation*. 2nd edition. Oxford: Aspen. p 189–211.
- Holden MK, Dyar T. (2002) Virtual environment training: a new tool for neurorehabilitation. *Neurol Rep* **26**: 62–74.
- Iacoboni M, Woods RP, Brass M, Bekkering H, Mazziotta JC, Rizzolatti G. (1999) Cortical mechanism of human imitations. *Science* **286**: 2526–2528.
- Jones TA, Schallert T. (1994) Use-dependent growth of pyramidal neurons after neocortical damage. *J Neurosci* **14**: 2140–2152.
- Kim S-G, Hendrick K, Hu X, Merkle H, Ugurbil K. (1994) Potential pitfalls of functional MRI using conventional gradient-recalled echo techniques. *NMR Biomed* **7**: 69–74.
- Kim YH, Jang SH, Han BS, Kwon YH, You SH, Byu WM, Park JW, Yoo WK. (2004) Ipsilateral motor pathway demonstrated by functional MRI, transcranial magnetic stimulation, and diffusion tensor tractography in a patient with schizencephaly. *NeuroReport* **15**: 1899–1902.
- Kim YH, Jang SH, Chang Y, Byun WM, Son S, Ahn SH. (2003) Bilateral primary sensorimotor cortex activation of post-stroke mirror movements: an fMRI study. *NeuroReport* **14**: 1329–1332.
- Leinsinger GL, Heiss DT, Jassoy AG, Pfluger T, Hahn K, Danek A. (1997) Persistent mirror movements: functional MR imaging of the hand motor cortex. *Radiology* **203**: 545–552.

- Liepert J, Bauder H, Miltner WH, Taub E, Weiller C. (2000) Treatment-induced cortical reorganization after stroke in humans. *Stroke* **31**: 1210–1216.
- Maegaki Y, Seki A, Suzaki I, Sugihara S, Ogawa T, Amisaki T, Fukuda C, Koeda T. (2002) Congenital mirror movement: a study of functional MRI and transcranial magnetic stimulation. *Dev Med Child Neurol* **44**: 838–843.
- Merians AS, Jack D, Boian R, Tremaine M, Burdea GC, Adamovich SV, Recce M, Poizner H. (2002) Virtual reality-augmented rehabilitation for patients following stroke. *Phys Ther* **82**: 898–915.
- Muller K, Kass-Iliyya F, Reitz M. (1997) Ontogeny of ipsilateral corticospinal projections a developmental study with transcranial magnetic stimulation. *Ann Neurol* **42**: 705–711.
- Page SJ, Levine P, Sisto S, Bond Q, Johnston MV. (2002) Stroke patients' and therapists' opinions of constraint-induced movement therapy. *Clin Rehabil* **16**: 55–60.
- Reid DT. (2002) The use of virtual reality to improve upper-extremity efficiency skills in children with cerebral palsy: a pilot study. *Techn Disabil* **14**: 53–61.
- Rizzolatti G, Fadiga L, Fogassi L, Gallese V. (1999) Resonance behaviors and mirror neurons. *Arch Ital Biol* **137**: 85–100.
- Scheker LR, Chesher SP, Ramirez S. (1999) Neuromuscular electrical stimulation and dynamic bracing as a treatment for upper extremity spasticity in children with cerebral palsy. *Br J Hand Surg* **2**: 226–232.
- Taub E, Wolf S. (1997) Constraint-induced movement technique to facilitate upper extremity use in stroke patients. *Topics Stroke Rehab* **3**: 38–61.
- van der Lee JH, Beckerman H, Knol DL, de Vet HC, Bouter LM. (2004) Clinimetric properties of the motor activity log for the assessment of arm use in hemiparetic patients. *Stroke* **35**: 1410–1414.

List of abbreviations

BOTMP	Bruininks–Oseretsky Test of Motor Proficiency
FMA	Fugl-Meyer assessment
fMRI	Functional magnetic resonance imaging
M1	Primary motor cortex
NLTU	Never-learned-to-use
PMAL	Pediatric Motor Activity Log
PMC	Premotor cortex
ROI	Regions of interest
S1	Primary sensorimotor cortex
SMA	Supplementary motor area
SMC	Primary sensorimotor cortex
VR	Virtual reality

Appendix I: Functional MRI measure

Before neuroimaging, the child practised the prepared motor task paradigm, which involved a sequential elbow flexion and extension at a metronome-guided frequency of 0.5 Hz (cycle of 15s of rest and 15s of stimulus). Imaging data were acquired when, after being blindfolded, he performed the prepared motor tasks in supine position in the magnetic resonance (MR) scanner. Imaging data were collected before and after the VR therapy to probe neuroplastic changes as a function of intervention. If there was a mismatch between what the experimenter asked the child to perform and the actual performance the test was repeated.

Image signals were acquired using the Echo Planar Imaging (EPI) sequence in accordance with the blood oxygenation level dependent (BOLD) technique. A 1.5T MR scanner (Vision; Siemens, Erlangen, Germany) with a standard head coil was used. For the anatomic base images, 13 axial, 5mm thick, T₁-weighted, conventional, spin echo images were obtained with a matrix size of 128×128 and a field of view (FOV) of 210mm, parallel to the bicommissure line of the anterior commissure–posterior

commissure. The EPI BOLD T_2 -weighted functional MR images in the transverse plane were acquired over the same 13 axial sections for each epoch, producing 780 images for each subject using the parameters TE (echo time), 25ms; TR (repetition time), 111ms; field of view (FOV), $210^\circ \times 210^\circ$ /mm; matrix, 64×64 ; thickness, 5mm. A mask was applied to the imaging data such that any voxel variation in signal intensity less than 5% during the control period was discarded to remove the potential confounding influence of large cerebral arteries (Kim et al. 1994). Functional MRI data were analyzed using SPM99 software (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK) running under the Matrix Laboratory programming environment (Mathwork, Inc., Natick, MA, USA). Statistical parametric maps were obtained and voxels were considered significant at a threshold of $p < 0.001$, with an additional requirement of a minimum cluster size of 5 voxels. Predetermined regions of interest (ROIs) were bilaterally drawn around the primary motor cortex (M1), the primary sensory cortex (S1), the primary sensorimotor cortex (SMC), the premotor cortex (PMC), and the supplementary motor area (SMA), because the areas have been reported to have neuroplastic potentials (Cramer et al. 1997, Carey et al. 2002, Kim et al. 2003, 2004). Because of a large within-patient variability in the BOLD signal, a normalized index, the laterality index, was used to determine any relative shift in the symmetry of cortical activation between the two hemispheres for the ROIs as a function of intervention (Cramer et al. 1997, Carey et al. 2002). This index is expressed as $(C-I)/(C+I)$, where C is the active voxel count for the ROIs in the hemisphere contralateral to the forearm performing the movement and I is the active voxel count for the corresponding region in the hemisphere ipsilateral to the performing forearm. The possible range is from -1.0 (all activity in the ipsilateral hemisphere) to $+1.0$ (all activity in the contralateral hemisphere; Cramer et al. 1997, Liepert et al. 2000, Carey et al. 2002).

Appendix II: Virtual reality therapy

Three virtual environments were interfaced with the bird-ball, conveyor, and soccer exercise games. These tasks were designed to improve the development of different motor skills, with each game programmed to exercise one of the aspects of the affected upper-extremity movement with emphasis on intensive, repetitive range of motion, mobility, and strengthening in the shoulder, elbow, and wrist movement (Hedenberg and Ajemian 2003). Specifically, the *bird-ball* exercise (Fig. 2b) simulates functional reaching and touching motor tasks. The VR scene was set on an idyllic pastoral hill with a snow-covered mountain range behind. In this game, as small round balls flew towards the child from different directions, he was only allowed to use his affected right hand to burst them. The balls transformed into birds and flew away when touched gently in a coordinated fashion, but burst if contact pressure was not properly graded. The number, direction, and speed of the balls were customized, based on the child's baseline performance (Reid 2002, Hedenberg and Ajemian 2003). The goal was to track visually and locate all the target balls and grade the amount of applied pressure of the hand. Thus, this VR exercise was designed to facilitate development of coordinated reaching and touching motor skills. The output reports generated from this game included the number of hits versus misses of the balls and accuracy. Information on knowledge of result (KR) and knowledge of performance (KP) was graphically presented to the child as feedback at the end of each trial when appropriate.

Conveyor (Fig. 2c) is a virtual scene which has multiple applications for exercising real-life functional tasks such as reaching, grasping, holding, and lifting an object. This exercise was adapted from the patterns of proprioceptive neuromuscular facilitation movement (diagonal patterns 1 and 2). This exercise also involves total body exercise, such as bending, twisting, jumping, weight shifting, and stepping. The goal of this VR exercise was to reach and grasp, lift and transfer the conveyor box from one conveyor belt to

the other belt. As with the bird-ball game, the clinician instructed the child in the proper body mechanics and task performance. Initially, the child performed symmetrical reaching and lifting activity and gradually switched to asymmetrical use of the affected hand to reach and lift the box. Thus, this VR exercise was designed to promote development of more complex reaching, grasping, and lifting motor behaviors. The output reports generated from this game included the number of lifting versus misses of the boxes as well as the weight of box (resistive force). Additional hand weights were added as the child progressed in his muscle strength and motor skills (Hedenberg and Ajemian 2003).

Soccer exercise (Fig. 2d) is a virtual scene, which simulates a soccer goalkeeper attempting to block balls from entering the net. In this program, the child was allowed to use only the involved hand to block the balls as soccer balls were launched at him. The output reports generated from this game included the number of blocking versus misses of the balls (Hedenberg and Ajemian 2003).

Joint kinematics during each VR task were recorded by sophisticated camera technology that captured the child's 'mirror' image on a computer monitor. This allowed the child to see himself move and interact with the objects in a virtual environment. Force output data were manually computed by determining the weight of hand/cuff weights or the conveyor box. VR provides an augmented feedback about KR and KP including error rate, speed, direction, joint position, and resistive force feedback. Because these motor tasks required complex intersegmental coordination, and were initially difficult for him due to synergistic patterns, we made a series of variations in the VR parameter specifications (speed, angle, lifting force) based on his performance and progress (Reid 2002, Hedenberg and Ajemian 2003). For example, exercise progression was also obtained by increasing resistive force using hand/cuff weights. Initially, a high frequency (greater than 90%) of augmented KP or KR feedback was given, but the frequency was gradually lessened as his performance improved (Holden and Dyar 2002, Merians et al. 2002). Because mild and temporary cyber sickness from full VR immersion has been reported (Cobb 1999), a partial immersion technique was used in this study.

Virtual environments are computer-generated fully immersive or partly immersive surroundings; a full-immersion system is designed to envelop the patient using a head-mounted visual display (HMD). The hardware of a conventional full-immersion VR system includes a computer, HMD, a hand-held input device, and a tracker. The full-immersion system presents inherent lags and associated delayed latency, which potentially produce symptoms similar to motion sickness. In addition, several practical problems with the full-immersive VR system include the heavy weight and contact of HMD with the head, motion restriction due to multicore cables, resolution of display, and high cost (Holden and Dyar 2002, Reid 2002). On the other hand, the IREX system is a partly immersive environment that offers an alternative to the problems existing in other full-immersion VR systems. Participants do not require HMD, data gloves, or other peripheral devices that connect to the computer. This enables them to move freely about in the real world while allowing manipulation of the virtual objects and navigation in the three-dimensional virtual world (Holden and Dyar 2002, Reid 2002).

Each VR protocol is composed of three major components. In the first part the participant's exercise focus, the maximum target movement and range of motion (ROM), and the target muscles are established. In the second part, the required mobility and muscle strength are determined based on the initial assessment of the participant's baseline performance. The last part includes accessory exercise items that can be incorporated into the VR exercise regime. Based on the child's baseline performance, the protocol was then systematically customized to provide specific types of movement, maximal potential ROM, and muscle strengthening exercises in order to improve functional target reaching mobility. The accessory exercise items such as cuff-weights, or Theraband, (rubber band) were used to provide resistive force as the participant improved

coordination, strength and mobility, and incorporated the accessory items into the VR exercise regime.

In the present study, on the first day the child was familiarized with the virtual exercise and movements. Once the child was familiarized, he was instructed to practice a VR exercise that was broken down step-by-step. Thus, movements could initially be worked on individually and then progressively integrated together toward the targeted reaching motor behavior. For the bird-ball game, designed to improve reaching, the segmental shoulder flexion and elbow extension and wrist extension motion were practised individually and later coordinated

together in progressive steps to produce a successful reaching motion. The VR stimulus was randomized in terms of speed, direction, and distance. As the child advanced in ability to perform the target VR tasks and increased strength, we systematically increased resistive force by applying a light child cuff-weight around the wrist. The feedback frequency was gradually lessened. Behavioral techniques such as verbal praise, cheers, and clapping, or rewarding with toy coupons were incorporated. Initially, the child was praised for any reaching motion; as his ability improved, he was required to demonstrate gradually more accurate reaching attempts to receive a reward.

Letters to the editor

'Efficacy of botulinum toxin A, serial casting, and combined treatment for spastic equinus: a retrospective analysis'

SIR—I read this paper¹ with interest. We use all three treatment strategies for paediatric contracture of the calf muscle-tendon complex.

It would appear from this study that casting alone or in combination with botulinum toxin A is superior to toxin alone in promoting an improved joint range in these retrospectively-studied patients. However, I am not sure that the patients in each group are directly comparable as the toxin alone group had the mildest mean contractures, i.e. they only lagged by a mean of 2° short of the neutral angle at the ankle, compared with mean contractures of 5 and 6° respectively for the casting alone or casting and toxin groups respectively. Not surprisingly, the joint range achieved by the toxin alone group was less than that in the other treatment modalities.

Can the figures be reworked to show how toxin alone works for mean contractures of 5 to 6° compared with casting alone or combination treatment?

DOI: 10.1017/S0012162205211295

Jean-Pierre Lin

Consultant Paediatric Neurologist, Newcomen on Borough, Guy's & St Thomas' NHS Foundation Trust, London, UK

Correspondence to:

Jean-Pierre.Lin@gstt.sthames.nhs.uk

References

1. Glanzman AM, Heakyung K, Swaminathan K, Beck T. (2004) Efficacy of botulinum toxin A, serial casting, and combined treatment for spastic equinus: a retrospective analysis. *Dev Med Child Neurol* 46: 807–811.

'Glanzman replies'

SIR—Dr Lin brings up a good point. However, the confound that Dr Lin describes would be based on the fact that the more contracted group had a greater amount of range to gain in order to reach a normal or functional range of motion. Our data, however, showed not only that the casting groups produced a greater change but also that, on average, they had a greater posttreatment range of motion (100° vs 50°). One could make the assertion from this that as the botox group fell short of the two casting groups in their end range, the initial magnitude of the contracture was not a significant factor contributing to the differences we saw. Certainly, a prospective trial would be able to address this issue in a more satisfactory manner through the use of randomization or stratification to control the difference in initial contracture. This was not possible in a retrospective study. We have felt here that botulinum toxin A (BTX-A) alone has not been a robust enough treatment to correct the most significant contractures. As a result of this, at our institution, serial casting has been used in addition to BTX-A to treat the most severe contractures. Because of our clinical practice our data was skewed in this way and is a reflection of the treatment choices we make.

DOI: 10.1017/S0012162205221291

Allan Glanzman PT DPT PCS ATP

Clinical Specialist, Physical Therapy Department, Children's Seashore House of The Children's Hospital of Philadelphia, Pennsylvania, USA

Correspondence to: glanzmana@email.chop.edu