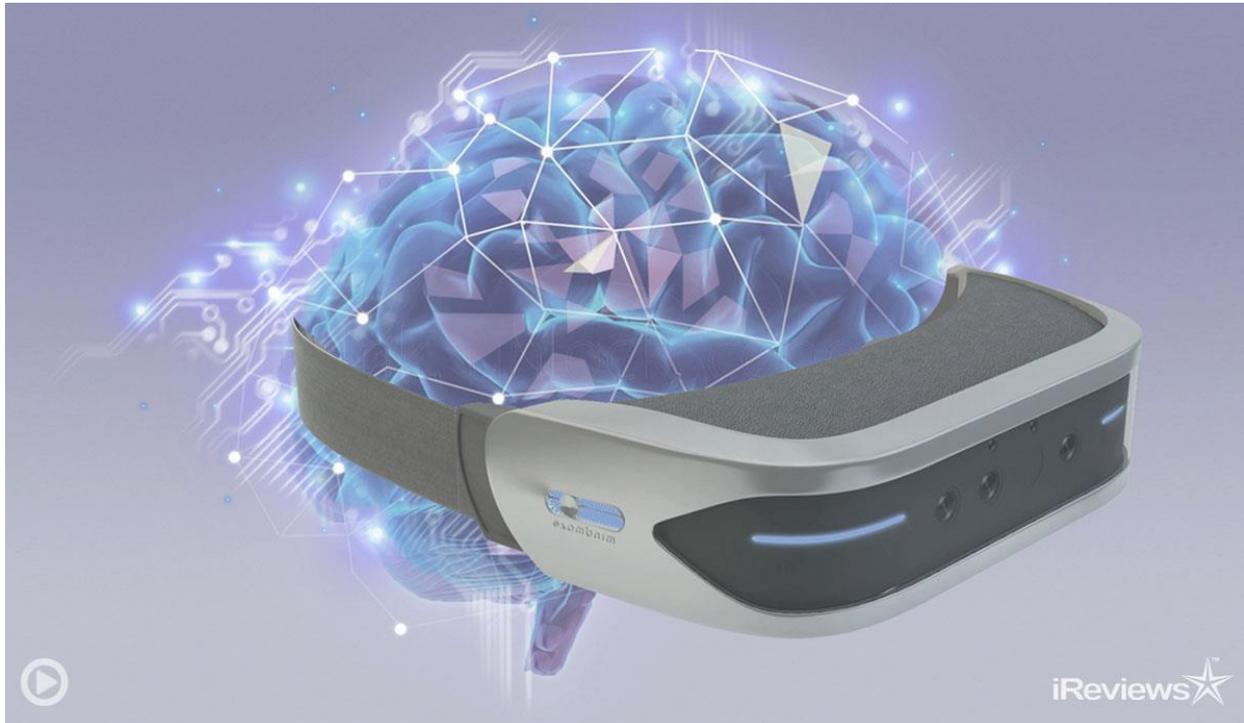




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## Virtual reality as a treatment

### The effects of virtual reality on motor rehabilitation.

Bachelor scriptie Life Science and Technology, Neurowetenschappen

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## **Abstract**

The use of virtual reality (VR) is now a days not limited to pleasure. The use of VR for rehabilitation is one of these applications. With the use of specific VR, rehabilitation of patients suffering from neuronal and motor disorders could possibly be improved. But does the use of virtual environments and virtual reality actually improve neuronal and muscular rehabilitation? Studies regarding the rehabilitation of stroke patients, cerebral palsy patients and spinal cord injury patients using VR for rehabilitation showed that VR application led to an improvement of motor function and neuroplastic changes. VR therapy also showed effects in healthy subjects. These effects caused by VR therapy suggest that the use of VR therapy in stroke patients, cerebral palsy patients and spinal cord injury patients improves the rehabilitation of the patients.

## **Introduction**

In daily life we depend on our eyes and visual stimuli. The visual information and cues we observe, control our movements and our decisions. The visual stimuli is processed and a signal is sent to our muscles to react. Due to for example a stroke this process is disrupted. The likelihood of improvement after stroke varies with the nature and severity of the initial deficit. Approximately 35 percent of survivors with initial paralysis of the leg do not regain useful function, and 20 to 25 percent of all survivors are unable to walk without full physical assistance. Six months after stroke, about 65 percent of patients cannot incorporate the affected hand into their usual activities (Dobkin, 2005). Full motoric use of the affected areas is ideal. This means that full neuronal and muscular rehabilitation in these patients would be the goal. However, full recovery is hard because movement is needed to enhance these rehabilitary processes that are needed to restore full motoric function. With the use of a virtual environment of virtual reality this problem may be solved. This research will focus on the use of this technology in combination with several other known treatments to enhance the chances of a full recovery. The main research question that will be addressed through this research is “Does the use of virtual environments and virtual reality improve neuronal and muscular rehabilitation? “.

## Virtual or reality?

Before clinical application can be discussed, the definition of the terms virtual environment and virtual reality need to be set. Previous research state that in the domains of psychotherapy and rehabilitation, virtual environments (VEs) are applied to treat patients. Virtual reality (VR) enables the therapist to create real world scenarios which can be manipulated freely and quit immediately if required. (Beck et al., 2009). This means that, in this context, virtual reality creates a virtual environment to be used for treatment. In this research both are important. To understand the possibilities of treatment with VE and VR the effect on the body needs to be researched.

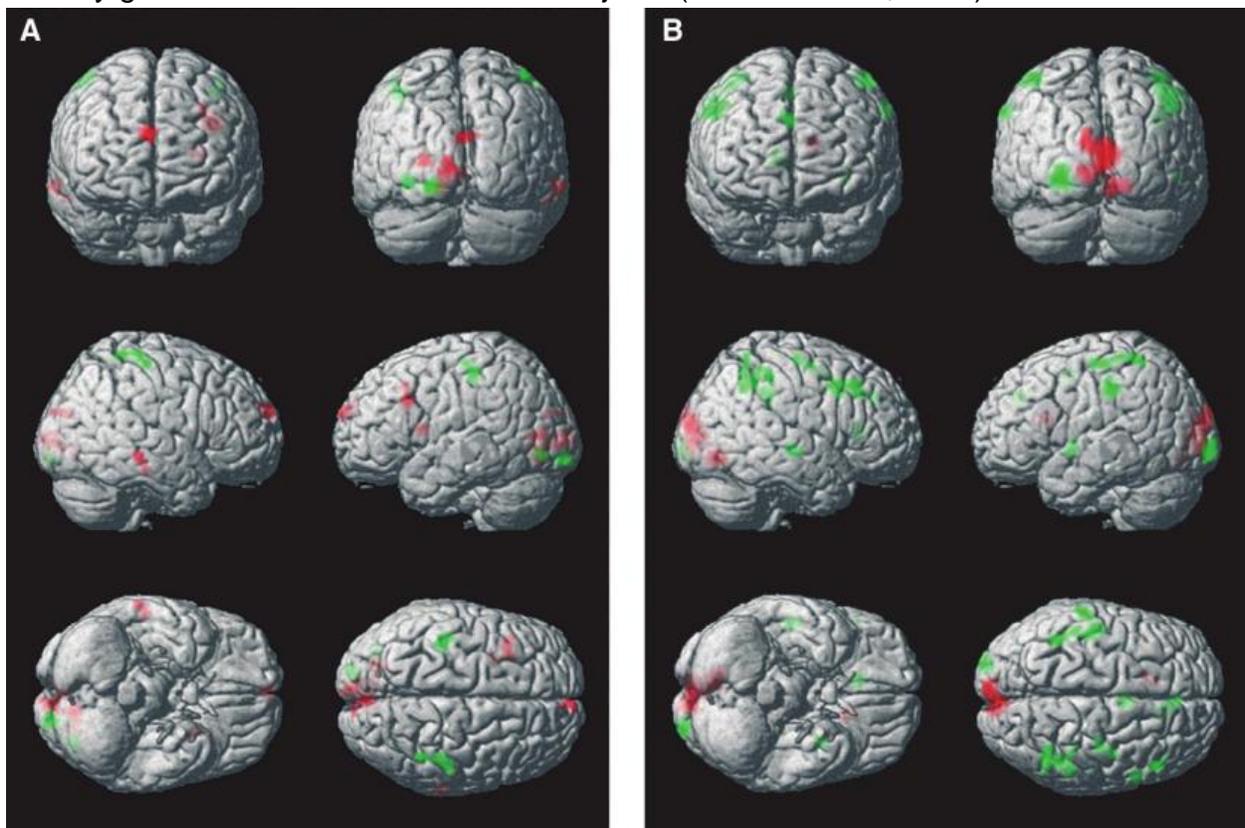
When discussing the quality of VR applications, the terms presence and immersion are important. Immersion refers to the technical performance of a VR application, presence describes the user's subjective psychological response to a VR system (Slater et al., 2005). These two terms determine the ecological validity. If the ecological validity is high, that means that the VR experience is close to a real-world experience. It is assumed that high levels of immersion cause an increased sense of presence and a more realistic experience (Bowman et al., 2007). Because presence is an individual and context dependent user response, it is usually assessed by subjective interrogation. It is presumed that ecological validity is limited by the fact that VR does not perfectly mimic the real world. Heterogeneous results have been reported concerning the equivalence of perception and action in VR and the real world (Beck et al., 2009).

A well-known difference when using stereoscopic displays is the contorted depth perception induced by presenting images on one surface. Focus cues such as accommodation and blur in the retinal image specify rather the depth of the display than the depth of the simulated objects (Hoffman et al., 2008). Furthermore, there is a mismatch between accommodation and convergence on a virtual object. While eye convergence is the angle with which both eyes fixate an object, accommodation is the refraction of the lenses, which adapts to differential distances (Beck et al., 2009). In VEs, eyes converge to the object of interest, but accommodation is always adapted to the projection screen, not the object. This vergence-accommodation conflict was recently proven to cause visual fatigue and discomfort (Hoffman et al., 2008). It is thus unclear if 3D objects in VR are processed analogically to the real world. A method for the investigation of this question is functional magnetic resonance imaging (fMRI), which can serve as an evaluation method for the quality of VR applications (Beck et al., 2009).

Differences and commonalities of brain processes in VR and the real world can be identified. This sheds a light on human processing and helps identify crucial aspects of VR that are required to simulate real-world processing. The investigation of human

processing in a spatial VR task by using fMRI demonstrates that brain imaging methods can be used as indicators for the ecological validity and presence of VR applications. If the prerequisites for ecological validity are fulfilled, it enables the therapist to treat patients suffering from impaired spatial processing after brain damage. The VR task could then be used as a training tool for restoring activations in damaged areas of the brain (Beck et al., 2009).

In the real world, differential brain activations were found for near and far space (i.e., near space was associated with the so-called dorsal visual stream and far space with the ventral stream). The ventral stream, which projects from the primary visual area to the inferotemporal cortex, is associated with the perceptual identification of objects; the dorsal stream projecting from visual areas to the posterior parietal region is linked to visually guided actions directed at such objects (Goodale et al., 1992).



**Figure 1. Near-space activations versus far-space activations. A: Horizontal task. B: Vertical task. Activations in red indicate stronger activations for near space, activations in green indicate stronger activations for far space.**

## **Neurorehabilitation.**

Neurorehabilitation applications have been focused on two areas: balance disorders and their underlying multisensory integration mechanisms and recovery of function after stroke (Bohil et al., 2011). VR simulations can be highly engaging, which provides crucial motivation for rehabilitative applications that require consistent, repetitive practice. Furthermore, the tracking systems used in VR provide an excellent tool for recording and following minute changes and improvements over time. Indeed, immersive multimodal VRs that link head, hand and body movement to changes in visual and auditory stimuli have proven useful for the recovery of motor function and postural stability (Bohil et al., 2011). For example, in postural and gait disorders. Several studies have shown that postural sway exhibits greater variance with age and in patients with balance disorders. Selective modification of one or more sensory channels has been found to reduce the amount of variance exhibited (Bohil et al., 2011). There is evidence that VR helps to engage primary and secondary motor areas related to recovery of muscle control after stroke (August et al., 2006) (Adamovich et al., 2005). Similar studies have examined children with gait disorder due to cerebral palsy (Baram et al., 2009). After walking on a track while observing a virtual tile floor for 20 minutes, participants showed improvements in walking speed and stride length, particularly those with the lowest baseline speed and stride lengths (as measured before the VR task). Similar trends have been reported for patients with gait disturbances related to multiple sclerosis (Baram et al., 2006). Again, the results seem to indicate that the timing of multimodal stimulation in VR (seeing a virtual tile floor under foot while hearing footsteps on the floor) provides feedback that helps the patient to understand that they are currently walking steadily, and helps the brain to bypass damaged areas to some extent in those cases where the sensorimotor vividness of the environment engages reflexive responses (Bohil et al., 2011).

VR has also found promise in stimulating the recovery of function in patients who have suffered a stroke (Bohil et al., 2011). To interact with the virtual environment, patients were given a force-feedback-enabled data glove (containing an exoskeleton of computer-controlled finger actuators that modify forces to simulate surface resistance), and after 2 weeks of desktop-VR tasks, improvements in individual finger control, thumb and finger range of motion, and thumb and finger speed were observed (Merians et al., 2006) (Adamovich et al., 2009). These results were retained after a week, highlighting the benefits of VR for rehabilitation. These authors attribute much of the improvement to increased motivation to engage in rehabilitative exercises. The exercises are embedded in a real-world context or a game and can be more engaging than a sterile medical office (Bohil et al., 2011). Several studies on the use of VR for upper-body exercise with feedback (for example, visual, auditory or haptic information indicating how close a patient has come to a desired performance goal) show significant improvement in the

movement, use and control of patients' hands, relative to baseline and to other rehabilitation approaches such as patient-guided exercise and group physical therapy (Henderson et al., 2007) (Merians et al., 2002). Other studies concerning rehabilitation using VR in stroke patients, cerebral palsy patients and spinal cord injury patients will further be discussed later.

## **Virtual reality treatment**

To understand and support the use of virtual reality in rehabilitation, the use of VR needs to be researched in different cases. The effectiveness of VR may not be homogenous for patients suffering from different disorders. Therefore, the use of VR in stroke patients, cerebral palsy patients and patients suffering from a spinal cord injury will be discussed.

### **Virtual reality in stroke patients**

#### **Motor rehabilitation using VR in stroke patients**

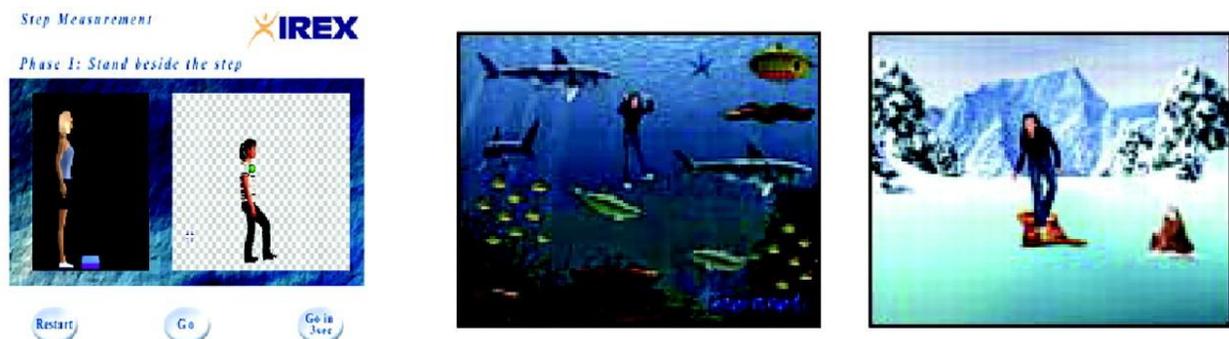
To determine the effect of VR on rehabilitation of motor function in stroke patients first the locomotor function was determined by the standardized FAC (functional ambulation category) and MMAS (modified motor assessment scale). A separate MWW (The Mann–Whitney-Wilcoxon) test revealed that there was significant difference in the interval changes in the FAC and MMAS scores between the groups ( $P < 0.05$ ), suggesting that the VR-trained group performed significantly better as a function of the intervention (Sung et al., 2005). This suggests that VR treatment improves the motor function of stroke patients.

#### **VR intervention**

The VR intervention used for this experiment is shown in figure 2. The different mini games are a Stepping up/down, a Sharkbait and a Snowboard game (from left to right in figure 2). VR was added to facilitate range of motion, balance, mobility, stepping, and ambulation skills. The VR tasks were designed to focus on the development of the different skills as described previously, with each game programmed to exercise 1 or multiple aspects of trunk, pelvis, hip, knee, and ankle movement (Hedenberg et al., 2003) (Sung et al., 2005).

## Neuronal effect

To examine the neuronal effect of the VR intervention a fMRI was performed. Predetermined regions of interest (ROIs) were bilaterally drawn around the primary sensory cortex (S1), the primary motor cortex (M1), the primary sensorimotor cortex (SMC), the premotor cortex (PMC), and the supplementary motor area (SMA) because the areas have been reported to have neuroplastic recovery potentials (Sung et al., 2005). The results of this fMRI are shown in figure 3 and 4. Independent sample t test revealed that the VR group compared with the control group showed significantly greater group mean LI difference (post-test–pretest) for SMC ( $P < 0.001$ ), suggesting that VR may be effective to induce measurable neuroplastic changes. As shown in Figure 3, t test revealed that among the predefined ROIs, only LI in the primary SMC area was statistically significant ( $t = -2.60$ ;  $P < 0.05$ ). This finding indicated that the LI in the VR group compared with the control group showed a significant increase as a function of the VR intervention (Figures 3 and 4). However, the interval cortical activation changes in the other ROIs were neither significantly different within the control group nor between the groups ( $P > 0.05$ ) (Sung et al., 2005). The results of this study suggest that VR treatment is effective to induce neuroplastic changes needed for recovery.



A. Stepping up/down

B. Sharkbait

C. Snowboarding

Figure 2. VR exercise games. A, Stepping up/down; B, Sharkbait; C, Snowboarding. Reprinted with permission from IREX, JesterTek, Inc. (Sung et al., 2005)

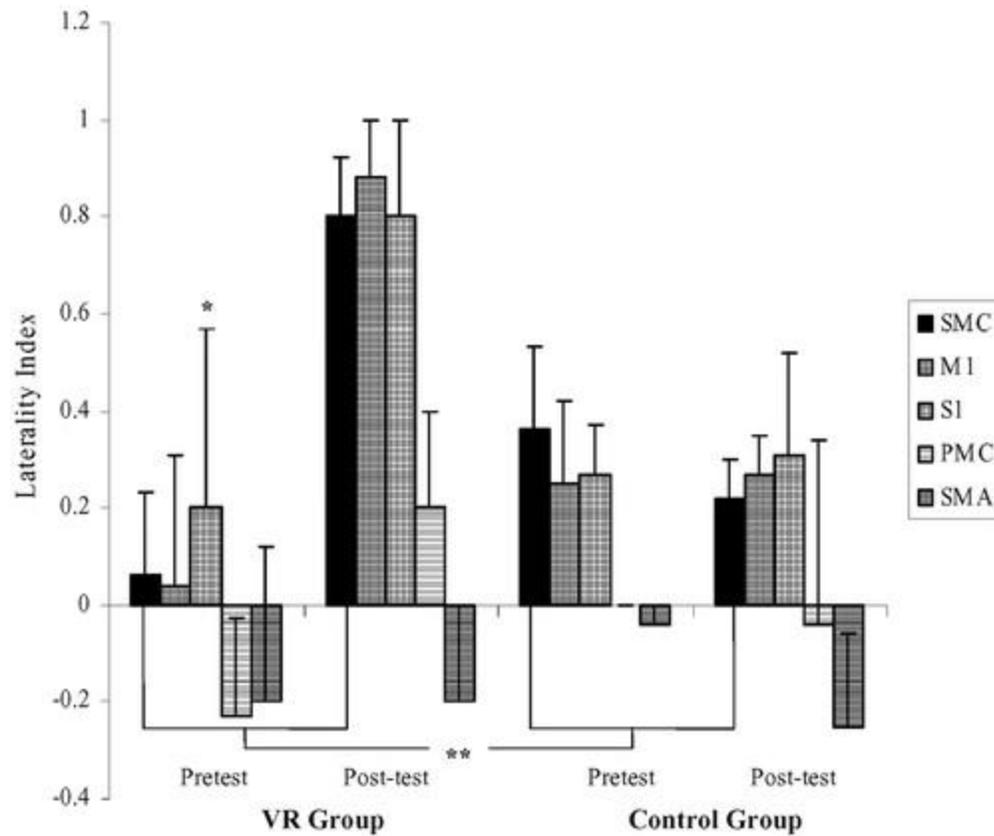
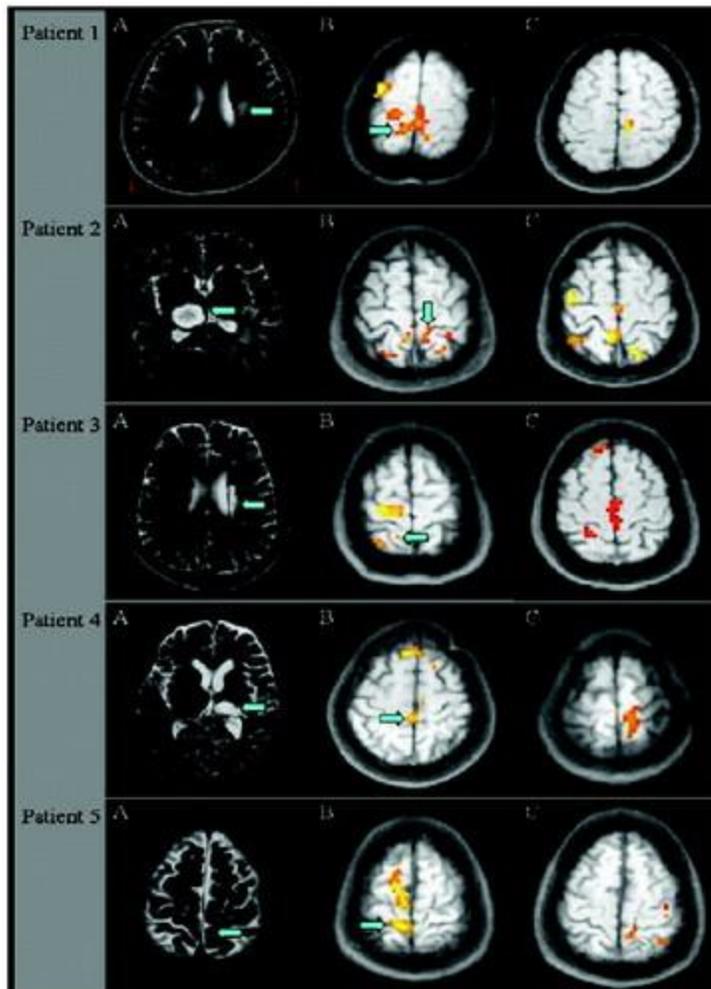


Figure 3. LI for each ROI during affected knee movement. \*SEM; \*\*independent sample t test revealed that the VR group compared with the control group showed significantly greater group mean LI difference (post-test–pretest) for SMC ( $P < 0.001$ ), suggesting that VR may be effective to induce measurable neuroplastic changes (Sung et al., 2005).



**Figure 4. A, T2-weighted diagnostic brain MRI images. The arrow indicates the lesion site. B, Before VR, all patients showed the ipsilateral activations (arrow) at primary SMCs. C, After VR, the ipsilateral SMC activity (arrow) disappeared (patient 1, 2, 4, and 5) or decreased (patient 3) during affected knee movement (Sung et al., 2005).**

## **Neglect**

Neglect is one of the factors that inhibits a patient from fully recovering. Neglect is when a patient (subconsciously) ignores a stimulus of the area affected by the stroke. This leads to a full loss of function. This loss of function inhibits the recovery of the patient. With VR this neglect can possibly be reduced. This would possibly help a patient in recovery. In IRF settings, spatial neglect impedes rehabilitation outcomes, prolongs hospitalization, increases safety risk, and decreases the likelihood of successful community reintegration (Chen et al., 2015). VR may be a solution to this problem. The aim of neglect treatment is to reduce the imbalance between the two hemispheres. VR can possibly help by stimulating affected brain areas and so reduce the imbalance between the two hemispheres (Johansson, 2012).

## Virtual reality in cerebral palsy patients

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). A study conducted by You et al. discusses the use of VR treatment in rehabilitation of patients suffering from cerebral palsy.

### VR intervention

The VR treatment used in a study by You et al. used a system called IREX VR therapy system. This system used cyber gloves, virtual objects, and a large screen. The video camera is used to capture and track movement and immerse the patient inside the VR scene. Several mini games were used to challenge the patient. The bird-ball, conveyor, and soccer exercise games (Fig. 5b–d) were interfaced with virtual environments to facilitate range of motion, mobility, and strength, which are important elements in developing reaching skills (You et al., 2005).



Figure 5 (a) Virtual reality experimental set-up; (b) bird-ball; (c) conveyor; (d) soccer.

## Motor function

Before VR therapy, the child had no functional use of the affected hand, which was evident in the PMAL (Pediatric Motor Activity Log) test score. After VR therapy, the BOTMP (Bruininks–Oseretsky Test of Motor Proficiency) 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 (Fugl-Meyer assessment) 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 (You et al., 2005).

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

**Table I. Bruininks–Oseretsky Test of Motor Proficiency (BOTMP), modified Pediatric Motor Activity Log (PMAL), and Fugl-Meyer assessment (FMA) scores for pre- and postvirtual reality (VR) therapy (You et al., 2005).**

## Neuroimaging

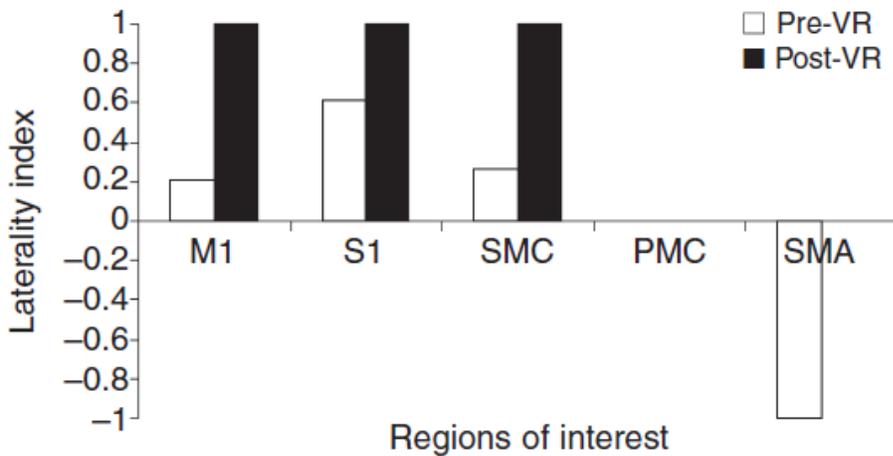
Cortical reorganization in the principal ROIs activated pre and post-VR therapy during either affected right elbow movement or unaffected left elbow movement is presented in Tables I and II respectively. In movement the affected elbow before VR therapy, the activated voxels were 121 for ipsilateral SMC 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. 6). 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. 6&7) (You et al., 2005).

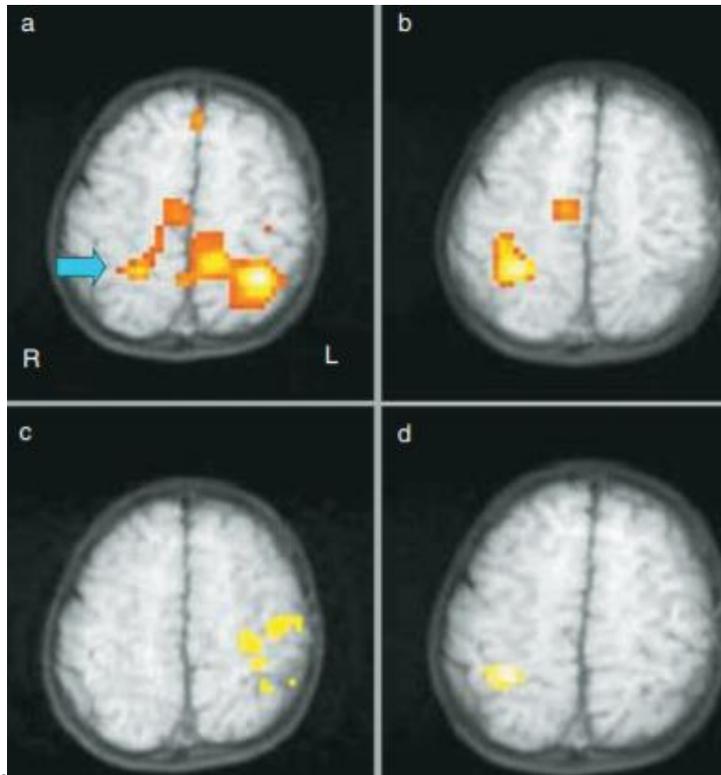
<i>ArEM</i>	<i>MI</i>			<i>SI</i>			<i>SMC</i>			<i>PMC</i>			<i>SMA</i>		
	<i>C</i>	<i>I</i>	<i>LI</i>	<i>C</i>	<i>I</i>	<i>LI</i>	<i>C</i>	<i>I</i>	<i>LI</i>	<i>C</i>	<i>I</i>	<i>LI</i>	<i>C</i>	<i>I</i>	<i>LI</i>
Pre-VR therapy	79	51	0.21	86	21	0.61	207	121	0.26	0	0	0	0	55	-1
Post-VR therapy	41	0	1	31	0	1	97	0	1	0	0	0	0	0	0
<i>UIEM</i>	<i>MI</i>			<i>SI</i>			<i>SMC</i>			<i>PMC</i>			<i>SMA</i>		
	<i>C</i>	<i>I</i>	<i>LI</i>	<i>C</i>	<i>I</i>	<i>LI</i>	<i>C</i>	<i>I</i>	<i>LI</i>	<i>C</i>	<i>I</i>	<i>LI</i>	<i>C</i>	<i>I</i>	<i>LI</i>
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

MI, primary motor cortex; SI, 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.

**Table II. 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) (You et al., 2005)**



**Figure 6 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 (You et al., 2005).**



**Figure 7. 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 (You et al., 2005).**

These 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 (You et al., 2005). 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 imitation mechanism (You et al., 2005). This mechanism is believed to facilitate the M1 via 'mirror' neuron circuits (You et al., 2005). The present findings suggest that the pictorial sensory feedback received during VR therapy facilitated internalization of the motor representation of the target motor behavior. 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 (You et al., 2005).

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 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).

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 (You et al., 2005). These findings suggest that VR therapy has a positive influence on the rehabilitation of cerebral palsy patients.

## Virtual reality in spinal cord injury patients

To examine the effect of virtual reality treatment subjects were selected with a chronic iSCI and a lesion level below C4, no assistive and supporting systems needed to sit in a chair, and American Spinal Injury Association Impairment Scale (AIS) C or D (i.e., sensorimotor incomplete) at time of inclusion (C = more than half of the key muscles below the neurological level have a muscle grade less than 3; D = at least half of the key muscles below neurological level have muscle grade  $\geq 3$ ) (Marino et al., 2003).

The VR system used for this experiment presented virtual representations of the feet and legs in a first-person perspective on a laptop computer and trained the lower limbs by combining action observation and execution (Figure 8)(Villiger et al., 2017).



**Figure 8: Overview of a virtual reality training setup and the different scenarios for training the various lower limb muscles and functions. Ankle dorsal flexion: Hamster Splash—launching hamsters into a swimming pool (A); Footbag—juggling a ball (B); and Get to the Game—walking from home via a tram station to a stadium (E). Knee extension: Star Kick—kicking balls toward stars (C). Leg ad-/abduction: planet drive—avoid touching oncoming cars (D).**

In collaboration with therapists, clinically relevant exercises for foot and leg while seated or in a standing position were generated. Five VR scenarios were provided on the

training system to train foot and leg movements in sitting and standing positions. The system contained applications to train different isolated movements as follows (Villiger et al., 2017).

At post-assessment, significant increases ( $P \leq 0.017$ ) in comparison with the averaged pre-baseline and baseline were found in the primary outcome measures such as muscle strength (LEMS,  $P = 0.008$ ), balance (BBS,  $P = 0.008$ ), and functional mobility (TUG,  $P = 0.005$ ). In addition, 7 out of 11 subjects improved (i.e., an increase of one grade at least) in ankle dorsiflexion (L4) and four of them reached the MCID of LEMS (overall) at post-assessment. The secondary outcome measures showed with respect to walking speed/distance and mobility no significant effects: 10MWT ( $P = 0.169$ ), 6minWT ( $P = 0.037$ ); SCIM III mobility ( $P = 0.018$ ), and WISCI II ( $P = 0.180$ ) (Villiger et al., 2017). Improvements were found in 64% of the subjects in ankle dorsiflexion (L4), and a general increase in lower limb muscle strength (LEMS) was achieved. In addition, an MCID by one-third of the subjects was reached. These changes may have been of relevance in enabling the observed gains in walking speed, stability, and mobility (reflected by improvements in TUG and BBS) (Villiger et al., 2017).

Virtual reality-based rehabilitation training combining action observation and execution and providing intensive, repetitive, and motivating training scenarios led to improvements in lower limb motor function. Therefore, the system may be of benefit as a neurorehabilitation tool for patients suffering from a spinal cord injury (Villiger et al., 2017).

### **Specific VR and Non-specific VR**

For clinical application it is important to distinguish between VR systems specifically built for rehabilitation (SVR) and off-the-shelf recreational VR systems (NSVR), based on the assumption that SVR systems incorporate principles of neurorehabilitation that potentially enhance learning and recovery, whereas NSVR systems do not. Our results demonstrate that SVR systems show a higher impact on recovery, on body function, and on activity than CT and that NSVR systems do not. (Maier et al., 2019). In all three cases examined in this study, specific VR was used. The VR used was focussed on improving rehabilitation by stimulating the patient in the area affected by their disorder. The VR systems used by these studies are specifically adjusted to help recovery and are not the “off the shelf” VR products that non-specific VR mentions. This needs to be taken into consideration when discussing possible clinical application of VR therapy.

## **VR in healthy patients.**

The effect of Virtual reality on neuronal activity is not limited to patients suffering from a disorder. Also, in healthy individual's virtual reality affected neuronal activity. A study conducted by Adamovich et al. showed three main findings when examining neuronal activity in the brain while interacting with virtual reality. First, both observation with intent to imitate and imitation with a real-time virtual avatar feedback, were associated with activation in a distributed frontoparietal network typically recruited for observation and execution of real-world actions. Second, there was noted a time-variant increase in activation in the left insular cortex for observation with intent to imitate actions performed by the virtual avatar. Third, imitation with virtual avatar feedback (relative to the control condition) was associated with a localized recruitment of the angular gyrus, precuneus, and extrastriate body area, regions which are (along with insular cortex) associated with the sense of agency. (Adamovich et al., 2009). These findings suggest that the effect of VR therapy does not limit to patients with a disorder.

## Discussion

The use of VR to help neuronal and muscular rehabilitation is very diverse. Different approaches are seen to try and reach the same effect on muscular and neuronal rehabilitation. This study addressed the following research question: “Does the use of virtual environments and virtual reality improve neuronal and muscular rehabilitation?”. To answer that question different cases were examined in which VR was used for treatment. Under all three cases improvement of rehabilitation was seen. Improvement in neuronal rehabilitation was seen in stroke patients and in cerebral palsy patients. Improvement of muscular rehabilitation was seen in stroke patients, cerebral palsy patients and in spinal cord injury patients. However, the conditions under which the patients were exposed to VR is important to take into account. Research states that not all VR is shown to improve effect on rehabilitation. Specific virtual reality showed more effect on rehabilitation than non-specific rehabilitation and control groups (Maier et al., 2019). All cases examined in this study used specific VR to help improve rehabilitation. For clinical application this is very important because the effect of non-specific VR on rehabilitation is not clear. Also, the quality of the VR needs to be taken into account. As shown by Beck et al. (Beck et al., 2005). By simulating a real-world experience with a high ecological validity, the effect of VR on the patient can be improved. This combined with a good motivation that results in a good psychological response to the VR system gives the patient the best rehabilitation chances (Beck et al., 2005).

However, it cannot be concluded that the use of VR in neuronal and muscular rehabilitation is universal. All cases in this study treated patients that already had a certain degree of mobility that allowed them to use the VR systems more freely. The use of VR systems in rehabilitation of patients with an absence of mobility is not yet proven to improve rehabilitation. The same approach in combination with helping devices and an improved VR system that simulates a more realistic real-world experience may offer the stimulation needed for rehabilitation of these patients, but this needs to be researched.

Based on the discussed studies, application of VR in rehabilitation of patients suffering from neuronal and muscular damage is helpful. VR offers a non-invasive, playful way of rehabilitating which offers an improvement in neuronal and muscular rehabilitation. In combination with a specific and realistic VR experience this offers the best perspective for treatment and clinical application. The research question addressed in this study stated, “Does the use of virtual environments and virtual reality improve neuronal and muscular rehabilitation?”. Based on this research virtual environments and virtual reality improve neuronal and muscular rehabilitation in stroke patients, cerebral palsy patients and spinal cord injury patients. More applications of VR therapy can be hypothesized but need to be studied. Future applications in other disorders than the disorders mentioned in this research need to be studied before clinical application is possible.

## References:

1. Adamovich, S. V. et al. Design of a complex virtual reality simulation to train finger motion for persons with hemiparesis: a proof of concept study. *J. Neuroeng. Rehabil.* 6, 28 (2009).
2. Adamovich, S. V., August, K., Merians, A., & Tunik, E. (2009). A virtual reality-based system integrated with fMRI to study neural mechanisms of action observation-execution: a proof of concept study. *Restorative neurology and neuroscience*, 27(3), 209–223. doi:10.3233/RNN-2009-0471
3. 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.
4. August, K. et al. fMRI analysis of neural mechanisms underlying rehabilitation in virtual reality: activating secondary motor areas. *Conf. Proc. IEEE Eng. Med. Biol. Soc.* 3692–3695 (2006).
5. Baram, Y. & Lenger, R. Virtual reality visual feedback cues for gait improvement in children with gait disorders due to cerebral palsy. *Proc. of the 19th Meeting of the European Neurological Soc. (Milan, Italy)* (2009).
6. Baram, Y. & Miller, A. Virtual reality cues for improvement of gait in patients with multiple sclerosis. *Neurology* 66, 178–181 (2006).
7. Beck, L., Wolter, M., Mungard, N.F., Vohn, R., Staedtgen, M., Kuhlen, T., Sturm, W., (2009). Evaluation of Spatial Processing in Virtual Reality Using Functional Magnetic Resonance Imaging (fMRI). *CyberPsychology & Behavior*. 091019095317065. 10.1089/cpb.2008.0343.
8. Bohil, Corey & Alicea, Bradley & Biocca, Frank. (2011). Virtual reality in neuroscience research and therapy. *Nature reviews. Neuroscience*. 12. 752-62. 10.1038/nrn3122
9. Bowman D, McMahan R. Virtual reality: how much immersion is enough? *IEEE Computer* 2007; 40:36–43.
10. Briellmann RS, Abbott DF, Caflisch U, Archer JS, Jackson GD. (2002) Brain reorganisation in cerebral palsy: a high-field functional MRI study. *Neuropediatrics* 33: 162–166.
11. 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.
12. Chen, P., Hreha, K., Kong, Y., & Barrett, A. M. (2015). Impact of spatial neglect on stroke rehabilitation: evidence from the setting of an inpatient rehabilitation facility. *Archives of physical medicine and rehabilitation*, 96(8), 1458–1466. doi:10.1016/j.apmr.2015.03.019

13. Dobkin B. H. (2005). Clinical practice. Rehabilitation after stroke. *The New England journal of medicine*, 352(16), 1677–1684. doi:10.1056/NEJMcp043511
14. Goodale M, Milner A. Separate visual pathways for perception and action. *Trends in Neurosciences* 1992; 15:20–5.
15. Hedenberg R, Ajemian S. IREX 1.3 Clinical Manual. New York, NY: JesterTek Inc; 2003.
16. 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.
17. Henderson, A., Korner-Bitensky, N. & Levin, M. Virtual reality in stroke rehabilitation: a systematic review of its effectiveness for upper limb motor recovery. *Top. Stroke Rehabil.* 14, 52–61 (2007).
18. Hoffman DM, Girshick AR, Akeley K, et al. Vergence accommodation conflicts hinder visual performance and cause visual fatigue. *Journal of Vision* 2008; 8:1–30.
19. Johansson B. B. (2012). Multisensory stimulation in stroke rehabilitation. *Frontiers in human neuroscience*, 6, 60. doi:10.3389/fnhum.2012.00060
20. Jones TA, Schallert T. (1994) Use-dependent growth of pyramidal neurons after neocortical damage. *J Neurosci* 14: 2140–2152
21. 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.
22. Liepert J, Bauder H, Miltner WH, Taub E, Weiller C. (2000) Treatment-induced cortical reorganization after stroke in humans. *Stroke* 31: 1210–1216.
23. Maier, M., Rubio Ballester, B., Duff, A., Duarte Oller, E., & Verschure, P. F. M. J. (2019). Effect of Specific Over Nonspecific VR-Based Rehabilitation on Poststroke Motor Recovery: A Systematic Meta-analysis. *Neurorehabilitation and Neural Repair*, 33(2), 112–129. <https://doi.org/10.1177/1545968318820169>
24. Marino RJ, Barros T, Biering-Sorensen F, Burns SP, Donovan WH, Graves DE, et al. International standards for neurological classification of spinal cord injury. *J Spinal Cord Med* (2003) 26:50–6. 10.1080/10790268.2003.11754575 [PubMed] [CrossRef] [Google Scholar]
25. Merians, A. S. et al. Virtual reality — augmented rehabilitation for patients following stroke. *Phys. Ther* 82, 898–915 (2002).M
26. Merians, A. S., Poizner, H., Boian, R., Burdea, G. & Adamovich, S. Sensorimotor training in a virtual reality environment: does it improve functional recovery poststroke? *Neurorehabil. Neural Repair* 20, 252–267 (2006).

27. 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.
28. Slater M, Wilbur S. A framework for immersive virtual environments (FIVE): speculations on the role of presence in virtual environments. *Presence: Teleoperators & Virtual Environments* 1997; 6:603–16.
29. Sung H. You, PT, PhD , Sung Ho Jang, MD , Yun-Hee Kim, MD, PhD , Mark Hallett, MD , Sang Ho Ahn, MD , Yong-Hyun Kwon, PT, MS , Joong Hwi Kim, PT, MS , and Mi Young Lee, PT. Virtual Reality–Induced Cortical Reorganization and Associated Locomotor Recovery in Chronic Stroke (2005) *Stroke*. 2005;36:1166–117
30. Villiger, M., Liviero, J., Awai, L., Stoop, R., Pyk, P., Clijsen, R., ... Bolliger, M. (2017). Home-Based Virtual Reality-Augmented Training Improves Lower Limb Muscle Strength, Balance, and Functional Mobility following Chronic Incomplete Spinal Cord Injury. *Frontiers in neurology*, 8, 635. doi:10.3389/fneur.2017.00635
31. You SH1, Jang SH, Kim YH, Hallett M, Ahn SH, Kwon YH, Kim JH, Lee MY. (2005). Virtual reality-induced cortical reorganization and associated locomotor recovery in chronic stroke: an experimenter-blind randomized study. *Stroke*. 2005;36:1166–1171.
32. You, S., Jang, S., Kim, Y., Kwon, Y., Barrow, I., & Hallett, M. (2005). Cortical reorganization induced by virtual reality therapy in a child with hemiparetic cerebral palsy. *Developmental Medicine & Child Neurology*, 47(9), 628-635. doi:10.1017/S0012162205001234