

Virtual reality rehabilitation system for neuropathic pain and motor dysfunction in spinal cord injury patients

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Abstract—Spinal cord injury (SCI) causes both lower limb motor dysfunction and associated neuropathic pain. Although these two conditions share related cortical mechanisms, different interventions are currently used to treat each condition. With intensive training using entertaining virtual reality (VR) scenarios, it may be possible to reshape cortical networks thereby reducing neuropathic pain and improving motor function. We have created the first VR training system combining action observation and execution addressing lower limb function in incomplete SCI (iSCI) patients. A particular feature of the system is the use of size-adjustable shoes with integrated motion sensors. A pilot single-case clinical study is currently being conducted on six iSCI patients. Two patients tested to date were highly motivated to perform and reported improved physical well-being. They improved in playing skill and in controlling the virtual lower limbs. There were post-intervention indications of neuropathic pain decrease, muscle strength increase, faster walking speed and improved performance on items relevant for ambulation. In addition functional MRI before and after treatment revealed a decreased activation pattern. We interpret this result as an improvement of neuronal synergies for this task. These results suggest that our VR system may be beneficial for both reducing neuropathic pain and improving motor function in iSCI patients.

Index Terms—Virtual reality, rehabilitation, spinal cord injury, neuropathic pain, motor dysfunction

I. INTRODUCTION

Injury of the spinal cord often leads to long lasting lower limb motor dysfunction and associated neuropathic pain. These problems are challenging to treat and new approaches are needed to relieve chronic pain. Over the past two decades it has

been established that observation of goal-directed actions, motor imagery and action execution activate overlapping cortical networks, known collectively as the mirror neuron system (for reviews see [1] - [3]). Hotz-Boendermaker et al. [4] showed that it was possible to activate these networks even in complete SCI patients during attempted, imagined and observed foot movements. These findings suggest that it may also be possible to activate cortical motor networks in iSCI patients that still project through non-injured parts of the spinal cord onto muscle effectors. In addition, there is evidence that neuropathic pain in SCI patients may be caused by a mismatch between motor output and sensory feedback, which may be reduced by employing motor imagery combined with visual illusions of virtual limbs [5]. Hence, neuropathic pain and motor dysfunction might share related cortical mechanisms, and interventions which directly address these mechanisms might bring substantial benefits to iSCI patients.

We believe that the best way to activate cortical areas related to both action observation and execution is using a VR-based interactive visuo-motor intervention. Due to technological progress the use of VR is currently expanding. VR systems are attractive for various research fields and applications in rehabilitation. Most lower limb rehabilitation systems using VR focused on posture, balance and walking and were used in a variety of populations, but less was done regarding goal-directed movements [6]-[8].

Here, we focus on goal-directed movements and the application of VR technology in therapy to assist users with distraction from pain and automation of motor therapy by physical support of constricted movements and enhancement of patient motivation [9]. Clinical assessments before and after treatment aimed to test the hypothesis that training with the VR

rehabilitation system reduces pain and improves lower limb motor function in iSCI patients.

II. PATIENTS AND METHODS

A. Study design

The study was designed as a single-case series of up to six iSCI patients. The main inclusion criteria were:

- Incomplete SCI (AIS C/D) with preserved motor function below the lesion level.
- Normal or corrected-to-normal visual acuity.
- No history of psychiatric or other neurological disorders.
- Right handed (test applied according to the Edinburgh Inventory [10]) and footed (preferred kicking foot).

All patients were aware of the purpose of the study. Informed consent was obtained from the patients and the experimental protocol was in accordance with the Declaration of Helsinki and performed with the approval of the local Ethics Committee.

B. VR rehabilitation system (intervention)

The participants were trained 16-20 times during a period of 4 weeks (4-5 x 45 minutes per week). The VR rehabilitation system consists of a PC and a large-screen display (132 cm diagonal) showing life-size virtual representations of the feet and legs. Adjustable shoes incorporate inclination angle sensors (accelerometers) in the foot and lower leg. Due to elastic components built into the shoes, it can be quickly fitted to patients with different-sized feet (Fig. 1).

A menu system based on a virtual assistant was developed to make the system as easy to use as possible for therapists. In consultation with physical therapists, motivating VR scenarios were created to provide clinically relevant interactions for training foot and leg movements in a sitting or standing position. The existing scenarios are (Fig. 2):

1) *Footbag*: A simple exercise in which the patient juggles a bag between the left and right foot, using dorsal ankle flexion movements (tibialis anterior (TA) contraction), a necessary exercise to prevent foot dragging. The trajectory of the bag is pre-set so that it always moves correctly through the air between the left and right feet.

2) *Hamster splash*: Hamsters run up to the patient's toes. The patient's task is to perform a dorsal flexion of the ankle to launch each hamster into a swimming pool. The reward for launching the hamsters higher (faster ankle movement) is a higher score and more elaborate hamster movements (somersaults, swimming patterns).

3) *Star kick*: The patient performs a knee extension by kicking a ball towards the displayed stars. For every hit, the patient receives a reward.

4) *Planet drive*: Cars are moving on a planet highway towards the virtual feet. The patient's task is to avoid touching the cars by displacing the foot and legs sideways.

In each session, scenario acceptance level, performance and pain level were collected. Additionally, patients filled in a questionnaire after the session to measure how well they could immerse in the tasks, whether they had the feeling that the presented virtual feet and legs were theirs and how well they could control them as previously showed [11].

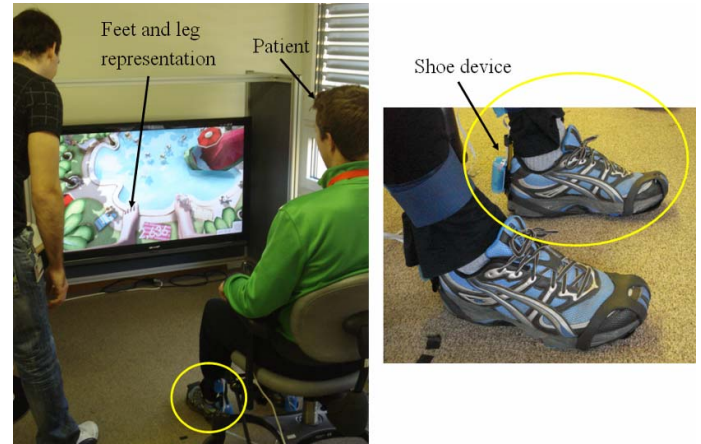


Fig. 1. Overview of VR rehabilitation system.

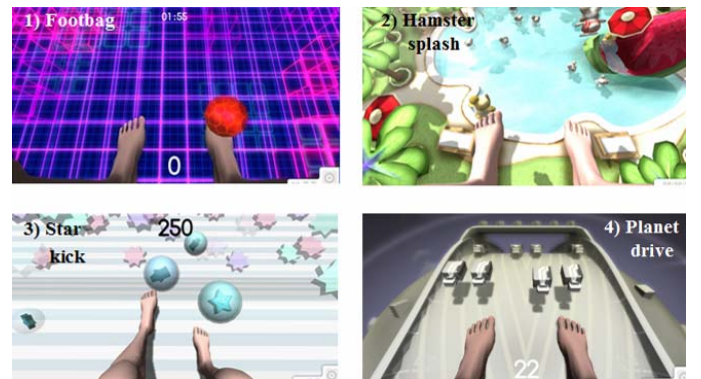


Fig. 2. Scenarios for the various lower limb muscles and functions:

- 1) Footbag - juggling a bag
- 2) Hamster splash - launching hamsters
- 3) Star kick - kicking balls towards stars
- 4) Planet drive - (avoiding) touching the cars

C. Clinical assessments

Besides the training program, both pain and motor function were investigated to test for possible transfer effects between the two. Data on pain were collected using a structured interview called the Pain Protocol which was developed at Balgrist University Hospital and is currently being evaluated in a multicenter study within the EM-SCI framework (European Multicenter Study about Spinal Cord Injury, www.emsci.org) and the 'Neuropathic Pain Scale' (NPS) assessing distinct pain qualities associated with neuropathic pain [12]. The following measurements were performed to quantify motor function:

- American Spinal Cord Injury Association Impairment Scale (AIS) - classification of individuals with SCI

(A-E): information about the motor level of the lesion determining effort from 0 (total paralysis) to 5 (active movement, full range of motion, against gravity and provides normal resistance) of key muscles (for lower limb: hip flexors, knee extensors, ankle dorsiflexors, long toe extensors and ankle plantar flexors) and information on the sensory levels of the lesion tested with light touch and pin prick [13]-[14].

- Spinal Cord Independence Measure (SCIM) - assessing activities of daily life and independence in subjects with spinal cord lesion [15].
- Walking Index for Spinal Cord Injury II (WISCI II) - assessing the need to rely on walking aids and/or personal assistance [16].
- Berg Balance Scale (BBS) - assessing balance during functional activities [17].
- 10 Meter Walking Test (10MWT) - examining gait speed over 10 m [18]-[19].
- Transcranial Magnetic Stimulation-Motor Evoked Potential (TMS-MEP) - noninvasive method to excite cortical neurons and measure changes in corticospinal tract function [20]-[21].
- Video analysis (VA) - assessing locomotion.

In addition, to gain insight into possible cortical reorganizational processes before and after the intervention, each patient was asked to play the ‘Footbag’ scenario in a 1.5T Magnetic Resonance Imaging (MRI) scanner. These fMRI data were analysed using SPM 5.

III. RESULTS

To date, the training sessions have been completed by two chronic iSCI patients (AIS D) with preserved motor function below the lesion level and at least half of the key muscles below the level of lesion have the full range of motion against gravity (Table I). In addition, Patient 2 complained about neuropathic pain at the lesion level.

A. VR rehabilitation system (intervention)

The patients tested so far enjoyed the scenarios, were highly motivated to perform the VR tasks and reported improvements in their physical well-being. Fig. 3 displays the performance of the patients during the ‘Footbag’ scenario (game time = 120 sec); the patients also improved similarly in the other scenarios. Over time, the patients reported better identification with the presented virtual feet and legs as demonstrated by the results of the questionnaires regarding control and feelings for the VR lower limbs. In parallel, enhanced ability to play the scenarios resulted in stronger feelings of controlling the virtual limbs. In addition, Patient 2 was also distracted from pain while playing and reported a decreased sense of pain after playing.

TABLE I. CLINICAL DATA OF THE ISCI PATIENTS

Pat	Sex	Age (years)	Age at injury (years)	Lesion level	AIS	Pain
1	m	70	68	C8	D	no
2	f	60	58	T4	D	yes

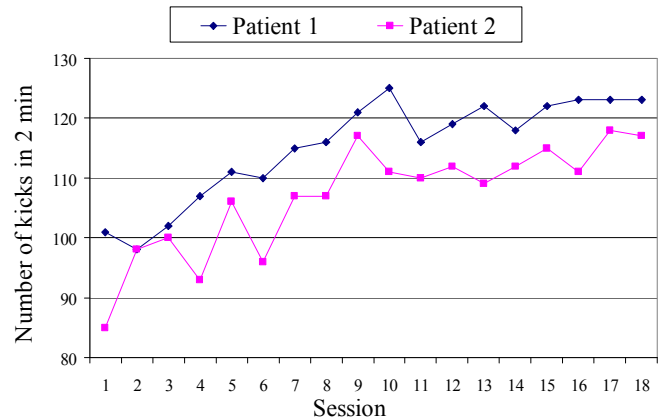


Fig. 3. Scenario results of Patients 1 and 2 in ‘Footbag’

B. Clinical assessments

Table II shows the key clinical results of the pain and motor function assessments. Patient 2 reported a slightly decreased pain sensation after the intervention on the Numerical Rating Scale (NRS). Overall, the muscle strength (AIS - lower limb motor score) increased - especially for the TA muscle. Hence, foot lifting was easier to perform, a finding also reflected in better locomotion (WISCI II, VA) and walking speed (10MWT) in both patients. They also improved in balance tasks (BBS, e.g. standing on one leg) which is important for ambulation and in daily life activities (SCIM). Interestingly, the relative MEP latency of the TA muscle improved significantly in patient 2 (Latency MEP / height). The fMRI measurements showed a similar but weaker activation pattern after intervention (Fig. 4, FWE correction, $p < 0.05$, extent threshold $k = 10$).

TABLE II. CLINICAL ASSESSMENTS BEFORE AND AFTER INTERVENTIONS

	Patient 1		Patient 2	
	Before intervention	After intervention	Before intervention	After intervention
Pain intensity on a NRS (0-10)	0	0	5	4
AIS (points) - lower limb motor score	47 / 50	49 / 50	48 / 50	49 / 50
10MWT (sec)	12.9	10.8	10.7	9.3
WISCI II (points)	16 / 20	19 / 20	16 / 20	19 / 20
BBS (points)	50 / 56	54 / 56	53 / 56	55 / 56
SCIM (points)	33 / 40	34 / 40	29 / 40	31 / 40
Latency MEP / height (msec)	Left TA: 21.3 Right TA: 22.3	Left TA: 22.2 Right TA: 23.6	Left TA: 26.1 Right TA: 23.9	Left TA: 22.9 Right TA: 19.4

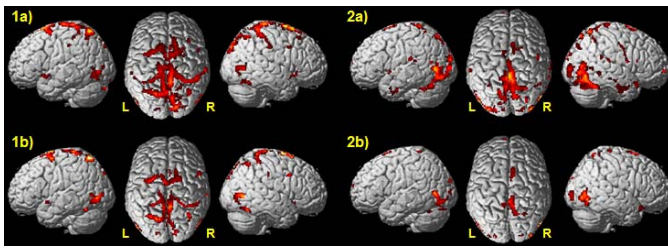


Fig. 4. Activation pattern while playing ‘Footbag’ scenario in a 1.5T MRI-Scanner - 1a) Patient 1 before intervention, 1b) Patient 1 after intervention, 2a) Patient 2 before intervention, 2b) Patient 2 after intervention.

IV. DISCUSSION

The testing of the VR rehabilitation method combining action observation with execution showed promising results. The new training system was well accepted by the patients and seemed to be enjoyable even when they were not familiar with VR. The motivational aspect is high, which is promising for simple training of repetitive movements. In addition, goal-oriented scenarios (rather than just locomotion) and adaptable difficulty levels in the VR system might improve patient concentration and the efficacy of the rehabilitation. The VR rehabilitation system requires active patient effort at all times and the results demonstrated improvement of lower limb motor functions that are relevant in ambulatory functions and a small reduction of pain intensity. The similar but weaker activation pattern after intervention measured with fMRI revealed a direct effect of treatment as an improvement of neuronal synergies on cortical activity.

As the single cases showed promising results, further randomized controlled trials will be conducted to gain evidence for future therapeutic applications of this system in acute and chronic iSCI patients. Furthermore, testing of the efficacy of the transfer effects between motor functioning and neuropathic pain evaluation will be extended. The optimization of the training will maximize the potential benefits of the VR system for neurorehabilitation.

REFERENCES

- [1] G. Rizzolatti, and L. Craighero, “The mirror-neuron system,” *Annu RevNeurosci*, vol. 27, pp. 169-192, 2004.
- [2] G. Buccino, A. Solodkin, and S. L. Small, “Functions of the mirror neuron system: implications for neurorehabilitation,” *Cogn Behav Neurol*, vol. 19, pp. 55-63, 2006.
- [3] S. Caspers, K. Zilles, A. R. Laird, and S. B. Eickhoff, “ALE meta-analysis of action observation and imitation in the human brain,” *Neuroimage*, vol. 50, pp. 1148-1167, 2010.
- [4] S. Hotz-Boendermaker, M. Funk, P. Summers, P. Brugger, M.-C. Hepp-Reymond, S. S. Kollias, and A. Curt, “Preservation of motor programs in paraplegics as demonstrated by attempted and imagined foot movements,” *Neuroimage*, vol. 39, pp. 383-394, 2008.
- [5] G. L. Moseley, “Using visual illusion to reduce at-level neuropathic pain in paraplegia,” *Pain*, vol. 130, pp. 294-298, 2007.
- [6] S.V. Adamovich, G. G. Fluet, E. Tunik, and A. S. Merians, “Sensorimotor training in virtual reality: a review,” *NeuroRehabilitation*, vol. 25, pp. 29-44, 2009.
- [7] J. E. Deutsch, J. A. Lewis, and G. Burdea, “Technical and patient performance using a virtual reality-integrated telerehabilitation system: preliminary finding,” *IEEE Trans Neural Syst Rehabil Eng*, vol. 15, pp. 30-35, 2007.
- [8] M. K. Holden, “Virtual environments for motor rehabilitation: review,” *Cyberpsychol Behav*, vol. 8, pp. 187-211 and discussion 212-219, 2005.
- [9] K. Eng, E. Siekierka, P. Pyk, E. Chevrier, Y. Hauser, L. Holper, M. Cameirao, K. Hägni, L. Zimmerli, A. Duff, C. Schuster, C. Bassetti, P. Verschure, and D. Kiper, “Interactive visuo-motor therapy system for stroke rehabilitation,” *Med Biol Eng Comput*, vol. 45, pp. 901-907, 2007.
- [10] R. C. Oldfield, “The assessment and analysis of handedness: the Edinburgh Inventory,” *Neuropsychologia*, vol. 9, pp. 97–113, 1971.
- [11] M. Tsakiris, M. R. Longo, and P. Haggard, “Having a body versus moving your body: neural signatures of agency and body-ownership,” *Neuropsychologia*, vol. 48, pp. 2740-2749, 2010.
- [12] B. S. Galer, and M. P. Jensen, “Development and preliminary validation of a pain measure specific to neuropathic pain: the Neuropathic Pain Scale,” *Neurology*, vol. 48, pp. 332-338, 1997.
- [13] R. J. Marino, T. Barros, F. Biering-Sorensen, S. P. Burns, W. H. Donovan, D. E. Graves, M. Haak, L. M. Hudson, and M. M. Priebe, ASIA neurological standards committee 2002, “International standards for neurological classification of spinal cord injury,” *J Spinal Cord Med*, vol. 26, pp. 50-56, 2003.
- [14] R. Labrüyère, A. Agarwala, and A. Curt, “Rehabilitation in spine and spinal cord trauma,” *Spine*, vol. 35, pp. 259-262, 2010.
- [15] A. Catz, M. Itzkovich, L. Tesio, F. Biering-Sorensen, C. Weeks, M. T. Laramee, B. C. Craven, M. Tonack, S. L. Hitzig, E. Glaser, G. Zeilig, S. Aito, G. Scivoletto, M. Mecci, R. J. Chadwick, W. S. El Masry, A. Osman, G. A. Glass, P. Silva, B. M. Soni, B. P. Gardner, G. Savic, E. M. Bergström, V. Bluvstein, and J. Ronen, “A multicenter international study on the Spinal Cord Independence Measure, version III: Rasch psychometric validation,” *Spinal Cord*, vol. 45, pp. 275-291, 2007.
- [16] P. L. Dittuno, and J. F. Dittuno Jr, “Walking index for spinal cord injury (WISCI II): scale revision,” *Spinal Cord*, vol. 39, pp. 654-656, 2001.
- [17] K. Berg, S. Wood-Dauphinee, and J. I. Williams, “The Balance Scale: reliability assessment with elderly residents and patients with an acute stroke,” *Scand J Rehabil Med*, vol. 27, pp. 27-36, 1995.
- [18] H. J. van Hedel, M. Wirz, and V. Dietz, “Assessing walking ability in subjects with spinal cord injury: validity and reliability of 3 walking tests,” *Arch Phys Med Rehabil*, vol. 86, pp.190-196, 2005.
- [19] H. J. van Hedel, M. Wirz, and A. Curt, “Improving walking assessment in subjects with an incomplete spinal cord injury: responsiveness,” *Spinal Cord*, vol. 33, pp. 352-356, 2006.
- [20] S. L. Thomas, and M. A. Gorassini, “Increases in corticospinal tract function by treadmill training after incomplete spinal cord injury,” *J Neurophysiol*, vol. 94, pp. 2844-2855, 2005.
- [21] M. Villiger, S. Chandrasekharan, and T. N. Welsh, “Activity of human motor system during action observation is modulated by object presence,” *Exp Brain Res*, vol. 209, pp. 85-93, 2011.