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Cortical activation during visual illusory walking in persons with spinal cord injury: A pilot study

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Abstract

Objective—To determine the location of cortical activation during a visual illusion walking paradigm, a recently proposed treatment for spinal cord injury (SCI)-related neuropathic pain, in persons with SCI compared to able-bodied controls.

Design—Pilot experimental fMRI trial.

Setting—Outpatient rehabilitation clinic.

Participants—Three persons with paraplegia and five able bodied participants were included in this study.

Interventions—Not applicable.

Main Outcome Measures—Cortical activation as measured by blood oxygenation-level dependent (BOLD) method of fMRI.

Results—During visually illusory walking, there was significant activation in the somatosensory cortex among those with SCI. In contrast, able-bodied participants showed little to no significant activation in this area, but rather, in the frontal and pre-motor areas.

Conclusions—Treatment modalities for SCI-related neuropathic pain that are based on sensory input paradigms such as virtual or visual illusory walking may work by targeting somatosensory cortex, an area that has been previously found to functionally reorganize following SCI.

Keywords

spinal cord injuries; neuropathic pain; somatosensory cortex; fMRI

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There are no known conflicts of interest.

Introduction

Approximately 70% of persons report pain following spinal cord injury (SCI).¹ Neuropathic pain is one form of post-SCI pain that is experienced in a region of sensory disturbance around or below the zone of injury. SCI-related neuropathic pain is often refractory, with many individuals experiencing only modest to minimal responsiveness to currently available treatments.² It is for this reason that novel treatment approaches to address SCI-related neuropathic pain are now being explored with promising initial results.

Novel treatments for SCI-related neuropathic pain are based on the assumption that cortical activity is continuously modulated by afferent, intersensory processes.³ When disruptions in this cortical-afferent operating feedback system occur, such as in amputation, the brain can functionally reorganize – a phenomenon thought to underlie the pain that is experienced.⁴ Reinstating sensory input, via visual illusion (e.g., mirror box therapy for phantom limb pain) has been found to promote pain relief^{5,6} and, moreover, some sensory input paradigms have been shown to reverse the reorganization thought to underlie phantom pain.⁷ Similarly, functional cortical reorganization in the somatosensory cortex has been linked to SCI and to a greater degree among those with SCI-related pain.⁸ Additionally, existing evidence suggests that when persons with SCI-related neuropathic pain are provided the visual illusion that they are walking, the severity of their pain is reduced.^{9,10}

If in fact SCI-related neuropathic pain is alleviated by reinstating sensory input through visual illusion walking paradigms, then it remains to be understood how these treatments affect the cortical correlates of SCI-related neuropathic pain and perhaps reverse maladaptive functional reorganization. It has been shown that mirror box therapy results in sensorimotor activation contralateral to the virtual hand, supporting the theory that perception plays a large role in sensorimotor cortical activity.¹¹ Providing the visual illusion of walking may have a similar effect as mirror box therapy, yet the cortical region of activation has not been characterized. Therefore, the aim of this study was to determine the location of cortical activation during a visual illusory walking paradigm in persons with SCI compared to able-bodied controls. We hypothesized that the visual illusion of walking would activate the sensorimotor cortex in persons with SCI and that the patterns of activation would be different than that of able-bodied participants.

Methods

Subjects

Three persons with SCI (2 male, 1 female) who were non ambulatory, manual wheelchair users were recruited from an outpatient rehabilitation center (Table 1). Additionally, data from five able-bodied controls (2 male, 3 female) were used for comparison. The study was approved by the institution's IRB and informed written consent was obtained from all participants for all of the procedures.

MRI scanning and image processing

Whole brain images were acquired using a Philips Achieva 3 Tesla MRI system^a and the blood oxygenation-level dependent (BOLD) method of fMRI was used to measure change in

cerebral blood flow during presentation of each stimulus. A block design was used, such that participants viewed separate 30-second blocks of fixation point (resting state), visual illusion of walking, and visual illusion of wheelchair use. The stimuli were projected to each participant on an MRI-compatible screen while lying on the scanner. The sequence of stimuli was repeated four times for a total of eight minutes.

Visual illusory walking

The visual illusory walking paradigm was adapted from an ongoing, larger study examining the effects of an immersive, simulated walking experience presented in 3D video to participants. Due to constraints of MR scanning and the necessity to have demagnetized video display equipment, the walking stimuli could only be presented in 2D format during scanning. The walking stimuli consisted of a video of an actor, in first person view, walking along a path. The control stimuli consisted of the same actor, in first person view, propelling a manual wheelchair along the same path for the same length of time (Figure 1). Prior to the presentation of the stimuli during scanning, participants were instructed to imagine that they themselves were performing the movements of the actor, but without actual movement of limbs. They were instructed to gaze at a fixation point during resting state scanning.

After scanning, participants were asked to rate how immersive/realistic the fMRI-adapted virtual scenes were on a 5-point Likert scale (1 = Not at all, 2 = Slightly, 3 = Moderately, 4 = Very Much So, 5 = Extremely). Participants were also asked to rate, using the same scale, how adequately they were able to imagine that they were performing the movements.

Analysis

fMRI images were processed using SPM8 software,^{12,b} correcting for motion artifact, normalized to the Montreal Neurological Institute (MNI) template and smoothed using a 8mm full-width half-max Gaussian filter. Using general linear modeling, a contrast was modeled between the walk and wheel conditions so that significant activations ($p < .01$) during the illusory walking condition, above and beyond that of the illusory wheeling condition, could be observed. Differences in the average signal intensity during walking, while controlling for wheeling, were then determined for each group.

Results

When the pattern of activation in the contrast (cortical activation during walking condition minus the wheeling condition) was examined, differences emerged. Among persons with SCI, there was significant activation along the bilateral somatosensory cortex and the paracentral lobule (right > left), and to a lesser extent, although still present, medial motor areas (Fig. 2). In contrast, able-bodied participants experienced significant activation in the bilateral frontal and premotor cortex. When examining individual scans of the participants, each participant with SCI consistently showed activation in the somatosensory cortex. The

^aSupplier List

Philips Achieva 3T scanner, Philips Healthcare, 3000 Minuteman Road, Andover, MA 01810-1099

^bFunctional Imaging Laboratory, Wellcome Trust Centre for Neuroimaging, Institute of Neurology, UCL, 12 Queen Square, London WC1N 3BG, UK, <http://www.fil.ion.ucl.ac.uk/spm/>

participant with incomplete SCI additionally showed premotor activation, similar to the able-bodied group. Questionnaire data revealed that both walking and wheeling visual illusory stimuli were experienced as more immersive among able-bodied participants compared to persons with SCI ($M = 3.6$ and 2.0 , respectively), a difference that was significant ($t = 3.0$; $p < .05$). On average, able-bodied participants reported greater ease of imagining that they themselves were performing the actor's movements compared to persons with SCI ($M = 4.0$ and 2.7 , respectively), although this was not significant ($p = .27$).

Discussion

This study has confirmed our hypothesis that paradigms based on the visual illusion of walking is associated with increased activation in sensorimotor areas among those with SCI, a region that reveals functional reorganization in persons with SCI and even more so among those with SCI-related neuropathic pain.⁸ Moreover, the overall pattern of activation was quite different from able-bodied participants, in that persons without SCI experienced increased activation in the frontal/premotor areas during the walking condition when controlling for the wheelchair condition. This suggests that treatment modalities based on sensory input paradigms (e.g. virtual walking or visual illusory walking) may work by targeting reorganized somatosensory cortex that occurs following SCI. However, able-bodied participants found the fMRI-adapted visual simulation to be more immersive and were better able to imagine themselves as the actor compared to persons with SCI. It is unclear whether these subjective reports were related to everyday, but yet very different experiences of mobility between able-bodied persons and those with SCI or if this could explain the differences observed cortically. While somatosensory activation was exclusive to and consistent among all participants with SCI, one individual with incomplete paraplegia had additional activation in premotor cortices, similar to able-bodied group in this study and healthy participants elsewhere.¹³ Although tempting to construe that this hybrid response is related to possible motor preservation, more data are needed to determine other factors.

Limitations

The study is of course small, and more data will be needed to confirm differences in cortical activation in response to sensory input paradigms such as illusory walking. As the aim of this study was simply to examine cortical activations in response to simulated walking, the effect on subjective pain levels were not measured here. A more comprehensive picture on the effectiveness of virtual walking or other visual simulated walking modalities will elucidate not only the mechanisms of how these treatments work, but equally important, the subjective benefit to the individual.

Conclusions

These results are certainly preliminary, but nonetheless demonstrate similarities in sensorimotor brain activation between illusory walking and other sensory input paradigms, such as mirror box therapy. It is important that investigation of the effectiveness of sensory input paradigms such as visual illusory walking be continued in order to determine whether this is a viable treatment alternative (or in combination) to pharmacotherapy for patients with SCI-related neuropathic pain.

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Abbreviations

SCI	spinal cord injury
fMRI	functional magnetic resonance imaging
BOLD	blood oxygen level dependent
MNI	Montreal Neurologic Institute

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Highlights

- We examined cortical activation during an illusory walking paradigm in persons with SCI.
- Persons with SCI showed activation in the somatosensory cortex.
- Able-bodied persons showed activation in the premotor cortical areas.

Figure 1.
Still-frames of first person walking (top) and wheeling (bottom) conditions.

Figure 2. Cortical activation during visual walking simulation, controlling for activation in the control (wheelchair) condition. Activation among able-bodied participants is shown in green; activation in persons with SCI is shown in red.

Table 1

Age and injury characteristics of participants.

	Age	Years since injury	Level of injury	ASIA* Impairment Scale (AIS) grade
Participants with SCI	32	6.9	T3	A
	25	1.0	T10	C
	30	0.8	T10	A
Control Participants <i>Mean (SD)</i>	31.6 (7.8)	--	--	--

* ASIA = American Spinal Injury Association classification of injury; A = complete, B–D = incomplete