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Clinical note

Using visual illusion to reduce at-level neuropathic pain in paraplegia

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Abstract

Neuropathic pain after spinal cord injury is not well understood and is difficult to treat. One possible cause is mismatch between motor commands and sensory feedback. This two-part study in five paraplegic patients investigated whether a visual illusion aimed to correct this mismatch reduces pain. In study 1, patients undertook three conditions: (i) virtual walking: with a mirror placed in front of a screen, patients aligned their own upper body with a film of a lower body walking. Patients imagined walking and 'watched themselves' walk; (ii) guided imagery; (iii) watching a film. One patient withdrew from virtual walking because of distress. For all patients, the mean (95% CI) decrease in pain (100 mm VAS) was 42 mm (~65%) (11–73 mm) for virtual walking, 18 mm(4–31 mm) for guided imagery and 4 mm (−3 to 11 mm) for watching the film. Mean (95% CI) time to return to pre-task pain was 34.9 min (20.1–49.8 min) for virtual walking; 13.9 min (−0.9 to 28.8 min) for the guided imagery and 16.3 min (1.5–31.2 min) for the film. To investigate its clinical utility, four patients underwent virtual walking every weekday for 3 weeks. Mean (95% CI) decrease in pain was 53 mm (45–61 mm) at post training and 43 mm (27–58 mm) at 3-month follow-up. Virtual walking may be a viable treatment for pain after spinal cord injury. A clinical trial seems warranted.

Keywords: Spinal cord injury; Physical therapy; Neuropathic pain; Paralysis; Visual input; Sensory-motor incongruence

1. Introduction

About 65% of spinal cord injured patients report chronic pain, a third of those report it as severe (Siddal et al., 2002) and a 10th report that their pain, rather than their paralysis, keeps them from work and activities (Rose et al., 1988). These pains sometimes respond to anticonvulsants (e.g. gabapentin/pregabalin) (Siddall et al., 2006), infrequently respond to opiates, rarely respond to spinal cord or brain stimulation, and do not respond to cordectomy or ablative procedures (Siddal et al., 2002).

There are many distinct pains associated with spinal cord injury. Lesions of the cauda equina can be associated with severe burning pain in the legs, feet, genitals and rectum. Because the pain is associated with lesion of the nerve roots, it is considered distinct to central pain due to spinal cord lesion (Siddal et al., 2002). In either case, the exact mechanisms underpinning pain are unknown. One model that may be relevant to both however is the cortical model of pathological pain (Harris, 1999). This model suggests that disrupted cortical proprioceptive representation underpins the pain, because it causes a mismatch between motor output and sensory feedback. In other groups, strategies that aim to correct this mismatch appear to reduce pain (Ramachandran et al., 1995; McCabe et al., 2003; Moseley, 2004, 2005, 2006) and normalisation of cortical proprioceptive representation correlates with recovery (Flor, 2000; Maihofner et al., 2004; Pleger et al., 2005).

This study had two parts. The first part was an experimental comparison of three treatments. This part investigated whether a treatment that aimed to correct any

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sensory-motor mismatch by providing patients with the visual illusion that they were themselves walking ('virtual walking') would reduce pain. The second part was a replicated case series of virtual walking, which aimed to determine whether virtual walking may be a treatment option worthy of further investigation.

2. Methods

Participants. A convenience sample of five paraplegic men (ASIA impairment scale level B) who had at or below level pain for 4 years (SD = 3 years) (Table 1) gave informed consent and participated.

Measures. The McGill Pain Questionnaire (Melzack, 1975) and a 100 mm visual analogue scale (VAS) for pain, anchored at left with "No pain" and at right with "Worst possible pain" with the question "How is your pain right now?" Subjects adjusted the VAS via left or right buttons, which moved a marker from a baseline position that was randomly allocated to the left or right end of the VAS. The change in pain VAS between pre and post training was the primary outcome measure. The time to return to pre-treatment pain was also recorded.

Because the visual illusion might also serve to normalise body perception disturbances, which are common in paraplegia, patients completed the following VAS before and after each condition: (i) Foreignness: how foreign do your legs feel now? (ii) Heaviness: how heavy do your legs feel now? (iii) Size: do your legs feel bigger or smaller than they should?

Finally, at the completion of data collection on the day on which patients underwent virtual walking, they complete a VAS in response to the question "How vivid was the illusion that you were watching yourself walking?" This VAS was anchored with "not at all" and "completely".

2.1. (A) Experimental comparison of treatments

Patients sat, with legs hidden by a board on which the buttons and VAS were mounted, 2.5 m in front of a vertical screen (Fig. 1). Three 10-min conditions were undertaken on separate days:

(i) Virtual walking: a film of an actor walking on a treadmill was projected onto the screen. A mirror placed over the top half of the screen meant that the patient could see the reflection of their own upper body. The location of the projector was adjusted so that the film and the reflection of the patient were aligned (Fig. 1). The patient moved their upper body in time with the lower body in the film so that it appeared to the patient as if they were watching themselves walk.
(ii) Guided imagery, undertaken by a psychologist who was not otherwise involved in the study. Individualised scripts took the patient through a scene in which they were pain-free and performing an enjoyable activity. This condition aimed to control for the distraction effect of virtual walking.
(iii) Watching an animated comedy film. This condition aimed to control for the effect of simply receiving visual input.

Patients reported pain every 30 s from 3 min prior, to 1 h after, each condition. Pain was not recorded during guided imagery. Conditions were ordered via concealed randomisation, which was balanced such that each patient performed the conditions in a different order. All procedures were approved by the Institutional Ethics Committee and complied with the Declaration of Helsinki.

2.1.1. Results

Patient (e) reported distress 45 s into virtual walking and withdrew from that condition. However, data for that patient were still collected and included in the group data. The most common descriptors from the McGill Pain Questionnaire were stabbing, cutting, burning, stinging and intense (scores in Table 1).

Change in pain VAS. Fig. 2 shows individual patient data for pain VAS from 3 min before treatment to 1 h after treatment, for each condition. Because guided imagery aims to distract the patient, pain was not recorded during that treatment. The mean (95% CI) decrease in pain VAS for virtual walking was 42 mm (11–73 mm), which equated to a decrease of ~65%. Pain decreased by 18 mm (4–31 mm) during guided imagery and 4 mm (−3 to 11 mm) while watching the film.

Time to return to pre-task pain VAS. The mean (95% CI) time to return to pre-task pain VAS was 34.9 min (20.1–49.8 min) after virtual walking; 13.9 min (−0.9 to 28.8 min) after the guided imagery and 16.3 min (1.5–31.2 min) after the film (Fig. 2).

Foreignness, heaviness and perceived size. The mean (95% CI) decrease in the perceived foreignness of the legs was 43 mm (11–74 mm) during virtual walking, 4 mm (−5 to 12 mm) during guided imagery and 3 mm (−7 to 12 mm) during watching the film. Finally, change in foreignness related to

Table 1
Subject characteristics

Subject	Years since injury	Age (years)	Level of lesion	McGill Pain Questionnaire			Prescribed medications	Non-prescribed medications
				Sensory	Affective	Evaluative		
A	6	32	L3	14	3	4	Gabapentin, morphine	Cannabis, paracetamol
B	20	45	L2	12	4	4	Gabapentin	
C	12	34	L1	15	2	4	Gabapentin, morphine	
D	13	24	L1	13	4	2	Nortriptyline	Cannabis
E	5	26	T12	16	6	5	Amitriptyline	Codeine
Mean	11.2	32.2						
Standard deviation	6.1	8.3						

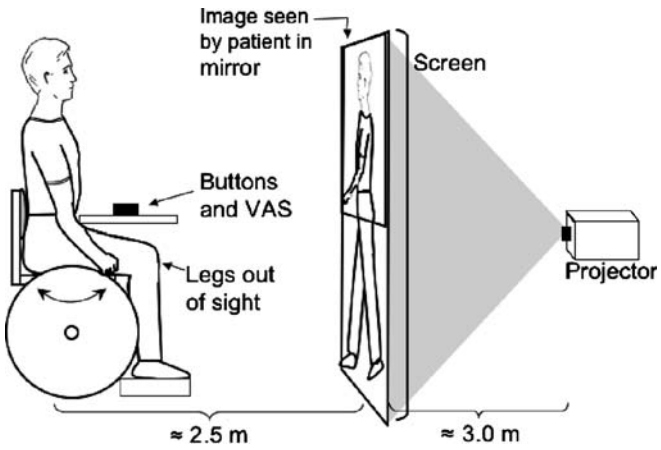

Fig. 1. Experimental set-up. The film was projected onto the screen. For virtual walking, a mirror was placed in front of the upper half of the screen so that, in the patient's view, their own upper body was aligned with the lower body in the film. Patients rated the intensity of their pain on an electronic visual analogue scale (VAS) by pressing a left or right button. The VAS and buttons were placed on a board that obstructed view of the legs.

change in pain during virtual walking (two-tailed Pearson $r = 0.84$, $p = 0.041$), but there were no other relationships. These results suggest that virtual walking decreases phantom pain. They are consistent with the proposal that the visual illusion corrects a mismatch between motor output and sensory feedback. Thus, virtual walking might be a clinically viable treatment option. To verify this possibility, a training study was undertaken with patients (a)–(d).

Vividness of the illusion. The illusion was reasonably vivid for all subjects (mean, 95% CI = 7.8 mm, 7.3–8.3 mm).

2.2. (B) Replicated case series of virtual walking

Patients (a)–(d) performed 10 min of virtual walking on 15 consecutive weekdays. Patients were advised to not alter their medication during the 3-week period. Pain VAS was measured before and after virtual walking, then every minute for 30 min and every 10 min until the sooner of 3 h or pain returned to pre-task level. The first outcome measure was pain VAS, as before, but with the question: "How would you rate your average pain over the last 24 hours?" This measure was also completed 3 months after the completion of the training study. The second outcome measure was the duration of pain relief.

2.2.1. Results

Fig. 3 (panels A and B) shows the effect of the virtual walking program over time, by splitting each patient's data at the median time point (day 8) and plotting the median score for the first 7 days against the median score for the last 7 days. Pre-task pain gradually decreased (Fig. 3A), the duration of pain relief gradually increased (Fig. 3B), and the area of pain was less at day 15 than it was before training (day 0, Fig. 3C). Mean (95% CI) decrease in pain VAS was 53 mm (45–61 mm) at post training and 43 mm (27–53 mm) at 3-month follow-up. On interview, Patients (b)–(d) reported that they had reduced their analgesic medication and patient (a) reported that he had undertaken virtual walking at home and ceased physical therapy, during the follow-up period.

3. Discussion

The first study suggests that using visual input to correct a mismatch between motor output and sensory feedback, 'virtual walking', reduces neuropathic pain due to root lesion in patients after spinal cord injury. The second study suggests that virtual walking may be an effective treatment for such patients. A randomised clinical trial of virtual walking appears warranted.

Patients reported that the illusion that they were watching themselves walk was reasonably vivid, which suggests that virtual walking may have been effective in correcting a mismatch between motor output and sensory feedback. That virtual walking relieved pain seems consistent with the cortical model of pathological pain (Harris, 1999), which has been used to explain the analgesic effect of mirror therapy in patients with phantom pain after amputation or in pain of complex regional pain syndrome (Ramachandran et al., 1995; McCabe et al., 2003; Moseley, 2004, 2005, 2006).

Three issues that are integral to the cortical model of pain (Harris, 1999) are also pertinent here: (i) that pathological pain is associated with changes in the organisation of primary somatosensory cortex (S1); (ii) that organisation of S1 returns to normal when pain subsides; (iii) that pathological pain is caused in part by the sensory-motor mismatch imparted by disrupted body schema. The first two issues are established (Flor et al., 1995; Flor et al., 2001; Maihofner et al., 2003, 2004), but the third is not. In fact, there is evidence to the contrary: phantom experience occurs in amputees for whom S1 is reorganised and in those for whom it is not (Flor et al., 1995) and the relationship between S1 representation and perceptual and behavioural capacity varies between and within individuals and conditions (Sterr et al., 1998). Further, that sensory-motor incongruence underpins

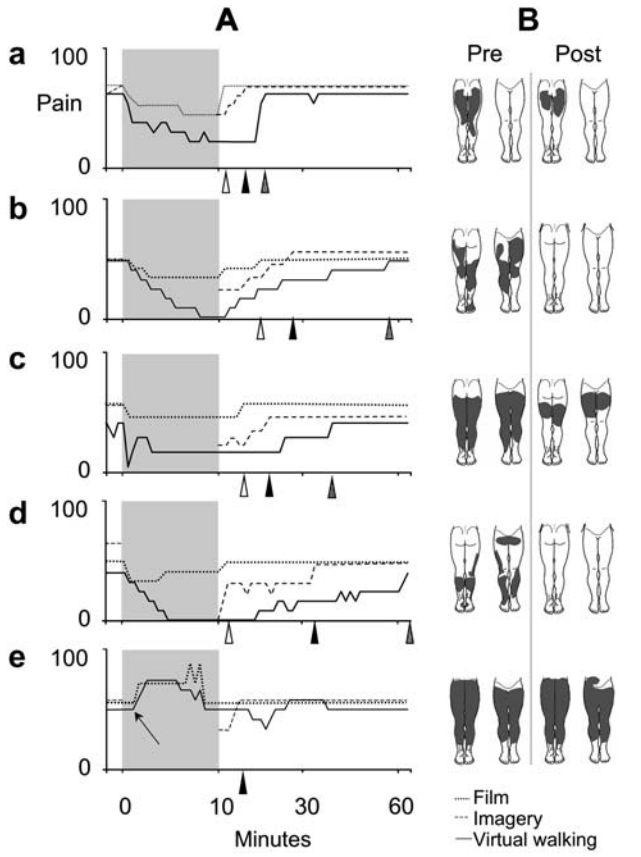

Fig. 2. The effect of three treatments on pain in five paraplegic patients. (A) Pain intensity on a 100 mm visual analogue scale (VAS) during guided imagery (dashed line, not recorded during the condition), watching the film (dotted line) and virtual walking (solid line) from 3 min before to 1 h after the task (the period during which the task was performed is shaded) and at 1 day later (final data point). By obtaining pain ratings every 30 s, it was possible to monitor the effect of each condition both during the treatment (10 min, shaded area) and then over the following hour or until pain had returned to pre-task level (marked here by triangles under the *x*-axis) (filled triangle = guided imagery; open triangle = the film; patterned triangle = virtual walking). Note (i) all conditions increased pain for patient (e) (bottom panel), who withdrew from virtual walking 45 s into the task (arrow); (ii) all three conditions relieved pain in subjects (a)–(d), (iii) pain relief was greater and lasted longer for virtual walking than for the other conditions for patients (a)–(d). (B) Body charts, showing the distribution of pain, completed by each patient 5 min before (pre), and immediately after (post), 10 min of virtual walking. Note reduction in the area of pain for patients (a)–(d) and increase in area of pain for patient (e).

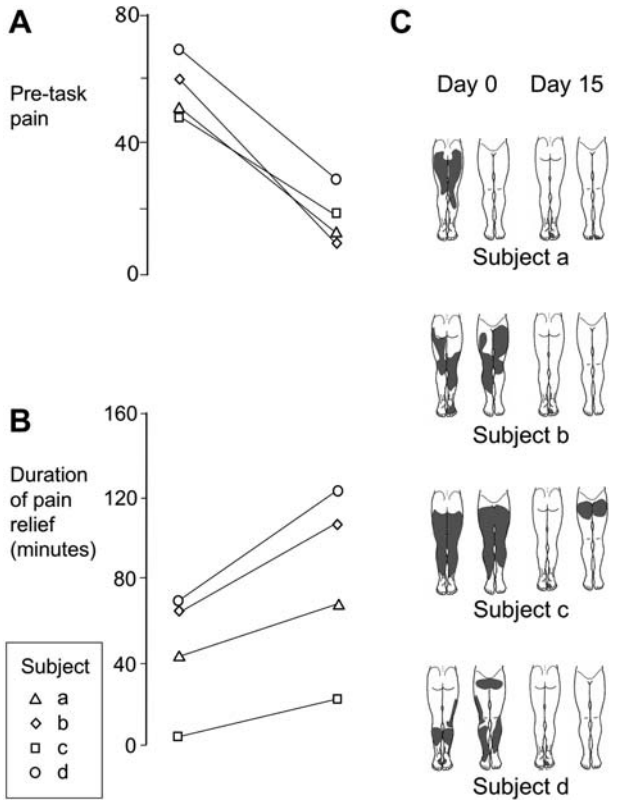

Fig. 3. Replicated case series – virtual walking training program. Change in pain (panel A) and change in the duration of pain relief (panel B) over 15 days of the virtual walking program. Individual subject data show median pre-task pain (100 mm VAS) (A) and median duration of pain relief (B) for the first 7 days (left) and the last 7 days (right) of the virtual walking program. (C) The distribution of pain reported by each subject prior to the first training session (day 0) and prior to the last training session (day 15).

pain after spinal cord injury depends on the assumption that the brain sends out motor commands to paralysed limbs. Why might the brain do this? Perhaps there is an innate drive to move or to perform some behaviours and pain occurs simply because the movement is not being executed. Reports that patients with congenitally missing limbs experience walking (Weinstein et al., 1964; Melzack et al., 1997) offer anecdotal support for that possibility. Even so, sensory-motor mismatch cannot always be sufficient to evoke pain, because imagined movements of intact limbs do not hurt.

There are other possible explanations for the analgesic effect of virtual walking. One is based on a broader understanding of pain as an experience that alerts the organism to tissue danger (Melzack et al., 2001) – perhaps virtual walking simply provides the illusion that all is as it should be. That patients did not consciously accept the illusion as reality – none believed he was now able to walk – suggests that if the mechanism involves reappraisal of tissue danger, then that reappraisal occurs outside of consciousness. Alternatively, perhaps virtual walking is sufficiently novel to distract the patient. That virtual walking imparted better effect than guided imagery, which explicitly exploits distraction as an analgesic strategy, appears contrary to that possibility. It also seems unlikely that upper body movement imparts the effect: each patient participated regularly in vigorous exercise that did not relieve pain. Although there is some evidence that long-term exercise programs can reduce pain in spinal cord injured patients (Hicks et al., 2003), there is probably no short term effect (Siddal et al., 2002).

The current studies raise three main implications. First, virtual walking can be used by paraplegic patients to reduce pain. Second, virtual walking may offer a new direction for treatment of a problem that has substantial personal and economic impact, and which hitherto has been considered almost untreatable (Siddal et al., 2002).

Importantly though, this possibility needs to be verified in a controlled trial. Third, virtual walking decreased pain in four patients and increased pain, and caused distress, in one. The reason for this is not obvious. It is notable that patient (e) also experienced a transient increase in pain while watching the film, although he did not become distressed by it. It may be relevant that patient (e) had a higher lesion (T12) than the other four patients (L1–L3). According to recommended taxonomy, patient (e)'s pain would be classified as below-level spinal cord injury pain, whereas the remainder of patients in this study would probably be classified as having cauda equina pain. Different mechanisms probably underpin the two – while the former is considered a central pain syndrome, the latter is considered a peripheral neuropathic pain (Siddal et al., 2002). Regardless of mechanism, that one patient became distressed and experienced a transient increase in pain emphasises the need for better understanding of how virtual walking might decrease pain in some patients, yet increase it in others. Further, it serves a caution to the use of virtual walking clinically, while these questions remain unanswered.

Finally, interpretation of the current work should consider its limitations. For example, a small, convenience sample, unblinded participation and measures and lack of a control condition in the training study all elevate the likelihood of bias. These issues reinforce the preliminary nature of this work and the need to undertake larger more controlled investigation.

In summary, virtual walking reduced phantom pain in paraplegic patients. The effect may be imparted by correction of sensory-motor mismatch, but other explanations are possible. Pain relief seems to increase with repeated performance, although further research is required to both clarify the long-term effects and to elucidate the mechanisms involved.

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