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Title: Illusory touch temporarily improves sensation in areas of chronic numbness: A brief communication.

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ABSTRACT

Background: Creating the visual illusion of touch can improve tactile perception in healthy subjects.

Objective: We were interested in seeing if creating the illusion of touch in an insensate area could improve sensation in that area.

Methods: Fourteen people with chronic numbness participated in a randomised cross-over experiment. The four conditions were: 1. Stimulation over the un-affected limb with mirror visual feedback (experimental condition). 2. Stimulation over the affected limb with mirror visual feedback 3. Stimulation over the un-affected limb without mirror visual feedback. 4. Stimulation over the affected limb without mirror visual feedback. Participants were assessed pre and post each condition using the Ten-Test and mechanical detection thresholds. Data were analysed using linear mixed models.

Result: Only the experimental condition produced a change in the Ten-Test (mean difference -1.1 95% CI: -1.8 to -0.4; $p=0.003$), corresponding to a 24% improvement in sensation. No differences were observed for any condition in mechanical detection thresholds.

Conclusion: Creating the illusion of touch may improve sensory function in areas of chronic numbness. This preliminary finding adds to the growing body of evidence supporting the use of techniques which directly target cortical function in people with peripheral nerve injury.

Key words: Nerve injury; mirror visual feedback; rehabilitation; sensory re-education; cortical reorganisation

Peripheral nerve injury (PNI) is associated with changes along the neuraxis, including peripheral nerve degeneration and regeneration as well as structural and functional changes within the spinal cord and brain^{1,2}. While ongoing tactile deficit after PNI is clearly attributable to incomplete peripheral repair³, cortical changes have also been shown to correlate with tactile function and may contribute to poor recovery³. Consistent with this, treatments that explicitly target the brain appear to reduce tactile deficit after PNI¹.

One way to facilitate cortical aspects of tactile function is to exploit the cross-modal interaction between vision and touch¹. Similar cortical areas are activated with touch of the hand and with watching a video of the hand being touched⁴. Furthermore, corresponding visual input enhances tactile sensitivity in healthy volunteers⁵, as does creating the illusion of touch using mirrors⁶. Here we report a randomised repeated-measures cross-over experiment in which we assessed tactile function in people with sensory loss before and after creating the illusion of touch in the insensate area via the manipulation of visuo-tactile input.

Fourteen people with persistent sensory loss after PNI participated. Most injuries were unforeseen complications from surgery and no nerve repair had been undertaken (supplementary Table 1). After signing consent, participants completed four different conditions, in random order, separated by at least two days (mean = 3.2 ± 1.7 days). Randomisation was concealed and counter-balanced. All procedures were approved by the institutional ethics committee.

Participants wore clothes that exposed the testing area and removed all jewellery. The area of sensory loss was mapped and the border and central point marked with a pen. The corresponding area on the *un-affected* limb was identically marked. Distances from bony landmarks were noted for standardization and participants were marked-up in an identical fashion before each session based on these measured distances.

The experimental condition involved placing a mobile mirror (lower-limb) or a mirror-box (upper-limb) in line with the participant's para-sagittal axis. The participants' limbs were placed either side of the mirror with the reflective surface facing the *un-affected* side. The *affected* limb was therefore hidden from view, and the reflection of the *un-affected* limb appeared spatially aligned with the location of the affected one (Fig. 1A). The marked area on the *un-affected* side was then stroked using a cotton swab, brushed with a paintbrush, and gently pricked with a medi-pin, each type of stimulation lasting two minutes. Participants watched the stimulation in the mirror, such that they had the visual illusion of being touched in the numb area while simultaneously receiving tactile input from an area of normal sensitivity.

The three control conditions were: sensory stimulation over the *affected* area with mirror visual feedback while the subject attended to the reflected image; sensory stimulation over the *un-affected* area with no mirror and sensory stimulation over the *affected* area with no mirror. In both non-mirror conditions, the participant attended directly to the area being stimulated. The stimulation protocol was standardised so the amount and type of stimulation was identical across all conditions.

Sensation in the numb area was assessed with the Ten-Test⁷ and mechanical detection threshold (MDT; using Semmes-Weinstein Monofilaments). For the Ten-Test, both the numb area and the corresponding area on the *un-affected* limb were stroked with a cotton swab while vision was occluded. The participant rated the sensation on the numb area, in comparison to the un-affected side, on an 11-point numerical rating scale, where 0 = no sensation and 10 = same as the other side (normal). Both outcomes were assessed prior to and immediately after completion of each treatment condition, All measurement was undertaken by the same independent investigator who was blinded to condition. At the completion of

each condition participants were informed by the treating therapist not to indicate to the assessor the treatment received at that or any previous session.

One participant did not attend all sessions and their data were excluded. For the remaining 13 participants, a linear mixed-model analysis compared Ten-Test scores across Time (pre-post) and Condition. There was a significant interaction between Time and Condition ($p = 0.015$) and a pre-post difference for the experimental condition only ($p = 0.003$, mean difference = -1.1, 95% CI: -1.8 to -0.4). This corresponded to a 24% increase in sensation (95% CI: 40% to 8%). There was no pre-post difference for any other condition ($p > 0.05$). An equivalent analysis on the MDT data was not significant. No carry-over or order effects were detected for either outcome measure ($p > 0.05$). Full details of the outcomes measures for each condition can be found in Table 1.

Our results show that a single session of illusory touch improved sensation in an area of persistent tactile deficit secondary to PNI. That only the illusory condition improved sensation strongly suggests that the improvement is mediated in the central nervous system, most likely the brain. Given that prolonged sensory deprivation influences the cortical representation of the affected area^{1,2}, and that cortical reorganisation can occur rapidly with sensory manipulation⁸, one might predict that the visuo-tactile illusion used here had a direct effect on the cortical representation of the affected area by enhancing the non-tactile contributions to the perception of touch.

We assessed sensation immediately after the treatment and would not predict a sustained improvement from one session, additionally we only saw a modest improvement in sensory function. However, an accepted tenet of neuroplasticity is that repeated training has a cumulative effect on cortical function and it is possible that repeated training might deliver larger and more sustainable benefits. Moreover, other innovative approaches to the

management of cortical changes in people with PNI such as audio-tactile retraining⁹ and temporary cutaneous anaesthesia of adjacent areas¹⁰ do show potentially sustainable benefits with long term application. We contend that the current results suggest that the investigation of repeated training using illusory touch is warranted, both in the early period post nerve repair, before sensation has begun to return, as suggested by Lundborg and Rosen¹, as well as in those with persistent sensory loss. Clearly, further research is needed to corroborate the current findings and explore whether repeated training leads to meaningful, long-term improvements.

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Figure Legends

Figure 1. Experimental set up. A = stimulation over the un-affected limb with mirror visual feedback (experimental condition). B = stimulation over the affected limb with mirror visual feedback. C = stimulation over the un-affected limb without mirror visual feedback. D = stimulation over the affected limb without mirror visual feedback.

Table 1. Mean change scores in outcome for each condition (Pre treatment – post treatment).

	Stimulation of un-affected limb with mirror (experimental condition)	Stimulation of affected limb with mirror	Stimulation of un-affected limb without mirror	Stimulation of affected limb without mirror
Change in Ten-test score Mean (95% CI) (N = 13)	-1.1 (-1.8 to -0.4)	-0.6 (-1.4 to 0.2)	-0.7 (-1.4 to 0.1)	0.7 (-0.3 to 1.8)
Changes in Mechanical Detection Threshold Mean (95% CI) (N = 13)	0.05 (-0.2 to 0.3)	-0.2 (-0.4 to 0.03)	0.02 (-0.2 to 0.2)	-0.1 (-0.3 to 0.1)

Supplementary Table 1. Individual patient characteristics

Subject number	Age	Gender	Duration of numbness (yrs)	Precipitating event	Area of sensory loss	Baseline Ten Test affected side (/10)	Baseline MDT affected side (mg)	Baseline MDT unaffected side (mg)
1	22	M	2	Orchiectomy	Upper medial thigh	3.0	4.4	3.7
2	18	F	10	ORIF radius	Anterolateral forearm	4.0	4.6	3.5
3	49	M	1	Repair laceration knee	Medial Knee	7.0	4.2	1.9
4	26	F	4	ACL reconstruction	Proximal anterolateral shin	4.5	5.2	3.6
5	51	M	3	Extended period of walking	Anterolateral thigh	4.0	4.5	1.9
6	59	M	30	Trauma to anterior hip	Anterolateral thigh	0.0	5.2	1.7
7	29	F	6	ORIF radius	Posterolateral hand	7.0	3.4	1.7
8	37	F	3	Tibial tuberosity transfer	Proximal anterolateral shin	4.0	4.5	3.5
9	33	M	16	ACL reconstruction	Medial knee	4.5	5.2	2.2
10	22	F	5	Repair laceration Knee	Anterolateral knee	3.0	4.4	4.0
11	24	F	2	Repair laceration	Anterior surface of	8.0	3.3	3.1

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				hand	third finger			
12	43	F	26	ORIF tibia /Fibula	Anterior foot	1.5	5.3	2.2
13	24	F	5	ACL reconstruction	Anterolateral shin	4.0	4.1	3.3
Mean (SD)	33.6 (13.1)		8.7(9.5)			4.2 (2.2)	4.5 (0.6)	2.8 (0.9)

MDT = Mechanical Detection Threshold, ORIF = Open Reduction Internal Fixation, ACL = Anterior Cruciate Ligament