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Neuropathic pain and primary somatosensory cortex reorganization following spinal cord injury

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ABSTRACT

The most obvious impairments associated with spinal cord injury (SCI) are loss of sensation and motor control. However, many subjects with SCI also develop persistent neuropathic pain below the injury which is often severe, debilitating and refractory to treatment. The underlying mechanisms of persistent neuropathic SCI pain remain poorly understood. Reports in amputees describing phantom limb pain demonstrate a positive correlation between pain intensity and the amount of primary somatosensory cortex (S1) reorganization. Of note, this S1 reorganization has also been shown to reverse with pain reduction. It is unknown whether a similar association between S1 reorganization and pain intensity exists in subjects with SCI. The aim of this investigation was to determine whether the degree of S1 reorganization following SCI correlated with on-going neuropathic pain intensity. In 20 complete SCI subjects (10 with neuropathic pain, 10 without neuropathic pain) and 21 control subjects without SCI, the somatosensory cortex was mapped using functional magnetic resonance imaging during light brushing of the right little finger, thumb and lip. S1 reorganization was demonstrated in SCI subjects with the little finger activation point moving medially towards the S1 region that would normally innervate the legs. The amount of S1 reorganization in subjects with SCI significantly correlated with on-going pain intensity levels. This study provides evidence of a link between the degree of cortical reorganization and the intensity of persistent neuropathic pain following SCI. Strategies aimed at reversing somatosensory cortical reorganization may have therapeutic potential in central neuropathic pain.

1. Introduction

Loss of mobility is often considered the most serious consequence of spinal cord injury (SCI). It is interesting to note, however, that people with SCI consistently rate pain as one of the most difficult problems to manage, despite the presence of other problems that interfere with daily life [26]. Although more than two thirds of people with SCI experience persistent pain after injury [23], our understanding of the mechanisms underlying SCI pain remain incomplete. As a result, available treatments are commonly ineffective [7]. Several types of pain may occur following SCI including musculoskeletal pain, visceral pain and two distinct types of neuropathic pain that occur at and below the level of SCI. Approximately one third of all people following SCI develop below-level neuropathic pain [22]. Of all the possible pain types, below-level neuropathic pain is the most likely type of SCI pain to be described as severe or excruciating [22].

While the amount of deafferentation varies between individuals, neuropathic pain occurring in the insensate region below a complete SCI is usually considered a central or deafferentation pain. In this situation, central nervous system mechanisms are likely to predominate in the production and maintenance of pain. Other deafferentation pains, such as phantom limb pain following amputation are thought to share some similar neurophysiological mechanisms. The literature relating to phantom limb pain is therefore of particular relevance to below-level neuropathic SCI pain.

Although very little is known about the central processes involved in the initiation or maintenance of persistent neuropathic pain, evidence suggests an association between primary somatosensory cortex (S1) reorganization and pain intensity. Using magnetoencephalography, Flor and colleagues [9] explored S1 reorganization in subjects with persistent neuropathic (phantom) pain following arm amputations. A significant correlation

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($r = 0.93$) between the amount of S1 reorganization and the intensity of phantom limb pain was found. An association between on-going pain intensity and cortical reorganization was further strengthened by the results of a more recent investigation by Lotze and colleagues. They reported that in subjects following arm amputation, use of a myoelectric prosthesis was significantly negatively correlated with both pain intensity and sensory and motor cortical reorganization [13]. These reports raise the possibility that reversal of cortical reorganization may be a crucial element of an effective treatment of deafferentation pain.

Although S1 reorganization has been shown to occur in patients with SCI [6,14,18,25], it remains unknown if there is a significant relationship between the degree of this reorganization and on-going pain intensity. The aim of this investigation was to use functional magnetic resonance imaging (fMRI) to determine whether the S1 reorganization that occurs following SCI is associated with pain intensity. We hypothesized that SCI subjects would display S1 reorganization and that there would be a significant positive correlation between S1 reorganization and on-going pain intensity.

2. Methods

2.1. Subjects

Twenty subjects with established complete thoracic SCI (18 males, 2 female; aged 22–63 years) and 21 healthy controls (20 males; 1 female; aged 23–60 years) were recruited for the study (Table 1). For the SCI subjects, the neurological level of injury was determined using the American Spinal Injury Association (ASIA) Impairment Classification [16]. Each subject was examined by a clinician (P.W.) in the research group. The standardized ASIA examination protocol was used to determine the most caudal level of the spinal cord with normal sensory and motor function on both sides of the body. An injury was termed complete when there was an absence of sensory and motor function which included the lowest sacral segments.

Ten of the 20 subjects with SCI experienced persistent neuropathic pain. All 10 subjects had below-level neuropathic pain as defined by the International Association for the Study of Pain SCI Pain Taxonomy [24]. These subjects experienced constant shooting, electric or burning pain in the region of sensory loss at least three segments below the neurological level of injury (Fig. 1). To assess the intensity of their pain, each subject completed a pain diary for one week prior to scanning in which they indicated, with a vertical pencil stroke on a 10 cm horizontal line, the intensity of their pain (0 cm = "no pain" to 10 cm = "maximum imaginable pain") three times a day. Each subject also rated their on-going pain intensity immediately prior to the MRI scanning session using the same intensity scale. The remaining 10 subjects with SCI did not have neuropathic pain. General functioning was also assessed using the Medical Outcome Short Form Health Survey (SF-36).

Informed written consent was obtained for all procedures, and the study was approved by the institutional Human Research Ethics Committees.

2.2. MRI scanning

MRI scans were acquired using a Philips Achieva 3 T MRI machine. Each subject lay in a supine position with their arms by their sides. Head movement was restricted by using tight fitting headphones, and foam padding placed between the subject's head and the MRI head coil. Multiple series of 130 gradient echo echo-planar fMRI image volumes using blood oxygen level dependent contrast were collected. Each image volume contained 43 axial slices covering the entire brain (voxel = $1.95 \times 1.95 \times 3.00$ mm thick, repetition time = 3000 ms; echo time = 40 ms). During each fMRI series,

Table 1
Spinal cord injury subject characteristics: Table indicating subject characteristics where Neurological level of SCI, the most caudal segment of the spinal cord with normal sensory and motor function on both sides of the body; ASIA, American Spinal Injury Association impairment scale where A, no motor or sensory function in the sacral segments S4–S5; motor/sensory level, the most caudal segment of the spinal cord with normal motor/sensory function; Sensory ZPP, zone of partial sensory preservation, which indicates the most caudal dermatome that remains partially innervated; VAS, visual analog scale.

Subject	Age	Years since injury	Neurological level of SCI	ASIA	Motor level		Sensory level		Sensory ZPP		Allodynia in ZPP	Mean pain intensity week prior to scan (10 cm VAS)	Pain intensity prior to scan (10 cm VAS)
					Right	Left	Right	Left	Right	Left			
SCI patients with below-level neuropathic pain													
1	40	5	T7	A	T1	T1	T7	T8	T12	T12	Yes	4.2	6.1
2	54	27	T2	A	T1	T1	T5	T2	T12	L2	Yes	2.8	1.6
3	29	4	T5	A	T1	T1	T6	T5	L1	L1	Yes	0.9	1.2
4	34	8	T4	A	T1	T1	T4	T4	T6	T5	Yes	4.6	3.9
5	57	32	T4	A	T1	T1	T4	T4	T5	T6	No	3.4	5.6
6	41	14	T3	A	T1	T1	T4	T3	T6	T6	No	3.5	5.2
7	27	2	T1	A	T1	T1	T1	T1	T5	T4	No	2.1	1.7
8	51	3	T9	A	T1	L2	T9	T9	S2	S2	Yes	3.2	0.2
9	63	5	T10	A	T1	T1	T11	T10	T12	T12	No	6.9	7.3
10	54	37	T3	A	T1	T1	T3	T4	T6	T5	No	2.3	4.4
Mean (±SEM)	45 (4)	14 (4)	5 (1)									3.4	3.7
SCI patients without neuropathic pain													
11	43	21	T8	A	T1	T1	T8	T9	T10	T10	No	0	0
12	26	7	T10	A	T1	T1	T10	T10	L1	T12	No	0	0
13	44	27	T5	A	T1	T1	T6	T5	L3	S2	No	0	0
14	52	9	T3	A	T1	T1	T3	T3	T4	T4	No	0	0
15	40	16	T3	A	T1	T1	T3	T3	T4	T4	No	0	0
16	32	7	T3	A	T1	T1	T3	T3	T5	T7	Yes	0	0
17	22	3	T5	A	T1	T1	T5	T5	T8	T11	No	0	0
18	37	11	T6	A	T1	T1	T6	T9	T11	T12	No	0	0
19	53	17	T6	A	T1	T1	T6	T6	T11	T12	No	0	0
20	32	3	T5	A	T1	T1	T5	T5	T12	L3	No	0	0
Mean (±SEM)	38 (3)	12 (3)	5 (1)									0	0

Table 2
Contralateral S1 activation MNI co-ordinates.

	MNI-co-ordinate			Cluster size	*T* value
	X	Y	Z		
Lip group					
Controls	−58	−16	38	1704	10.31
SCI without pain	−58	−24	34	704	8.66
SCI with below-level neuropathic pain	−56	−22	36	676	10.02
Thumb group					
Controls	−56	−22	42	4827	9.19
SCI without pain	−52	−18	46	121	6.85
SCI with below-level neuropathic pain	−46	−20	42	570	12.42
Little finger group					
Controls	−38	−32	62	49	3.09
SCI without pain	−42	−28	58	18	3.71
SCI with below-level neuropathic pain	−46	−30	62	64	7.76

either the right thumb pad down to the first joint, the right little finger pad to the first joint, or the right side of the bottom lip was brushed using a plastic brush at approximately 2 strokes/s. Each of these stimulation paradigms were performed for a period of 10 fMRI volumes (30 s) following a baseline period of 10 fMRI volumes (30 s). This was repeated a further 5 times for a total of 6 stimulation and 7 baseline periods. A 3D T1-weighted image set was also collected (voxel size: 0.90 × 0.90 × 0.90 mm).

2.3. MRI image processing

All fMRI images were processed using SPM5 software [10]. The images were motion corrected, global signal drifts removed using the detrending method described by Macey et al. [15] and spatially normalized to the Montreal Neurological Institute (MNI) template and spatially smoothed using a 6 mm full-width-at-half-maximum Gaussian filter. Significant increases in fMRI signal intensity were determined using a repeated box car model convolved with hemodynamic delay function.

Each subject's T1-weighted anatomical image set was spatially normalized to the MNI template and segmented into grey matter, white matter and cerebrospinal fluid images. The grey matter image was then co-registered to an individual's fMRI image set so that both the fMRI and T1-anatomical images were in the same three-dimensional space. For each fMRI scan, activated voxels ($p < 0.05$, FDR corrected) were overlaid onto a rendered view of each subject's co-registered grey matter T1-anatomical image. In 12 of the 123 fMRI scans, brushing did not result in any significantly activated voxels within the contralateral somatosensory cortex (3 lip; 0 thumb; 9 little finger). For group overlays, significant increases in signal intensity during each stimulus paradigm in each group were determined ($p < 0.001$, uncorrected, minimum cluster size 20 voxels) and overlaid onto an individual subject's T1 image set. Significant differences between the control and SCI

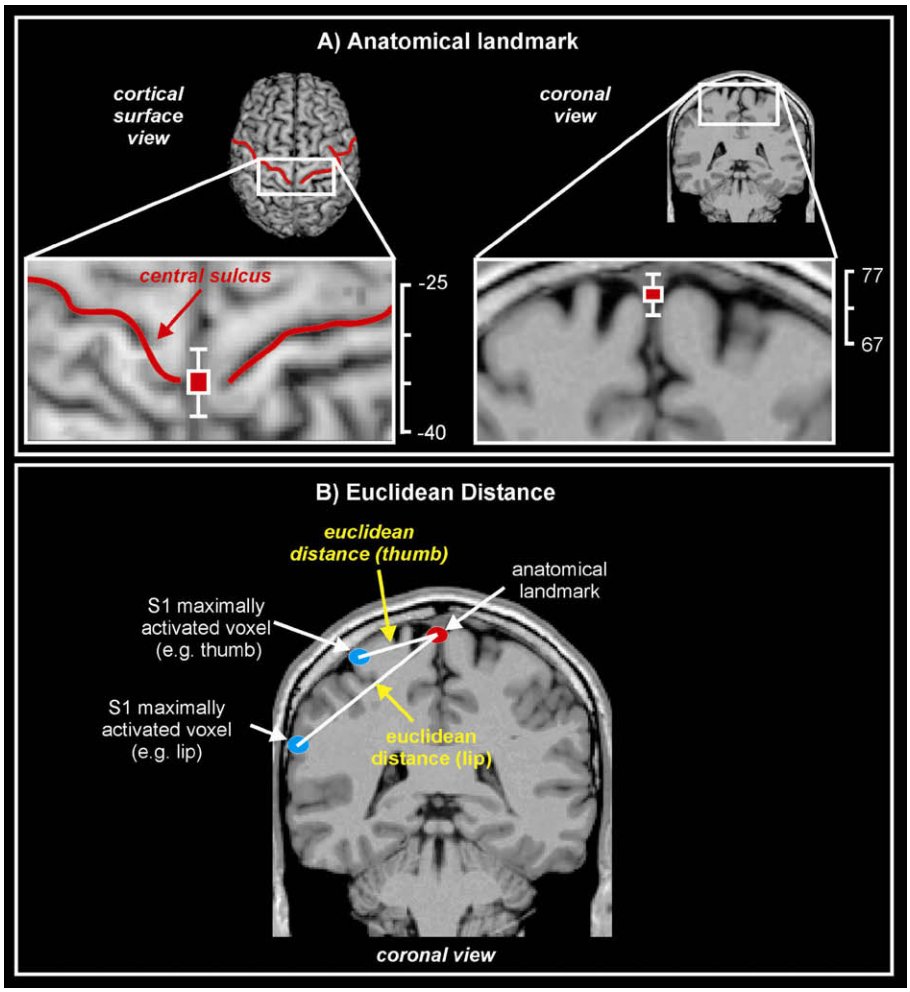

Fig. 1. Anatomical marker and Euclidean Distance: (A) Illustration demonstrating the location of the anatomical marker, i.e. where the central sulcus meets the midline and at the dorsal aspect of the brain. The variability in the location of this marker in each individual is represented by the mean (±SD) MNI co-ordinates. (B) Illustration of how Euclidean distance was calculated.

without pain groups and between control and SCI with pain groups during each three brushing stimulus paradigms were also determined ($p < 0.001$, uncorrected, minimum cluster size 20 voxels).

2.4. Determination of cortical distance

The point at which the central sulcus meets the longitudinal fissure at the dorsal aspect of the brain was used as a standardized anatomical marker. The Euclidean distance (ED) was calculated as the distance between the anatomical marker and the maximally activated voxel in the contralateral (left) post-central gyrus (S1). An illustration of the anatomical marker and the method used for calculating ED is shown in Fig. 1. In addition to ED, the polar angle (PA) between the three-dimensional MNI co-ordinates of the maximally activated voxel in the contralateral (left) post-central gyrus (S1) and the anatomical marker were calculated.

2.5. Statistical analysis

Using SPSS software, a two-sample *t*-test was used to determine significant differences ($p < 0.05$) in the ED as well as in the PA of S1 activations between controls, in SCI subjects with neuropathic pain and in SCI subjects without neuropathic pain. In addition, a one-tailed Pearson correlation test was used to determine significant ($p < 0.05$) correlations between these ED's as well as between the PA's and the mean pain intensity scores calculated from the pain diary and the pain intensity rating on the day of scanning.

3. Results

3.1. Pain and functional assessments

The mean (±SEM) pain intensity calculated from the seven day pain diary in the SCI pain subjects was 3.4 ± 0.5, and the mean pain intensity immediately prior to the MRI scanning was 3.7 ± 0.8. In each SCI subject with on-going pain, the pain was perceived to be located more than three segments below the neurological level of the spinal cord lesion. In eight subjects, the on-going pain was located in both the right and left feet, extending into the lower leg and into the hip and thigh region. In subject 7, pain was restricted to small regions on the left and right hips, and in subject 10, pain extended from the right hip to the right foot in a thin continuous band (Fig. 2).

3.2. Brain activation in response to brushing

Brushing of the right little finger, thumb and lip in controls, SCI subjects without pain and SCI subjects with pain evoked significant signal intensity increases in the contralateral thalamus, secondary somatosensory cortex (S2), primary somatosensory cortex, and in the ipsilateral cerebellar cortex (Fig. 3). These signal intensity increases were located in similar locations in all three groups during each brushing stimulus. Direct statistical comparisons of regional brain activation between the groups failed to demonstrate any consistent significant differences in signal intensity during each stimulation paradigm.

3.3. Location of S1 activation sites

When the pattern of activation was examined in the contralateral post-central gyrus (S1), brushing of the little finger, thumb and lip in controls, SCI subjects without pain and SCI subjects with pain evoked significant signal intensity increases in a medial to lateral pattern in a topographic distribution consistent with the sensory homunculus. In all three groups, the brushing was perceived as innocuous. Fig. 4 shows the location of these S1 activations in the control group rendered onto the brain surface, along with the mean (±SEM) signal intensity changes for each cluster. It is clear that during each brushing period, signal intensity increased by approximately 1% and returned to baseline in the intervening rest periods. Although the overall pattern of brain activation and the pattern of S1 activation was similar in all three groups, significant differences between the precise locations of these S1 activations occurred.

In control subjects, the mean (±SEM) *X*, *Y*, *Z* co-ordinates were lip: −58.0 ± 0.7, −15.6 ± 1.0, 39.4 ± 1.3; thumb: −57.6 ± 0.8, −19.9 ± 1.2, 46.6 ± 1.2; little finger: −54.8 ± 1.8, −23.9 ± 8.7, 47.7 ± 2.3, the mean ED between the anatomical marker and the

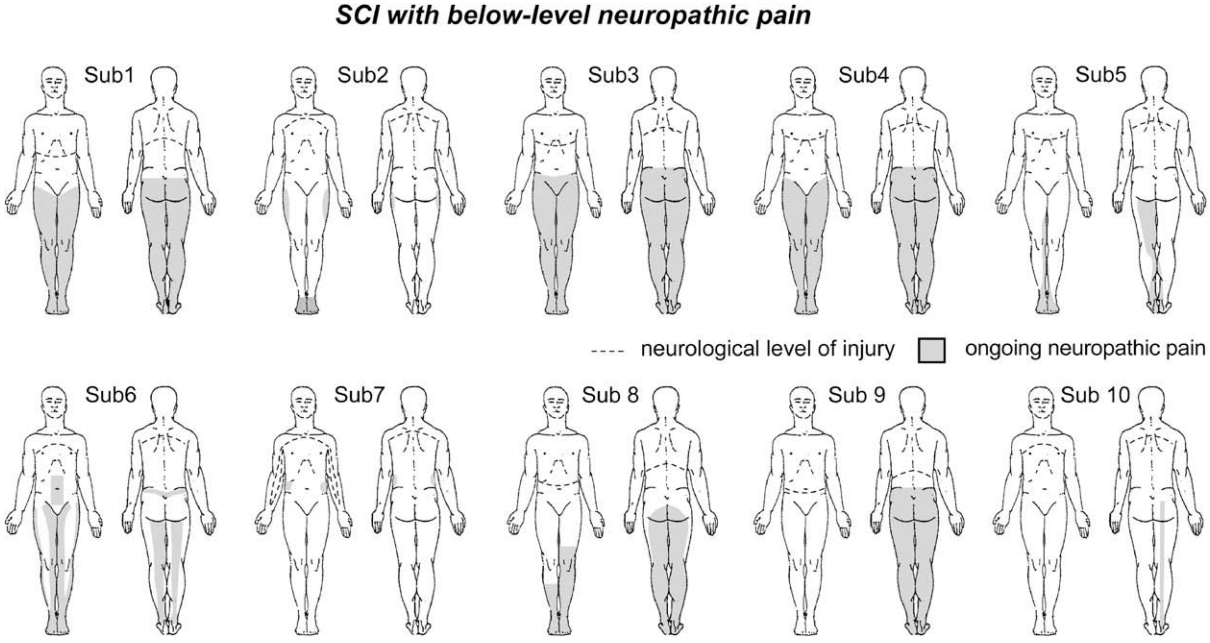

Fig. 2. SCI pain diagrams: individual illustrations of the distribution of pain in 10 SCI subjects with persistent SCI below-level neuropathic pain. The light grey shading indicates each SCI subject's on-going pain distribution.

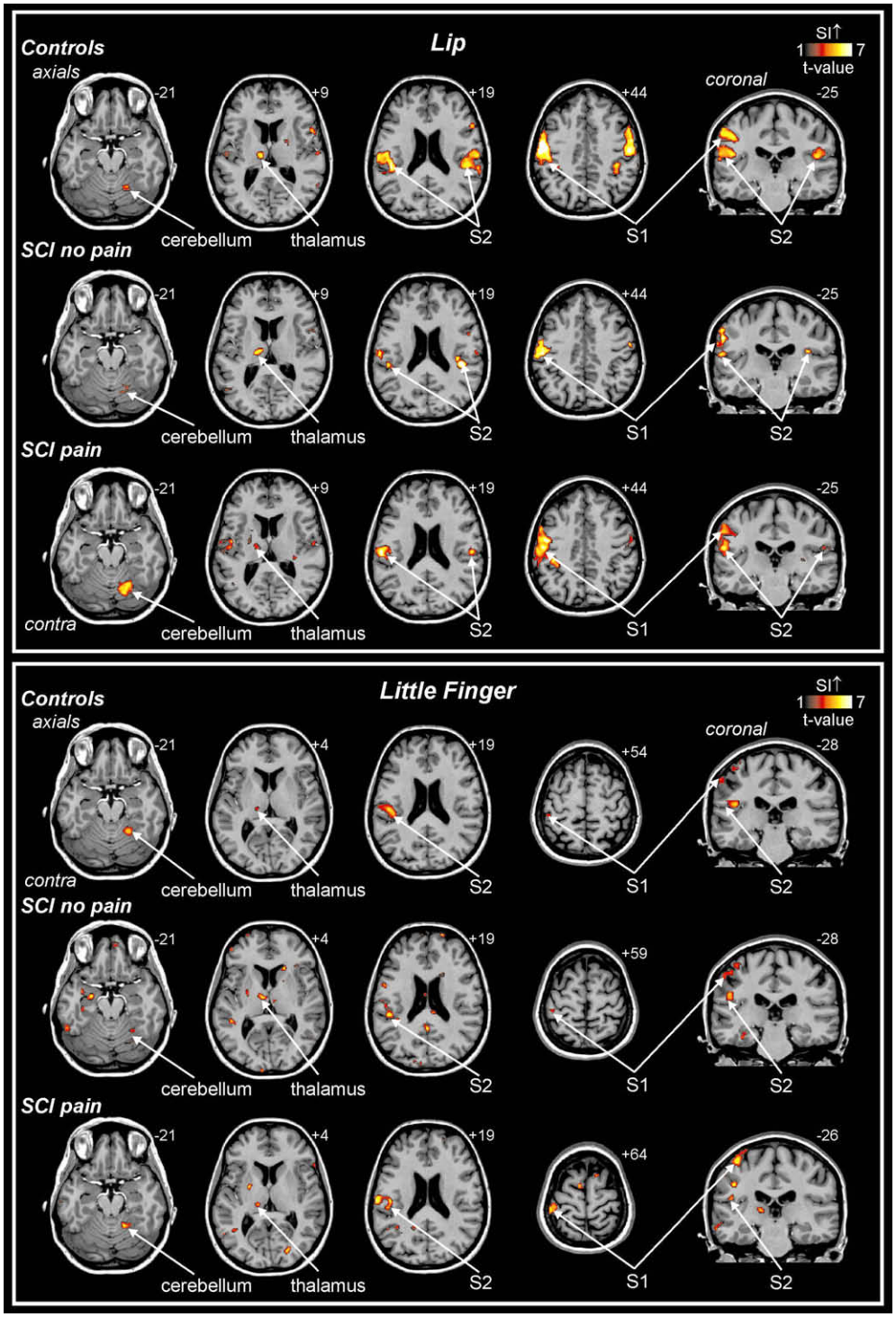

Fig. 3. Regional brain activation during brushing: signal intensity increases evoked by innocuous brushing of the lip and little finger in three groups: controls, SCI without pain, and SCI with below-level neuropathic pain. Note that brushing activates the ipsilateral cerebellar cortex, contralateral thalamus, secondary somatosensory cortex (S2), and primary somatosensory cortex (S1). The slice location is indicated by the MNI co-ordinate at the top left of each image.

MNI co-ordinates were lip 70.8 ± 1.0 mm; thumb 65.8 ± 1.2 mm; little finger 62.1 ± 2.4 mm, and the mean differences in PA between the anatomical marker and the MNI co-ordinates were lip 32.5 ± 1.4°; thumb 28.3 ± 1.4°; little finger 27.6 ± 2.3° (Fig. 5, Table 3). The ED's were significantly different from the lip to the thumb ($p < 0.01$) and lip to the little finger ($p < 0.01$), but not from the thumb to the little finger. The difference in the PA was significantly different from the lip to the little finger ($p < 0.01$) and from the thumb to the little finger ($p < 0.01$).

In SCI subjects without pain, the mean *X*, *Y*, *Z* co-ordinates were lip: −58.6 ± 1.0, −16.3 ± 1.3, 39.7 ± 0.9; thumb: −52.6 ± 2.8, −20.1 ± 2.5, 47.6 ± 2.3; little finger: −49.5 ± 2.5, −29.0 ± 2.2, 54.9 ± 3.0, the mean ED's were lip 70.5 ± 1.4 mm; thumb 62.6 ± 3.4 mm; little finger 54.0 ± 3.5 mm ,and the mean differences in the PA were lip 31.4 ± 0.9°; thumb 24.7 ± 2.2°; little finger 20.8 ± 2.8° (Fig. 5, Table 3). The mean ED as well as the difference in PA of the lip and thumb was not significantly different to controls. Brushing of the little finger in SCI subjects without pain evoked S1

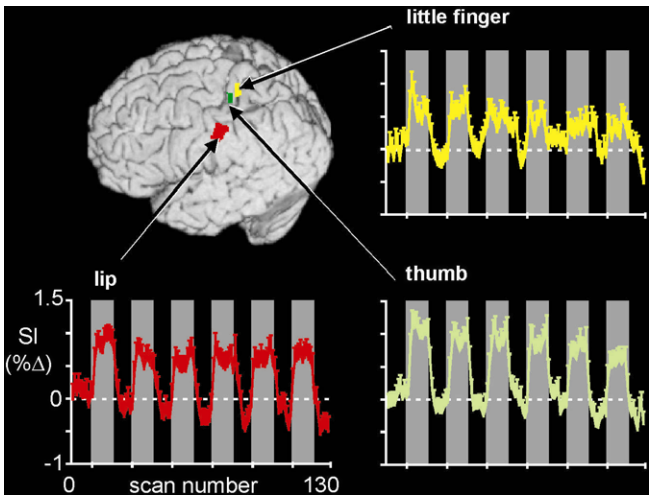

Fig. 4. S1 activation during brushing: illustration showing significantly activated regions of the contralateral primary somatosensory cortex during brushing of the lip, thumb and little finger in the control group. The mean (±SEM) percentage change in signal intensity for each cluster is also shown. The vertical grey bars indicate each brushing period.

activations that were not statistically different when compared to controls.

In SCI subjects with pain, the mean *X*, *Y*, *Z* co-ordinates were lip: −55.2 ± 2.0, −17.1 ± 3.3, 36.7 ± 1.6; thumb: −49.8 ± 3.3, −20.9 ± 2.3, 53.6 ± 2.8; little finger: −41.8 ± 2.0, −28.0 ± 2.8, 63.1 ± 1.7, the mean ED's were lip 68.5 ± 2.8 mm; thumb 56.2 ± 3.5 mm; little finger 44.2 ± 2.2 mm, and the mean differences in PA were lip 33.4 ± 2.0°; thumb 22.2 ± 2.1°; little finger 14.7 ± 2.5° (Fig. 5, Table 2). The ED and PA to the lip activation were not different to either the control or SCI without pain groups, the ED and PA to the little finger were, however, significantly smaller (shifted medially) when compared with controls ($p < 0.01$). Furthermore, the ED to the little finger activation was shifted medially compared to the SCI subjects without pain ($p < 0.01$). Brushing of the thumb in SCI subjects with pain evoked S1 activations that were medially placed when compared with controls ($p < 0.01$) but were not significantly displaced when compared with SCI subjects with pain.

3.4. Correlation with pain intensity and other variables

A significant correlation occurred between the amount of cortical reorganisation of the little finger activation and both the mean 7 day pain intensity prior to scanning (ED: $r = -0.52$, $p < 0.05$; PA: $r = -0.44$, $p < 0.05$) and the pain intensity immediately prior to scanning (ED: $r = -0.57$, $p < 0.05$, Fig. 6). There was no significant correlation between the level of SCI and the amount of cortical reorganisation. Additionally there was no correlation between reorganisation of the thumb and lip representations and pain.

Table 3
Euclidean distance (EM) and polar angle (PA) values.

Group	Lip	Thumb	Little finger
Euclidean distance (mean ± SEM)			
Controls	70.8 ± 1.0 mm	65.8 ± 1.2 mm	62.1 ± 2.4 mm
SCI without pain	70.5 ± 1.4 mm	62.6 ± 3.4 mm	54.0 ± 3.5 mm
SCI with below-level neuropathic pain	68.5 ± 2.8 mm	56.2 ± 3.5 mm	44.2 ± 2.2 mm
Polar angle (mean ± SEM)			
Controls	32.5 ± 1.4°	28.3 ± 1.4°	27.6 ± 2.3°
SCI without pain	31.4 ± 0.9°	24.7 ± 2.2°	20.8 ± 2.8°
SCI with below-level neuropathic pain	33.4 ± 2.0°	22.2 ± 2.1°	14.7 ± 2.5°

4. Discussion

This study has shown that subjects with complete SCI and below-level neuropathic pain demonstrate reorganization of the primary somatosensory cortex that correlates with pain intensity. In all subjects, brushing of the skin in selected sites evoked a pattern of somatosensory cortex signal increase consistent with the conventional sensory homunculus, with the lip represented lateral to the little finger. Although this pattern of sensory activation was preserved in all subjects, complete thoracic SCI resulted in a medial shift of the thumb and the little finger compared with controls (combined results not included). This shift is consistent with the hand region shifting towards the area of S1 which would normally innervate the region below the level of the injury. In subjects with a SCI and neuropathic pain, the medial shift of the little finger representation was statistically different to control subjects and those with a SCI without neuropathic pain. Furthermore, in subjects with SCI and neuropathic pain, little finger medial displacement was found to correlate positively with the pain intensity.

Cortical reorganization following deafferentation is a well-known phenomenon described many times by previous investigators. Over two decades ago, Merzenich and colleagues [17] used microelectrode mapping techniques to show that, following digit amputation in the owl monkey, S1 skin representation in the region adjacent to the amputated digits expands into the region pre-

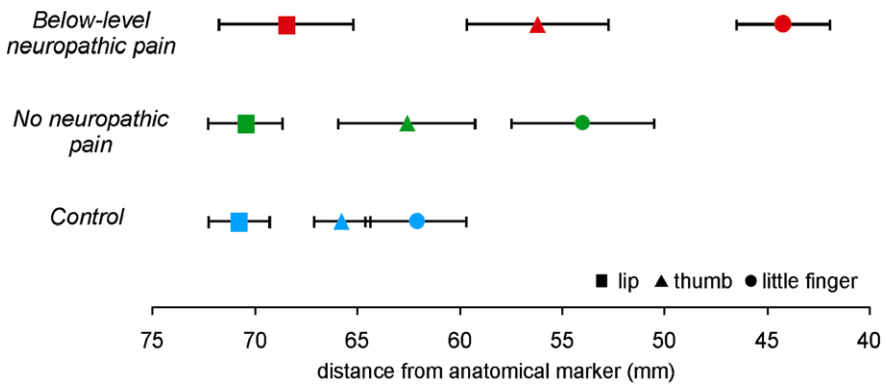

Fig. 5. Comparison of Euclidean distances: graph displaying the mean (±SEM) Euclidean distances in mm from the anatomical marker to the mean activation points in the contralateral post-central gyrus during lip, thumb and little finger brushing in control subjects (blue), SCI subjects without neuropathic pain (green) and SCI subjects with below-level neuropathic pain (red).

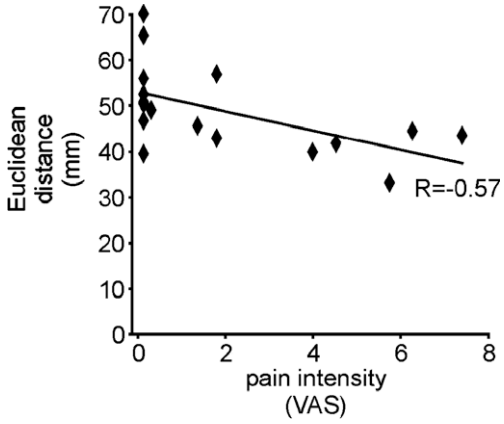

Fig. 6. Correlation between S1 reorganisation and neuropathic pain: Graph of the Euclidean distances from the anatomical marker to the mean activation points in the contralateral post-central gyrus during little finger brushing in all SCI subjects plotted against on-going pain intensity measured immediately prior to MRI scanning.

viously receiving input from the amputated digits. In a similar study, Calford and Tweedale [3] described rapid changes in the organization of the cortex of flying foxes following digital amputation. Consistent with these reports, we found that only the area that was located immediately adjacent to the deafferented region displayed a significant reorganisation, i.e. the region representing the little finger.

Although the precise mechanisms underlying cortical reorganization remain unknown, several possibilities exist. Evidence suggests sprouting of new neurons into the region of deafferented cortex is responsible for at least part of the cortical reorganization seen after injury [4,5,6,12]. Long-term structural changes do not, however, account for the rapid changes in cortical reorganization in some reports [3,21]. Calford and Tweedales' work in flying foxes suggests that rapid functional changes in local inhibition may occur. In addition, Rossini et al. [21] reported that brief anaesthesia of a finger resulted in expansion of the remaining fingers' S1 representation which reversed on removal of the block. It has been proposed that these rapid changes may result from the unmasking of dormant connections secondary to several possible mechanisms including changes in membrane conductance, increases in excitatory neurotransmitter release [12] and excitatory disinhibition, due to reduced gamma-amino butyric acid (GABA)-ergic inhibition [4,6,11].

Several studies have been performed using functional imaging to determine whether SCI is associated with cortical reorganization. An early study used positron emission tomography to investigate cortical activation in response to hand movements in a group of subjects with cervical and thoracic injuries [2]. This study found evidence of cortical plasticity with expansion of the region of activation into the leg region of the sensorimotor cortex following hand movements. Despite this positive finding, two subsequent studies using sensory stimulation of the hand in subjects with complete thoracic spinal cord injuries failed to find evidence of a significant medial shift in cortical representation [18,25]. However, in these studies, the link with neuropathic pain was not examined. In the study by Moore et al., some subjects had neuropathic pain but were not examined separately and in the study by Turner et al., subjects were not assessed for the presence of neuropathic pain. Given the findings of the present study, which also failed to find a significant change in subjects without pain, it appears that the presence of neuropathic pain is a crucial ingredient in detecting a significant shift in representation.

Despite many studies demonstrating that deafferentation results in changes in cortical organization, only a few studies have suggested that these changes are associated with the presence of persistent pain. In 1995, Flor et al. [9] demonstrated somatosensory cortical reorganization in amputees with phantom pain. In addition, they showed that the degree of S1 cortical reorganization was strongly correlated to pain intensity ($r = 0.94$). Furthermore, Birbaumer et al. [1] reported that the S1 reorganization associated with phantom limb pain could be reversed within 20 min following the elimination of pain by regional blockade. This study also supported the view that cortical reorganization following deafferentation results at least partly from rapid mechanisms that can be swiftly reversed.

In some situations, changes in cortical organization can result in a positive compensatory brain response, such as the S1 change in Braille readers linked to improved Braille reading ability [20]. In contrast, the "compensatory" reorganization demonstrated in this study appears to be maladaptive in nature correlating with increased on-going pain (Fig. 3).

Given the poor efficacy of currently available pharmacological treatments for persistent neuropathic pain, manipulating the degree of cortical reorganization provides an important potential alternative treatment approach. Indeed, Lotze et al. [13] showed that greater use of a myoelectric prosthesis in arm amputation subjects correlated with a reduced on-going pain intensity. Similarly, it has recently been demonstrated that 2-point discrimination training in both phantom limb pain and CRPS patients can result in a return of S1 reorganization to its "control" state and an associated decrease in on-going pain [8,19]. Whether a similar approach will be effective in reducing on-going pain intensity levels in central neuropathic pain conditions such as neuropathic SCI pain remains to be determined.

Although the causal relationship between pain and cortical reorganization remains unclear, there is accumulating evidence of an association between the degree of cortical reorganization following nervous system injury and the presence and severity of neuropathic pain. Despite several studies demonstrating cortical reorganization following SCI, no studies have examined the relationship between this reorganization and pain. The present study provides further evidence of a link between the degree of cortical reorganization and pain in central neuropathic pain conditions.

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