Title: Mislocalisation of sensory information in people with chronic low back pain: A preliminary investigation.

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ABSTRACT

Objectives: The purpose of this study was to establish if people with chronic low back pain (CLBP) demonstrate impairments in the ability to localise sensory information delivered to the back more than healthy controls and determine whether any sensory abnormalities are related to pain-related variables.

Methods: Vision was occluded and participants were stimulated using light touch or pinprick over a number of body areas in random order. To assess for mislocalisations participants were asked to nominate the location of each stimulus in reference to a marked body chart. To assess for referred sensations participants were asked whether they experienced any sensations elsewhere during stimulation. If referred sensations were reported, testing was repeated with visualisation of the stimulated area.

Results: While a small number of CLBP subjects demonstrated referral of sensations, this was not statistically different from what was observed in a healthy control group ($p = 0.381$). In contrast, mislocalisations were very common in the patient sample and statistically more common than we found in healthy controls ($p = 0.034$). No statistically significant associations were detected between sensory function and the measured pain-related variables (all $p > 0.05$).

Discussion: These data add to a growing body of evidence suggesting that disturbed self perception is a feature of CLBP. It is plausible that altered self perception is maladaptive and contributes to the maintenance of the problem and may represent a target of treatment for CLBP.

Key words:

Low back pain; referred sensations; sensory perception; cortical reorganisation; body image

INTRODUCTION

A key property of the somatosensory system is the ability to localise the site of sensory input [1]. This is particularly significant for the nociceptive system where accurate localisation of the stimulus is likely to be very adaptive [2]. Evidence suggests that the ability to localise sensory information is impaired in people with chronic pain problems. Referred sensations, which are somatosensory feelings that are perceived to emanate from a body part other than the one being stimulated [3], have been reported in a range of painful conditions such as phantom limb pain [4-9], neuropathic pain following spinal cord injury [10], brachial plexus injury [11, 12] and complex regional pain syndrome [3, 13]. Referred sensations are thought to represent the clinical correlate of cortical [4, 14, 15] and subcortical [16, 17] reorganisation, a feature of a number of chronic pain syndromes [18].

In reports of referred sensations, subjects commonly perceive sensation both at the stimulated site as well as a remote referral site. Clinically, we have observed a different type of localisation deficit, in which people with chronic back pain experience only one site of stimulation but are unable to accurately localise where on the body surface the stimulation occurred, a phenomenon termed atopognosia [1]. This finding is generally displayed in neurological patients following definitive brain injury [19-21]. However, it is also described in people with complex regional pain syndrome of one arm. Those people have not sustained brain damage, yet when a single finger is stimulated, their ability to correctly identify the stimulated finger is lower on the affected hand than on the unaffected hand [22], suggesting this phenomenon may also be present in subjects with pain-induced cortical reorganisation.

Chronic low back pain (CLBP) involves extensive changes in central nervous system structure and function [23, 24] and there is increasing interest in identifying clinically accessible markers of cortical dysfunction. There is some evidence, from retrospective chart review, that referred sensations are a feature of CLBP [25], but we are not aware of any empirical investigation of the presence of atopognosia in people with CLBP. This study aimed to determine if people with CLBP demonstrate impairments in the ability to localise sensory information and whether these sensory impairments relate to clinical status. We hypothesised that CLBP patients would be poorer at localising sensory input, and would experience referred sensations more often, than healthy controls. We also hypothesised that the extent of these particular sensory impairments would relate to clinical status.

MATERIALS AND METHODS

Design:

This cross-sectional case-control cohort study received institutional ethical approval. Participants provided informed consent and all procedures conformed to the Declaration of Helsinki.

Participants:

A convenience sample of 24 non-specific CLBP patients was recruited from the Department of Pain Management at The Sir Charles Gairdner Hospital, Perth, Western Australia, and from community physiotherapy practices as part of a randomized cross-over experiment exploring the effect of visual feedback on movement related back pain [26]. The sample size was determined by the power calculation for that cross-over experiment. Participants were eligible if they were aged

between 18 and 60 years of age; were proficient in written and spoken English; reported back pain as their main complaint; had experienced non-specific low back pain for a minimum of six-months; rated their back pain as at least moderate on a modified version of item seven of the Short-Form 36 [27] and were able to provide consent. Participants were excluded if they presented with nerve root pain or evidence of specific spinal pathology (such as malignancy, infection, fracture, inflammatory disease, etc); were pregnant or less than six-months post-partum; had undergone any lumbar surgery or invasive procedure within the previous 12-months; were currently involved in litigation in relation to their back pain; were judged by their treating clinician to be unsuitable for performance of a repeated movement assessment; had significant medical or psychological illness or significant visual impairment.

Twenty-four healthy volunteers drawn from staff and students of The University of Notre Dame Australia also participated. Control subjects were invited to participate if they were currently low back pain free, reported no back pain at all in the last six-months, had not experienced any episode of low back pain sufficient to restrict work or leisure within the last two-years, were proficient in written and spoken English and were able to provide consent. Control subjects were excluded if they were pregnant or less than six-months post-partum or had any significant extant medical condition.

Participant profile

Treating medical or physiotherapy staff identified potential patients and checked the study criteria. Potential participants were then seen by a research assistant who clarified inclusion and exclusion criteria, obtained consent and collected basic demographic data. Volunteers completed

a questionnaire, which solicited information about the length of the current episode, pain distribution, work status and current pain medications. In addition, patients completed a set of standardized questionnaires that assessed disability, pain and psychological functioning. Low back pain related disability was measured using the Roland Morris disability questionnaire [28]. Back pain intensity was measured using a visual analogue scale for average pain over the last week, anchored at left with 0 = 'no pain' and at right with 100 = 'pain as bad as you can imagine'. Kinesiophobia was estimated using the Tampa Scale of Kinesiophobia [29]. The level of pain-related catastrophization was measured using the Pain Catastrophizing Scale [30] and depression and anxiety were assessed with The Hospital Anxiety and Depression Scale (HADS) [59]. The control population provided the same demographic information and completed The HADS [31].

Procedure

The protocol was based partly on that used by McCabe et al. [3]. All testing occurred in a closed room in which ambient noise was kept low and distractions minimised. Prior to testing, participants undressed to their underwear and were shown an A3 size schematic diagram of a posterior view of the body with different anatomical areas marked (figure 1). The areas were: lower thigh (popliteal line to mid femur); upper thigh (mid femur to gluteal crease); low lumbar (posterior superior iliac spine to spinous process of L2); upper lumbar (L2 to T10); low thoracic (T10 to T6); upper thoracic (T6 to T2) and shoulder (posterior acromium to mid humerus). The subjects were thoroughly orientated to the labels for each body area and the anatomical demarcation between the areas. The verbal descriptions were reinforced by tactile input from the

researcher identifying both the boundaries between the areas and the centre of each area where the formal stimulation would occur.

Participants were then positioned comfortably in prone on an examination table. A pillow was placed under the stomach to flatten the lumbar spine and standardise lumbar position. A large mobile mirror was placed adjacent to the table so that patients could view a reflection of their back and legs by turning their head to the side. For initial testing participants were instructed to lay prone with their face through the hole at the end of the examination table, occluding vision of the back. The schematic diagram of the body was placed on the floor visible to the patient through the face hole. In this position further verbal and tactile reinforcement was given of the boundaries and centre of the marked body areas. For the final stage of preparation, the research assistant lightly marked the centre of each body area to ensure standardisation of stimulation site.

For CLBP patients, the sensory examination was conducted on the side of worst back pain. If patients were unable to differentiate between sides, the side of testing was determined by coin toss. The side of testing for control participants was determined by coin toss. Testing of light touch was undertaken first in all participants using a software generated sequence that ensured each body area was assessed twice in randomised counterbalanced order. Superficial pain was then assessed in a similar manner using a different random sequence, resulting in 28 stimulations in total. As the participants were recruited from different facilities, the tester was not blind to subject's clinical status.

Light touch was assessed by applying five slow horizontal strokes with a cotton swab to the centre of each body region marked on the body chart and superficial pain by five light depressions with a Medipin (Medipin Ltd, Bushey Hertfordshire, UK) in the same area. Five stimuli were chosen as pilot testing established that participants had difficulty judging both referred sensations and localisation based on a single stimulus. To enhance consistency in sensory stimulation the size of the cotton swabs used and the way they were held was standardised and attempts made to ensure uniformity of applied pressure. For superficial pain testing we attempted to control the depth of depression by use of the Medipin, which is a single use neurological testing pin where the point is surrounded by a flattened annulus, thus limiting the depth of depression. Each stimulation was applied at a rate of approximately one per second and a five second pause was used between each set of stimulations.

For each series of five stimuli, participants were asked to state in which body area they felt the stimuli. If the stated body area was different to the stimulated site this was recorded as a mislocalisation. Participants were then asked whether they perceived a stimulus area anywhere else. If participants responded in the affirmative, it was recorded as a referred sensation. When referred sensations were reported, participants were asked to describe the referred sensations and indicate their location. The identical stimulation site was then reassessed, using the same modality, but with visualisation of the back and legs, so as to measure the effect of visual feedback on the referred sensation. The effect of vision on mislocalisation was not assessed as it was assumed that all mislocalisations would likely be corrected by visual feedback. Subjects were informed that the purpose of the study was to investigate the sensitivity of the back in

CLBP patients and they were naïve to the concept of referred sensations, and blinded to the study hypotheses.

Data analysis

All analyses were undertaken using PASW for Windows version 18 (SPSS, Chicago IL, USA) or Stata/IC 10.1 for Windows (Statacorp LP, College Station TX, USA). The demographic and clinical profile of patients and controls were summarised with means and standard deviations for continuous data and ratios and percentages for categorical data. The two outcome variables were counts of i) mislocalisations or ii) referred sensation with sensory stimulation. Data from light touch and superficial pain testing were combined for analysis. A comparison of the distribution of the number of mislocalisations and referred sensations between patient and control groups was made using Fisher's exact test. Due to the small number of mislocalisations and referred sensations, the nonparametric Kendall's tau-b coefficient was used to test if the number of mislocalisations or referred sensations were associated with pain-related variables (intensity, duration, disability, kinesiophobia and pain-related catastrophization). Statistical significance was set at α=0.05.

RESULTS

Group characteristics

Table one describes the demographics of all study participants and the clinical status of the participants with CLBP. Of note, 62.5% of the patient sample complained of back pain and referred leg pain.

Differences in sensory function

Sixty seven percent of people with CLBP reported at least one mislocalisation, whereas only 25% of control participants mislocalised sensory information. This difference was statistically significant (Fisher's exact p=0.034). Figure 2 displays the frequency of participants experiencing up to five mislocalisations, by patient versus control group (although the maximum possible mislocalisations was 28, a maximum of only five was observed).

Referred sensations were experienced by 21% of people with CLBP and 12.5% of control participants. This difference was not statistically significant (Fisher's exact p =0.381). Figure 3 displays the frequency of participants experiencing up to nine referred sensations, by patient versus control group (a maximum of nine referred sensations out of possible 28 was observed). Visual feedback reduced the perception of referred sensations in 71% of referred sensations experienced by the patient group and all referred sensations experienced by the control group.

Relationships between sensory function and clinical profile

Table 2 displays the associations between number of mislocalisations / referred sensations and pain–related variables in the patient group. No statistically significant associations were detected.

DISCUSSION

The results uphold our first hypothesis, that CLBP patients would be poorer than healthy controls at localising sensory input. Sixty-seven percent of people with CLBP but only 25% of healthy controls, made at least one error when asked to indicate where on a body chart they had been

touched. That is, atopognosia seems to be a feature of CLBP. Our results do not uphold the second hypothesis, that people with CLBP would report more referred sensations than healthy controls. Twenty one percent of people with CLBP and 12.5% of healthy controls reported referred sensations at some time during the testing protocol but this difference was not statistically significant. Our third hypothesis was also not supported as we found no relationship between sensory function and pain-related variables.

Whilst quite high rates of referred sensations are reported for phantom limb pain [5-7], previous research has suggested that only around 30% of people with CLBP experience some form of referred sensations [25], a figure very similar to what has been reported in people with CRPS [3, 13] and neuropathic pain related to spinal cord injury [10]. The lower rate reported in our study may represent a difference in severity between the patients in our sample and those in other investigations. In our study, subjects were only included if the referring clinician felt they were suitable for performance of a repeated movement assessment. This may have led to the exclusion of more disabled and distressed subjects. This is particularly relevant as researchers have previously found evidence of somatosensory cortical reorganisation in people with CLBP who were distressed but not in those who were not [32]. Further investigation of referred sensations in people with CLBP may still be indicated, utilising larger samples of more severely affected patients.

While there are anecdotal reports of referred sensations in healthy subjects [33], none of the experimental studies we identified found evidence of referred sensations in the healthy control groups [4, 10, 13] or in non-painful patient controls [5, 10]. Most studies, including our own, have used

modest sample sizes and it may be that the failure of other researchers to identify referred sensations in control groups reflects the difficulty of identifying uncommon phenomena in small populations. Alternatively, it might be related to the body area tested. All stimulation in our study was provided to the posterior surface of the body and primarily to the spine and thighs. The relatively small representation of these regions in primary sensory cortex, and the fact that these regions are rarely visualised, might make referred sensations from stimulating these segments more likely in healthy controls than they are from regions with larger representations, most notably the hand and mouth [15]. Additionally, the high prevalence rates of low back pain means that identification of a truly healthy control group is likely to be more difficult than with other much less common pain conditions such as CRPS or brachial plexus injury. We did not screen for the absence of back pain beyond two years and it is likely that some of the healthy controls had previously experienced episodes of low back pain and this may have influenced our results. Finally, the protocol we adopted used a series of five stimulations which may have influenced the results; different outcomes might be seen with a single stimulation protocol. Clearly further research of referred sensations on large groups of healthy controls stimulating a variety of body areas is required.

This is the first report of atopognosia in patients with CLBP, and our data suggest it is a common phenomenon. Previous studies have found normal tactile detection thresholds yet deficits in two point discrimination [34, 35] and graphaesthesia [35] over the back in CLBP patients and the findings of the present study add to this growing body of evidence suggesting that deficits in complex sensory function are a feature of the CLBP experience. Investigations of atopognosia in neurological patients suggest a dissociation between tactile detection and tactile localisation.

Several authors have described neurological cases in which detection of sensory stimulation is minimally affected yet subjects are unable to indicate where they have been touched [19-21]. This would seem consistent with the data available for CLBP.

Evidence also suggests primary somatosensory cortex disruption may be implicated in deficits of localisation. Large parietal infarcts involving the primary somatosensory cortex have been identified in some neurological patients who demonstrate atopognosia [19, 20]. In addition, Braille readers who use three fingers simultaneously for reading display a greater degree of mislocalisation of tactile stimulation of the fingers than single finger Braille readers and non-Braille readers. Importantly, the three finger Braille readers demonstrated far greater reorganisation in the primary somatosensory cortex than the other two groups as well as a significant relationship between cortical reorganisation and mislocalisations [36]. Schweizer et al. [37] have noted a worsening of mislocalisations to near threshold tactile stimulation of the hand when healthy subjects engage in a training task known to disrupt normal somatosensory cortical maps. Also, Schaefer et al [38] used a visual illusion to induce mislocalisation of sensory stimulation to the hand in healthy subjects. Neuromagnetic source imaging showed that representation of the hand in the primary somatosensory cortex changed during the illusion in comparison to control stimulation which did not induce mislocalisation. Finally, temporary disruption of somatosensory cortex function using trancranial magnetic stimulation has been shown to effect both detection and localisation of tactile stimulation, though the effect on localisation is more profound and long lasting [39]. Reorganisation [32, 40] and degeneration [41] within the primary somatosensory cortex appear to be a feature of CLBP and the presence of

atopognosia in CLBP patients may be the clinical correlate of these observed central nervous system changes.

The presence of atopognosia may simply be a consequence of ongoing pain and related emergent behaviours. However, it is plausible that atopognosis is maladaptive and contributes, at least in part, to the maintenance of the CLBP experience. Recent models of pain emphasise the importance of threat perception in generation of the pain experience [42] and the loss of ability to accurately localise where nociceptive information is coming from might contribute to perceived threat. Consistent with this idea visualisation of the stimulated body part, which improves tactile acuity [43] and is very likely to improve localisation, has been shown to be effective in reducing the intensity of experimental pain [44, 45].

Some researchers have emphasised the role of cortical mechanisms in maintaining various chronic pain states [46, 47]. Specifically, it has also been argued that movement-related pain may arise as a result of incongruence between predicted and actual sensory feedback by virtue of disrupted body maps and disturbed body schema [46, 47]. A deficit in localisation of sensory information from the back is a likely contributor to a mismatch between actual and expected sensory feedback and could contribute to ongoing movement related pain via this mechanism. In addition, poor sensory function is likely to negatively impact on control of the spine with movement and during static tasks. This may lead to abnormal and noxious loading of spinal tissue and contribute to the maintenance of peripheral nociceptive input as a driver to the chronic pain state.

One final interpretation of the current results relates to the recent discovery of spatially-defined deficits in sensory processing in people with back pain [48]. This work, undertaken in people with unilateral chronic low back pain, revealed that tactile stimuli from the painful side were processed more slowly than identical stimuli from the non-painful side. Importantly, the same was true when the stimuli were delivered to the hands and the hands were held next to the painful, and non-painful side of the back. This spatially-defined deficit has also been observed in people with CRPS of one hand [49] and implicates a deficit in the integration of somatotopically-based frame of reference with a space-based frame of reference (see [2] for review). Such a deficit may also explain problems that people with chronic pain have in performing motor imagery tasks relating to the painful area. The most studied motor imagery tasks involve making left/right judgements of pictured body parts. These tasks require the individual to mentally manoeuvre their own body part to match the posture of the part shown in the picture. This manoeuvre requires the transformation of location data between frames of reference, a task that is thought to depend on posterior parietal mechanisms (see [50] for review). Performance in this task is disrupted in people with CRPS [51, 52], chronic back pain [53] and chronic knee pain [54]. Sensory discrimination training, which aims to improve sensory localisation ability and is likely to sharpen the somatotopically-based frame of reference, has been shown to be effective in managing phantom limb pain [55] and complex regional pain syndrome [56, 57]. Our data suggest these or similar approaches may be worth testing in people with CLBP.

The results presented here need to be interpreted in light of the study limitations. As data collection for patients and controls largely occurred at separate sites, it was not possible to blind the tester to participants' clinical status, the rigor of this study would have been improved by the

use of a blind assessor. It is also possible that attentional problems may underpin the results seen. Attentional functioning is known to be susceptible to pain interference [58] and the poorer performance by patients on the localisation task may have been influenced by the distracting influence of pain. We attempted to mitigate this confounder by ensuring patients were comfortably positioned throughout testing. Furthermore, the lack of association between pain intensity and mislocalisation suggests this might not be an important issue, though assessing present rather than average pain would have enabled better control of this issue. This study was conducted alongside a randomised experiment looking at the influence of mirror visual feedback on movement related pain and the sample size and patient characteristics were determined based on this experiment. As mentioned previously, this might have influenced the severity of subjects accepted in to the study and decreased the representativeness of our sample, most significantly by excluding the more severe and distressed participants. The sample size might also not have been large enough to detect group differences in referred sensations as it appears to be a phenomenon with a fairly low incidence amongst chronic pain populations.

In summary, mislocalisations are more common in CLBP than in healthy controls, but referred sensations are not. These data add to a growing body of evidence suggesting that disturbed self perception is a feature of CLBP.

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Figure legends:

Figure 1. Body chart with anatomical area marked

Figure 2. Frequency of 0-5 mislocalisations in Control and Patient Groups

Figure 3. Frequency of 0-9 Referred Sensations in Control and Patient Groups

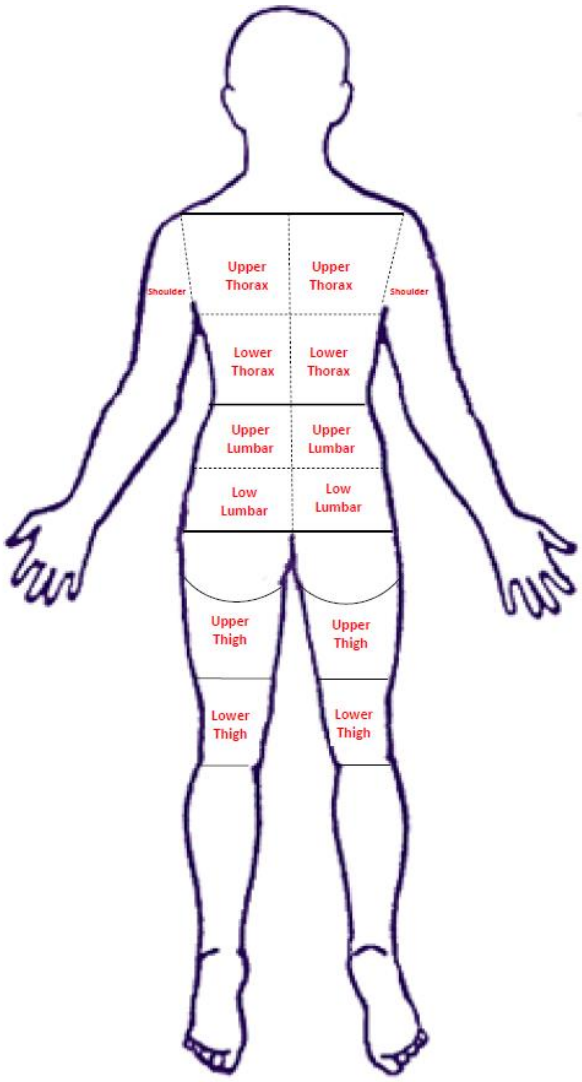

Upper Thorax
Upper Thorax
Shoulder
Shoulder
Lower Thorax
Lower Thorax
Upper Lumbar
Upper Lumbar
Low Lumbar
Low Lumbar
Upper Thigh
Upper Thigh
Lower Thigh
Lower Thigh

Figure 1

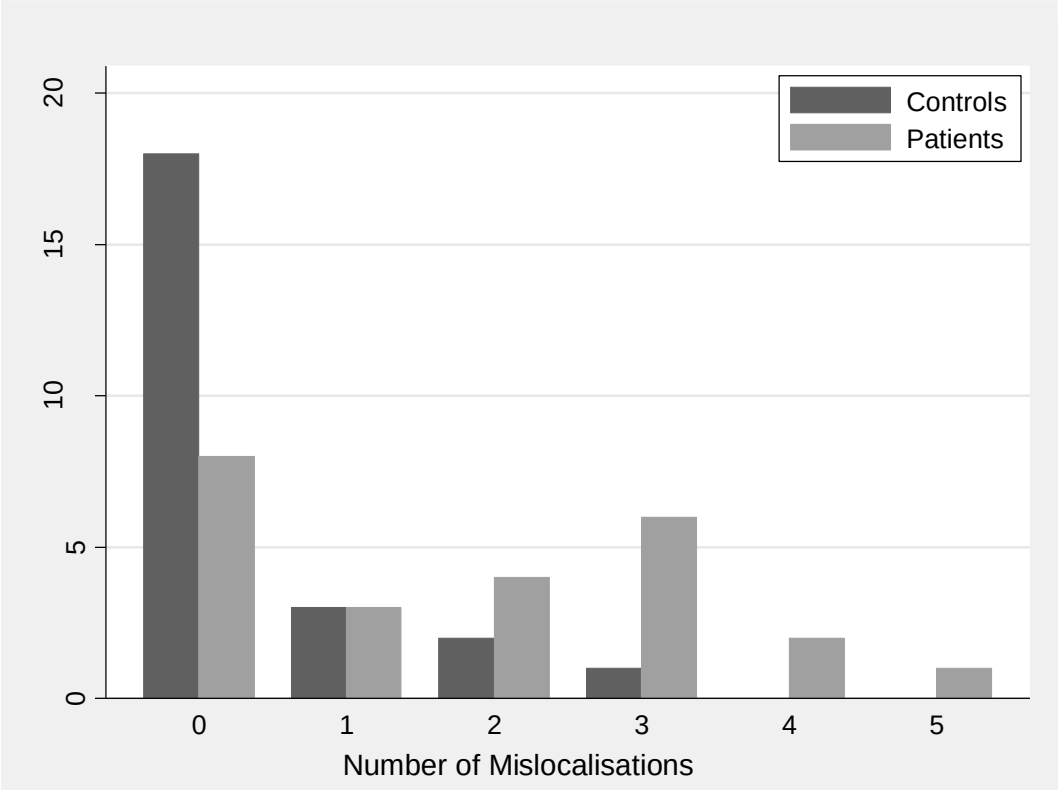
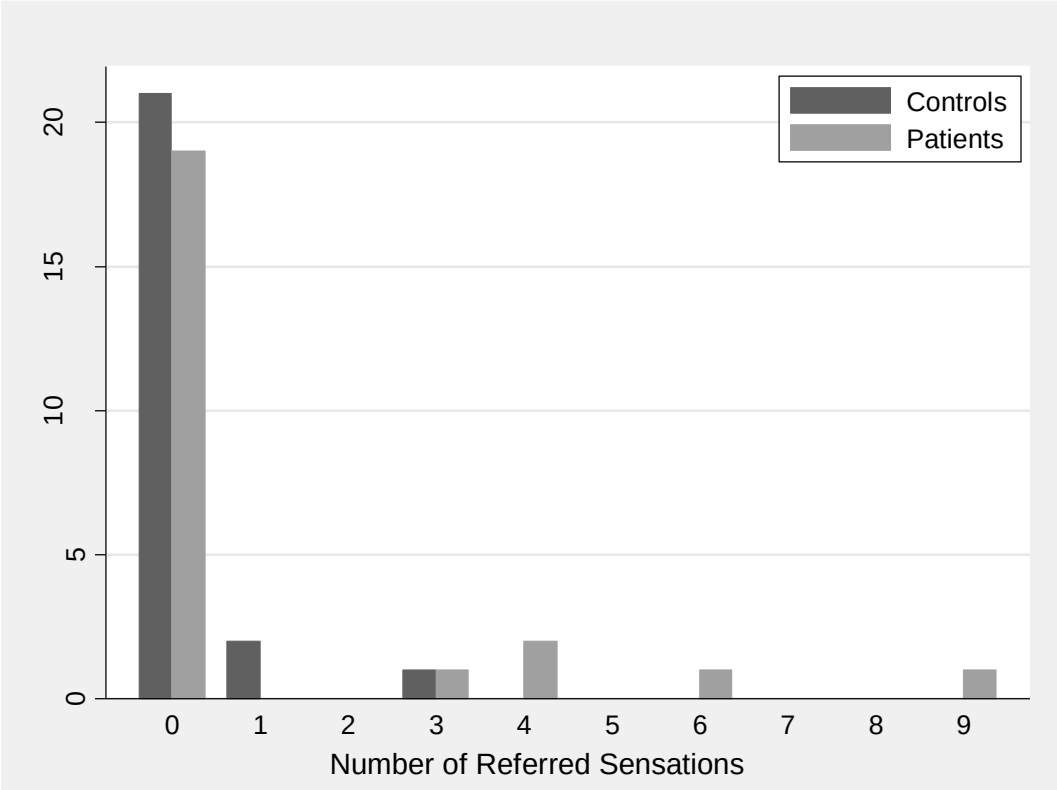

Controls
Patients
0
5
10
15
20
0
1
2
3
4
5
Number of Mislocalisations

Figure 2


Controls
Patients
0
5
10
15
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0
1
2
3
4
5
6
7
8
9
Number of Referred Sensations

Figure 3

Table 1: Demographics and clinical status of participants (mean(SD) or n(%))

	Controls (n=24)	CLBP patients (n=24)
Age (years)	42.0 (14.7)	41.8 (15.0)
Female Gender	10 (41.7%)	10 (41.7%)
Height (m)	1.75 (0.11)	1.73 (0.10)
Weight (Kg)	77.5 (14.4)	80.2 (14.5)
Body Mass Index (Kgm^{-2})	25.1 (2.8)	26.9 (5.0)
Anxiety (HADS, 0-21)	4.9 (2.7)	6.8 (4.4)
Depression (HADS, 0-21)	1.4 (1.8)	4.8 (3.3)
Side tested: right	10 (41.7%)	12 (50.0%)
CLBP Patient Clinical Status		
Side of pain:		
Unilateral		8 (33.3%)
Bilateral with dominance		12 (50.0%)
Bilateral and equal		4 (16.7%)
Length current episode (years; Median (IQR))		5.5 (17.5)
Taking Opiods		9 (18.8)
Symptom Distribution		
Back only		9 (37.5%)
Above knee		6 (25.0%)
Below knee		9 (37.5%)
Off work due to LBP		3 (12.5%)

Pain intensity (VAS, 0-100)	45.0 (19)
Disability (RMDQ, 0-24)	9.9 (5.6)
Kinesiophobia (TSK, 17-68)	40.4 (6.5)
Catastrophisation (PCS, 0-52)	18.2 (12.2)

HADS = The Hospital Anxiety and Depression Scale

VAS = Visual Analogue Scale

RMDQ = The Roland Morris Disability Questionnaire

TSK = The Tampa Scale of Kinesiophobia

PCS = The Pain Catastrophizing Scale

Table 2: Associations between number of mislocalisations/referred sensations and pain-related variables in the patient group (n=24)

	Mislocalisations		Referred Sensations	
	Kendall's tau-b	p-value	Kendall's tau-b	p-value
Pain intensity	0.008	0.980	0.071	0.699
Duration of current episode	0.161	0.327	-0.097	0.596
Disability	-0.066	0.699	0.061	0.750
Kinesiophobia	-0.053	0.757	0.307	0.077
Catastrophisation	0.183	0.258	-0.012	0.972