Title: Tactile thresholds are preserved yet complex sensory function is impaired over the

lumbar spine of chronic non-specific low back pain patients. A preliminary

investigation

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**ABSTRACT** 

**Objectives**: To investigate impairments in sensory function in chronic non-specific low back

pain patients and the relationship between any impairment and the clinical features of the

condition. **Design**: A cross-sectional case-control study. **Setting:** Laboratory based study.

Participants: Nineteen chronic non-specific low back pain patients and nineteen healthy

controls. Main Outcome measures: Tactile threshold, two point discrimination distance and

accuracy at a task involving recognizing letters drawn over the skin of the lower back

(graphaesthesia) were assessed over the lumbar spine in both groups. Pain duration, pain

intensity, physical function, anxiety and depression were assessed by questionnaire in the

back pain group **Results**: We found no difference in tactile threshold between the two groups

(median difference 0.00~95% CI -0.04-0.04). There was a significant difference between

controls and back pain patients for two point discrimination (mean difference 17.85 95% CI

5.93 – 29.77) and graphaesthesia accuracy (mean difference 6.13 95% CI 1.27-10.99). Low

back pain patients had a larger lumbar two point discrimination distance threshold and a

greater letter recognition error rate. In the patient group, we found no relationship between

clinical profile and sensory function and no relationship between the sensory tests.

**Conclusions**: These data support existing findings of perceptual abnormalities in chronic non-

specific low back pain patients and are suggestive of cortical rather than peripheral sensory

dysfunction. Amelioration of these abnormalities may present a target for therapeutic

intervention.

**Key words**: low back pain; body image; neuronal plasticity; touch perception

#### INTRODUCTION

Chronic non-specific low back pain (CNSLBP) is a common and costly health care problem for which there are few effective interventions [1]. Recent evidence indicates significant structural and biochemical changes within the brains of patients with CNSLBP [2], as well as evidence of alterations in the representation of the back in the primary sensory cortex (S1) [3,4]. Sensory cortical representation is a plastic phenomenon that is dependent on the response profiles of neurons in S1. It is considered important in representing the consciously felt body and thus alterations in this representation may have consequences for the conscious body image [5]. One perspective that is gaining acceptance in other complex pain problems is that disruption of the cortical representation of the painful body part and the resultant body perception disturbance might contribute to the clinical condition [5,6]. Moreover, treatment approaches aimed at normalizing cortical representation and body perception seem to be effective in the management of other complex pain problems such as phantom limb pain and complex regional pain syndrome type I [7-10].

In light of these brain changes seen in the back pain population, we were interested in exploring whether patients with CNSLBP demonstrate evidence of altered perception of their back. One approach to investigating body perception is via 'cortical' sensory tests, such as two-point discrimination (TPD), which are dependent in part on the integrity of the cortical representation of that body area [5]. Recent studies have explored whether patients with CNSLBP exhibit evidence of altered perception of their back. Moseley [11] demonstrated deficits in TPD over the low back area along with marked alterations in body image in a small group of CNSLBP sufferers and more recently these deficits in tactile acuity have been found to be related to lumbo-pelvic motor control impairments in a similar patient population [12]. Importantly simple tactile threshold was unaffected in these studies indicating that deficits in

tactile acuity may not be due to any gain or loss in the peripheral transduction and transmission of sensory information but instead may have its origins in central processing.

The ability of the brain to manipulate the representation of the body is critical for normal function and perception. It is currently unknown whether this ability is compromised in patients with CNSLBP. A cortical sensory task that may offer a way to investigate this ability is graphaesthesia, or recognition of symbols drawn on the skin. It is a task that requires not only good tactile acuity but greater cortical manipulation of the sensory stimulus to construct an image of which letter has been drawn [13]. There is currently no data on graphaesthesia performance in CNSLBP patients or evidence of whether deficits in cortical sensory function extend beyond problems with tactile acuity. We were interested in establishing whether patients demonstrate a deficit in graphaesthesia and the relationships between graphaesthesia performance, tactile acuity and simple tactile thresholds.

The specific research questions investigated in this study were:

- 1. Do CNSLBP patients demonstrate a deficit in graphaesthesia ability over the lower back?
- 2. Does graphaesthesia performance relate to other sensory measures, specifically lumbar tactile acuity and simple tactile threshold?
- 3. Is graphaesthesia performance related to the severity of the clinical condition?

We hypothesized that CNSLBP patients would have normal tactile threshold, but demonstrate deficits in graphaesthesia and TPD. Furthermore, we predicted that graphaesthesia performance would be related to tactile acuity and to the severity of the clinical condition.

#### **METHODS**

# **Participants**

A convenience sample of nineteen volunteers with CNSLBP was recruited from the neurosurgical waiting list of a district general hospital in Perth, Western Australia and from a private physiotherapy clinic. Subjects were screened by a physiotherapist and included in the study if they were aged between 20 and 55 years, had experienced non-specific low back pain (LBP) for more than six-months, were proficient in written and spoken English and were able to provide written informed consent. Participants were excluded if they presented with signs and symptoms suggestive of nerve root pain, evidence of specific spinal pathology such as malignancy, fracture, infection, inflammatory joint or bone disease, were pregnant or less than six month post partum, had a coexisting major medical disease, or had undergone previous spinal surgery.

Nineteen healthy volunteers drawn from students and staff of The University of Notre Dame Australia also participated in the study. Subjects were invited to participate in the trial if they were currently LBP free, had not experienced any episode of LBP sufficient to restrict work or leisure within the last five years, were aged between 20 and 55 years old, were not pregnant or less than six months post-partum, had no major medical disease, were proficient in written and spoken English and were able to give written informed consent. All procedures received ethical approval from the Human Research Ethics Committee of the University of Notre Dame Australia and the Ethics Review Board of The Sir Charles Gairdner Hospital, all participants were fully informed of the experimental procedure and all gave written consent.

#### Measurements

**Questionnaires** 

Before any testing was carried out demographic information was obtained on all participants. In addition the LBP subjects were asked to indicate the duration of their current episode of back pain and completed three numerical rating scales to record the level of their current back pain, their usual level of back pain and their level of back pain at its worst. The scales were anchored with 0 = 'no pain' and 10 = 'pain as bad as you can imagine' [Cleeland 1991]. Physical function was measured using item three of the Medical Outcomes Study Short Form Health Survey (SF-36) [14]. This item lists ten functional activities and asks patients to indicate if their health problem limits performance of each task a lot, a little, or not at all during a typical day. These responses are scored as 1, 2 or 3 respectively yielding a score between 10 and 30, with the higher number indicating better physical function. Estimates of depression and state anxiety levels were obtained from the Hospital Anxiety and Depression Scale (HADS) [15]. This is a 14-item self report scale which contains seven items related to anxiety and seven items related to depression. Each item is scored on a 0-3 scale, yielding two sub scales ranging from 0-21. Higher scores indicate higher frequency of symptoms of depression and anxiety.

## Sensory testing

For all testing, subjects were positioned comfortably in prone lying on an examination table with their back exposed, ambient noise was kept low and distractions minimized. Pillows were positioned under the stomach to flatten the lumbar spine and to standardize lumbar position. Using a standardized palpation procedure, the examiner initially located and marked the position of the tip of the transverse processes of L1, L3 and L5, these markings served as reference points for all subsequent testing. The same examiner undertook all testing on control subjects and patients, and as patients and controls were recruited from separate facilities, was not blind to subject status. Tactile threshold was assessed first, then TPD and

finally letter error rate. For all subjects, testing was undertaken separately on the left and right sides of the back and the order of the side of testing was randomized. An *a priori* decision was made to discard data collected from the pain free side in patients with only unilateral back pain, both sides were tested to ensure equivalence in learning effects across all participants.

#### *Tactile threshold*

The sensory threshold to light touch was assessed using Semmes-Weinstein monofilaments (North Coast Medical, Morgan Hill, CA, USA) over the tip of the transverse processes at the levels of L1, L3 and L5. The filament was pressed at a 90° angle to the skin until it bowed and held in place for 1.5 seconds, subjects were instructed to say 'yes' when a stimulus was felt. The stimulus was applied up to three times at the same location for monofilaments 1.65 to 4.08 and one time only for filaments 4.17 and above [16]. The sites were tested in a random order and a threshold value calculated for each site using an ascending sequence starting with the lightest monofilament. The mean of these three sites was calculated for each side for use in subsequent analyses.

## *Two-point discrimination*

Two-point discrimination was assessed using aspects of the method described by Moberg [17] and Seltzer and Seltzer [18]. A set of mechanical calipers (Lafayette two point aesthesiometer, Lafayette Instruments, Layayette In, USA) with a precision of 1 mm was lightly applied to the back until the very first blanching of the skin. The calipers were parallel to the spine and the transverse process of L3 was maintained in the centre of the two calipers. Testing was commenced with 0 mm between the two calipers, and then the distance between them was increased in 2 mm increments until the subject was able to perceive two points instead of one.

Subjects were instructed to clearly say 'one' when they felt one point and 'two' when they felt two points. Catch trials were used to ensure that subjects were not guessing. The distance at which the subject first perceived two distinct points was noted as the initial threshold value. The process was then repeated using a descending sequence from a start point well above the initial threshold value, the distance at which patients first reported one distinct point during this sequence was noted. Testing then continued around these initial values using ascending and descending sequences until a consistent response was obtained.

## Graphaesthesia

Subjects were first shown a wall chart of the upper case letters of the alphabet and were instructed that this would be the way the letters would be drawn. They were then shown a diagram of the lumbar spine depicting the orientation and location of the letters. The letters were drawn with the blunt end of a monofilament on three sites centred on the tips of the L1, L3 and L5 transverse processes and did not extend across the midline, the height of the letters were such that there was no overlap in the area of skin in which the letters were drawn between the three sites. 20 random letters were traced at each of the three afore-mentioned sites and subjects were asked to clearly identify the letter that was drawn. The three sites were tested in a random order, and an error rate out of sixty was calculated for that side of the back.

## **Data analysis**

The distribution of data were checked for normality (Kolmogorov-Smirnov test). Subsequent statistical testing was determined by the distribution of the data. Differences in age and gender between patients and controls were investigated with an independent samples t-test and a Chi-square test respectively. The relationships between age and gender and TPD, tactile threshold

and graphaesthesia performance were investigated with Pearson's correlations. For patients with unilateral pain the values for the painful side only were used in the analyses. For patients with bilateral pain and all control subjects, data from both the left and right were utilised. In participants for whom bilateral data were used, two sample t-tests were employed to investigate within subject side to side differences for TPD and graphaesthesia. Within subject side to side differences in tactile threshold were investigated with the Mann-Whitney U test.

## Differences between groups

As tactile threshold data were not normally distributed, to test the hypothesis that it would not differ between controls and CNSLBP patients, we performed a Mann-Whitney U test. To test the hypothesis that cortical sensory function would be different between controls and CNSLBP patients, we performed a one-way between groups multivariate analysis of covariance. The two dependent variables were letter error rate and log transformed TPD distance. The independent variable was group (patients or controls) and age and gender were the covariates. Preliminary assumption testing was conducted to check for normality, linearity, univariate and multivariate outliers, homogeneity of variance-covariance matrices and multicollinearity. Besides one univariate outlier in the control group, no serious violations were noted once the TPD scores had been log transformed. A Bonferroni correction was applied to account for multiple statistical analyses. Effect sizes were explored using partial eta squared.

# Relationships between sensory tests

In the patient population, the relationships between graphaesthesia error rate, TPD and tactile threshold was examined using partial correlations controlling for age and gender.

## Relationships to clinical profile

In the patient population, the relationship between cortical sensory function and clinical status (pain duration, pain intensity, physical function, depression and anxiety) was explored with partial correlations controlling for age and gender. For all testing significance was set at p < 0.05

#### **RESULTS**

## Sample characteristics

Table one provides a summary of the characteristics of the study sample.

# **Methodological checks**

The two groups did not differ with respect to age (mean difference -7, 95% CI -15.09 to 1.09) or gender (odds ratio 0.49 95% CI 0.13 to 1.93). There was no significant correlation between age or gender and any of the sensory tests. There were no significant within participant side to side differences for any sensory test in either the control subjects or in the bilaterally distributed LBP patients (data not shown). As a result, in these participants the mean of left and right for each sensory test was calculated and this combined score was used in all subsequent analyses.

## **Sensory testing**

Table 1 provides the median and interquartile range for tactile threshold and means and standard deviation values for TPD and graphaesthesia organized by group. Actual TPD values rather than the log transformed values used in the analysis are provided for ease of interpretation.

## Differences in tactile threshold

There was no significant difference between patients and controls in tactile thresholds (median difference 0.00 95% CI -0.04 to 0.04)

# Differences in TPD and graphaesthesia

There was a statistically significant difference between controls and CNSLBP patients in cortical sensory function on the combined dependent variables: F(2, 33)=7.358, p=0.002; Wilks' Lambda = 0.69. When the results for the dependent variables were considered separately, using a Bonferroni adjusted alpha level of 0.025, TPD: F(1,34)=8.727, p=0.006 and letter error rate: F(1, 34)=6.389, p=0.016 were significantly different between groups. Inspections of the mean scores indicate that CNSLBP patients had a larger TPD distance and a greater letter recognition error rate (Table 1). The effect size statistic indicated that 20% of the variance in TPD and 16% of the variance in letter error rate could be explained by group. These data are represented graphically in Figure 1.

#### Relationships between sensory tests.

In the patient group we found no significant correlations between graphaesthesia and TPD or tactile threshold. These data are presented in Table 2.

## Relationships to clinical profile

One subject had ambiguous pain scores and one subject had not completed the HADS form fully, so were entered as missing values in this analysis. In the patient population we found no significant correlations between any aspect of cortical sensory function and symptom

duration, present, usual or worst pain intensity, physical function or anxiety and depression scores. Table 3 provides a summary of these data.

#### **DISCUSSION**

We found that TPD detection threshold was larger and graphaesthesia error rate greater over the lumbar spine in patients with CNSLBP compared to a control group of similar age and gender, but simple tactile thresholds were not significantly different between groups. These results confirm previous findings that patients with CNSLBP demonstrate specific deficits in sensory function over the lumbar spine. Moseley [11] and Luomajoki and Moseley [12] demonstrated impairment of tactile acuity along with marked alterations in body image in CNSLBP sufferers. In the first of these papers patients described the back as feeling smaller or even "missing" and it is proposed that these phenomena may indicate a disturbance of body perception. The current study extends these findings by demonstrating an additional deficit in a more complex perceptual task.

It is feasible that the deficits observed in TPD and graphaesthesia accuracy might result from peripheral abnormalities such as local reduction in cutaneous receptor field density. However we are not aware of any existing data that demonstrates such abnormalities and these impairments are apparent despite there being no difference in tactile thresholds between the two groups. Furthermore, there is a growing body of evidence demonstrating that tactile acuity is a dynamic phenomenon dependent on the integrity of the primary sensory cortex [13] and is largely determined by cortical representation in this region [19,20]. In CNSLBP patients the representation of the back in S1 is altered [3,4]. A reasonable interpretation of our findings is that the deficit does not primarily lie in transmission of the stimulus to the brain, but in the processing of that tactile input by the brain. It is possible that the disruption in

cortical representation seen in LBP patients may play a role in creating a body perception disturbance, and that the sensory deficits identified here may be a correlate of this process.

Graphaesthesia is a complex phenomenon and in simple terms involves encoding and transmission of the sensory stimulus peripherally, the reception of the stimulus in the cortex, the mapping of that stimulus in virtual space and the conversion of the stimulus into a semantic. Graphaesthesia performance has been shown to be dependent upon both tactile acuity and the integrity of S1, while the reverse is not the case, suggesting that graphaesthesia is a higher order task dependant on serial processing of sensory information from S1 [13]. The finding that TPD and graphaesthesia performance were unrelated suggests that impairment of graphaesthesia may not result simply from impairment of static tactile acuity and different deficits in cortical processes may underpin the impairments noted in these two sensory tasks.

Altered cortical representation and body perception is a potential target for therapeutic interventions. Studies in phantom limb pain [7], and complex regional pain syndrome (CRPS) [10] have demonstrated significant clinical improvements with sensory discrimination training. In these studies improvements in sensory performance were found to mirror improvements in pain. In addition, graded motor imagery programmes that aim to promote an incremental activation of cortical systems involved in body perception and movement have demonstrated efficacy in CRPS and phantom limb pain [8,9]. We are currently investigating the therapeutic application of these principles in CNSLBP. The identification of specific deficits in graphaesthesia performance in our study suggests that graphaesthesia training may be a valid addition to this type of therapeutic approach, particularly as a potential progression from tactile discrimination training.

The absence of a relationship between sensory performance and the clinical status of the patient cohort is an unexpected finding as previous studies have demonstrated a relationship between tactile perceptual disturbance and clinical profile [1,21,22]. Taken alone our results would suggest that the deficits are neither the cause nor the result of ongoing pain and might represent an epiphenomenon. In the light of the existing research it is possible that the current study may not have had sufficient power to demonstrate a relationship. In addition, rigorous standardisation of the testing procedure, coupled with variation of symptom location inherent in the sample, means that testing was not always performed directly over the area of maximal pain in the patient group. It is probable that sensory deficits are specific to the painful area, or more marked in this area [11] and our methodology may lack a degree of sensitivity in this respect. Furthermore Flor et al. [3] found cortical reorganization in a population considerably more chronic than ours and Lloyd et al. [4] only observed this phenomenon in patients who demonstrated abnormal illness behaviours. Levels of depression were low in our patient group and the average anxiety scores only just exceeded the threshold for normal scores [14], it may be that the clinical profile of our patient group made detection of relationships more difficult. In light of the relationship between cortical reorganisation and abnormal illness [4] it is interesting that the one clinical variable that approached a relationship to tactile acuity in the current study was anxiety (p=0.094).

Consideration must be given to the limitations of the study. The small sample size and lack of strict localization of testing to the site of maximum pain may have impaired our ability to detect relationships within the data. Additionally, the fact that the assessor was not blinded to the patient group may have introduced a degree of bias into the results however, no results were calculated or analysed until all 38 subjects' data had been collected in an attempt to minimize bias. It might be argued that tactile thresholds are a better control for possible

peripheral influences in static tests such as TPD than they are for dynamic tests such as graphaesthesia since encoding directional dynamic sensory stimuli involves the activation of additional populations of afferent receptors (slow adapting type 2 receptors) that are not required for static stimuli [23,24]. It is also possible that the deficits found in TPD and graphaesthesia may be due to alterations in attention, distraction and motivation, which would be less likely to affect the tactile threshold task. However, Peters and Schmidt [25] found no deficit in TPD on the forearm of patients with CLBP which suggests that this may not be the case and Moseley [11] found that deficits in tactile acuity and alterations of body perception were specific to the painful area on the back. Also, control subjects and patients potentially differ in medication use and it is possible that differences in the use of centrally acting analgesics may underpin some of the differences seen. Finally, the current study is cross-sectional and thus no causal inferences can be drawn.

We found evidence of poorer TPD and greater graphaesthesia error rates over the lumbar spine of patients with CNSLBP. These results are supportive of the notion that CNSLBP is characterized by dysfunction of sensory processing of information from the painful area. We also provide evidence that tactile thresholds over the lumbar spine are preserved, suggesting that that the dysfunction may be one of integration of sensory input at a central nervous system level. This interpretation is strengthened by evidence of reorganisation [3,4] and degeneration [26] within the primary sensory cortex of CNSLBP patients. Our results strengthen existing findings of a perceptual abnormality in CNSLBP and the suggestion that a disturbance in body perception may be part of the clinical condition. There is evidence from other chronic pain problems to suggest that these abnormalities may present a target for therapeutic intervention via sensory training. The identification of impairment in graphaesthesia suggests graphaesthesia training may be a valid addition to this type of

therapeutic	approach,	particularly	as	a	potential	progression	from	tactile	discrimination
training.									

# **Ethical approval:**

Ethical approval was obtained from the Human Research Ethics Committee of the University of Notre Dame Australia and the Ethics Review Board of The Sir Charles Gairdner Hospital.

# **Funding**:

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#### **Conflict(s) of interests:**

None declared

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# **TABLES**

Table 1 Characteristics of the sample and results of sensory testing for LBP patients and controls

Variable	LBP patients (N = 19)	Control subjects (N =	Difference between
		19)	groups (95% CI)
Age (yrs), mean (SD)	41 (12.5)	34 (12.1)	7 (-1.1-15.1)
Gender (female), N (%)	11 (57.9)	14 (73.7)	0.49 ( 0.13 - 1.93)
Duration of LBP episode (yrs), mean	9.33 (9.81)		
(SD)			
Usual pain intensity NRS(0-10), mean	3.9 (2.1)		
(SD)			
Current pain intensity NRS (0-10), mean	3.2 (3.0)		
(SD)			
Worst pain intensity NRS (0-10), mean	4.611 (2.85)		
(SD)			
SF36 Physical function (10-30), mean	21.8 (4.98)		
(SD)			
HADS Depression (0-21), mean (SD)	4.67 (4.93)		
HADS Anxiety (0-21), mean (SD)	7.44 (5.40)		
Tactile threshold log <sub>10</sub> Fmg, median (IQR)	1.65 (0.71)	1.65 (0.61)	0.00 (-0.04 – 0.04)
Two point discrimination mm, mean (SD)	62.03 (21.64)	44.18 (13.73)	17.85 (5.93-29.77)
Letter error rate /60, mean (SD)	25.47 (7.92)	19.34 (6.80)	6.13 (1.27-10.99)

Table 2. Correlations between each of the sensory tests for the CNSLBP patients (all non significant  $p \!>\! 0.05$ )

		Tactile threshold	Two point discrimination	letter error rate
Tactile threshold	Partial r		120	.337
	P value		.646	.185
Two point	Partial r	120		043
discrimination	P value	.646		.871
letter error rate	Partial r	.337	043	
	P value	.185	.871	

Table 3 Correlations between cortical sensory performance and clinical characteristics of the CNSLBP patients (all non significant p > 0.05)

		Duration Of LBP	Usual pain intensity	Current pain intensity	Worst pain intensity	SF 36 Physical function	HADS Depressi on score	HADS Anxiety score
Two point discrimination	Partial r	169	.030	.015	.032	241	.217	.432
discrimination	P value	.516	.914	.955	.907	.351	.420	.094
letter error rate	Partial r	188	041	063	062	.329	.172	.138
Tate	P value	.471	.879	.818	.818	.197	.523	.610

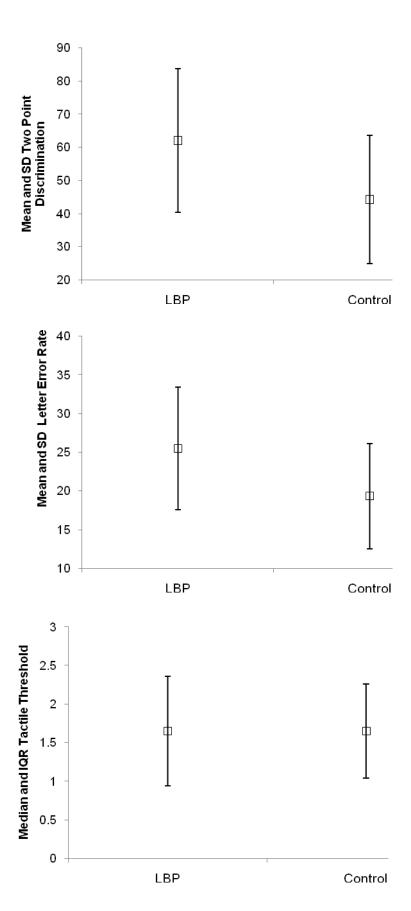


Figure 1. Comparison between CNSLBP patients and pain free controls for each of the sensory tests