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From acute to persistent low back pain: a longitudinal investigation of somatosensory changes using quantitative sensory testing—an exploratory study

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Abstract

Introduction: Chronic low back pain (LBP) is commonly associated with generalised pain hypersensitivity. It is suggested that such somatosensory alterations are important determinants for the transition to persistent pain from an acute episode of LBP. Although cross-sectional research investigating somatosensory function in the acute stage is developing, no longitudinal studies designed to evaluate temporal changes have been published.

Objectives: This exploratory study aimed to investigate the temporal development of somatosensory changes from the acute stage of LBP to up to 4 months from onset.

Methods: Twenty-five people with acute LBP (<3 weeks' duration) and 48 pain-free controls were prospectively assessed at baseline using quantitative sensory testing with the assessor blinded to group allocation, and again at 2 and 4 months. Psychological variables were concurrently assessed. People with acute LBP were classified based on their average pain severity over the previous week at 4 months as recovered (≤1/10 numeric rating scale) or persistent (≥2/10 numeric rating scale) LBP.

Results: In the persistent LBP group, (1) there was a significant decrease in pressure pain threshold between 2 and 4 months ($P < 0.013$), and at 4 months, pressure pain threshold was significantly different from the recovered LBP group ($P < 0.001$); (2) a trend towards increased temporal summation was found at 2 months and 4 months, at which point it exceeded 2 SDs beyond the pain-free control reference value. Pain-related psychological variables were significantly higher in those with persistent LBP compared with the recovered LBP group at all time points ($P < 0.05$).

Conclusion: Changes in mechanical pain sensitivity occurring in the subacute stage warrant further longitudinal evaluation to better understand the role of somatosensory changes in the development of persistent LBP. Pain-related cognitions at baseline distinguished persistent from the recovered LBP groups, emphasizing the importance of concurrent evaluation of psychological contributors in acute LBP.

Keywords: Low back pain, Acute pain, Chronic pain, Quantitative sensory testing, Conditioned pain modulation

1. Introduction

Low back pain (LBP) remains a clinical challenge and has the highest disability burden worldwide.[30,59] After an episode of LBP, up to two-thirds of people still experience variable levels of pain after 1 year[21,57] and a percentage of people (around 10%) will be significantly disabled as a result of LBP.[2] The reasons underlying failure to recover from an acute episode of LBP are not yet understood. Furthermore, consensus has not been achieved about which factors are most highly associated with poor outcome in LBP.[20] Although psychosocial and pain-related factors such as poor coping strategies, job dissatisfaction, leg pain, and higher pain intensity at LBP presentation have been shown to be significantly associated with delayed recovery, they explain only a limited proportion (ranging from 29% to 46%) of the variance in LBP outcomes.[27]

During the past few decades, research has demonstrated that several musculoskeletal chronic pain conditions, including LBP, are associated with generalised pain hypersensitivity,[46] most

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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likely reflecting increased excitability and/or changes in pain modulation within the central nervous system,[6] as well as with tactile acuity deficits deemed to reflect cortical reorganisation.[3] It is suggested that such somatosensory alterations are important determinants for the transition to persistent pain from an acute episode of LBP.[18] Previous prospective studies on acute whiplash injury have shown a differential development of pain hypersensitivity to cold and mechanical stimuli as well as spinal cord hyperexcitability in people reporting persistent pain and disability at 6 months compared with those who recover.[50,51] In LBP, although research investigating somatosensory function in the acute stage is developing, to the best of our knowledge, no longitudinal studies designed to evaluate temporal changes have been published. Therefore, the time course of sensory disturbances from early after onset of LBP to later stages when chronic pain develops remains unknown.

The aim of this exploratory study was to investigate and compare the temporal development of somatosensory changes in people with acute LBP from as early as 3 weeks from onset up to 4 months, with pain-free controls. This knowledge will assist in understanding mechanisms involved in the development of chronic LBP and factors associated with poor outcomes.

2. Methods

2.1. Study design

An inception cohort study was used to explore quantitative sensory testing (QST) responses in people with acute LBP followed up until 4 months. Three assessments were performed: at <3 weeks from LBP onset (baseline), 2 months (mean: 48 days from baseline) after pain onset, and 4 months (mean: 111 days from baseline) after pain onset. Pain-free controls were assessed at the same 3 time points: at baseline, 2 months later (mean: 58 days from baseline), and 4 months later (mean: 116 days from baseline).

The study protocol was approved by the human research ethics committee at Macquarie University (Approval Reference No. 5201400840).

2.2. Participants

Twenty-five people with acute LBP and 48 pain-free controls were enrolled in the study. People with LBP were recruited from primary care practices (medical, physiotherapy, and chiropractic clinics) and from the local community through advertisements in the Sydney metropolitan area from February 2015 to April 2016. Participants were enrolled consecutively if they: (1) were adults (≥18 years old); (2) had LBP for less than 3 weeks; and (3) had an average pain intensity during the last week of at least 3 on an 11-point numeric rating scale (NRS11, where 0 indicated no pain and 10 the worst pain imaginable). Acute LBP was defined as pain and discomfort localised below the costal margin and above the inferior gluteal folds with or without leg pain[56] lasting more than 24 hours but less than 3 weeks preceded by a pain-free period of at least 1 month.[7] Subjects were excluded if they had possible serious spinal pathology (ie, spinal fracture or malignancy) based on the presence of red flags,[8] previous back surgery, pregnancy, any pain condition that has lasted for more than 1 month over the last year affecting daily function and work ability, diabetes mellitus, diagnosed comorbid pain syndrome (eg, fibromyalgia, osteoarthritis, and irritable bowel syndrome), diagnosed neurological disease, unstable psychiatric disorder or psychosis, severe cognitive impairment (arising from head injury or other comorbidities), substance abuse problem in the past 24 months, long-term use of medications that may impact on cognitive or sensory function (eg, opiates intake greater than daily morphine equivalent 40 mg), and unable to read, write, and understand English. Participants were allowed to continue their usual care for LBP and medications and/or treatments received were recorded. All participants were provided with a copy of The Back Book (a resource recommended for use in primary care).[47] Pain-free controls were recruited from the local community through advertisements. The exclusion criteria for the control group were the same as the LBP group plus any pain at time of testing. All participants provided written informed consent.

2.3. Demographic, clinical, and psychological variables

Demographic information collected included sex, age, body mass index, race, and work status. People with LBP provided the following clinical information: LBP duration, pain intensity at time of testing, average pain intensity, and worst level of pain over the last week scored from 0 (no pain) to 10 (the worst possible pain) on an 11-point numeric rating scale (NRS11), level of function measured by the Functional Rating Index (FRI) scored from 0 (high functional level) to 40 (low functional level),[12] and disability level measured by the Roland-Morris Disability Questionnaire (RMDQ) scored from 0 (no disability) to 24 (high disability).[44]

All participants completed the following questionnaires: Depression, Anxiety and Stress Scale (DASS-21) scored from 0 (not at all) to 42 (extremely)[29] and Pain Catastrophizing Scale (PCS) scored from 0 (not at all) to 52 (all the time).[52] Participants with LBP also completed the Pain Self-Efficacy Questionnaire (PSEQ) scored from 0 (not at all confident) to 60 (completely confident),[36] the Short-Form McGill Pain Questionnaire to measure the sensory and emotional/affective dimensions of pain[34] and the PainDETECT questionnaire to screen for neuropathic features of LBP.[13] All questionnaires and clinical information (ie, pain intensity and functional/disability levels) were collected at all 3 assessments.

2.4. Quantitative sensory testing protocol

A rigorous protocol was followed for all QST testing and this has been reported in detail previously.[32] The protocol encompassed both static and dynamic QST (Ref. 55 for a review on QST measurement properties). The tests were conducted in the following order: cold pain threshold (CPT) and heat pain threshold (HPT), mechanical wind-up ratio (WUR), pressure pain threshold (PPT), two-point discrimination (TPD), and conditioned pain modulation (CPM). Cold pain threshold, HPT, WUR, PPT were performed according to the QST protocol of the German Research Network on Neuropathic Pain (DFNS).[45] Measurements were taken at 3 body sites: bilaterally at the back and at the dorsum of the left hand (except for PPT, which was tested at the thenar eminence). For people with LBP, the testing site at the back was in the area of maximal pain, nominated by participants and the level confirmed through palpation by an experienced physiotherapist. A random level at the back (from T12 to S1) was chosen for pain-free controls. Previous investigations have shown no significant differences in QST responses at different levels of the spine in healthy controls subjects.[40] A DFNS-certified researcher (AM) performed all tests blinded to participants' LBP or pain-free control status, and standardised instructions were used for all tests.

2.4.1. Thermal pain thresholds

A 30 × 30 mm ATS thermode (PATHWAY; Medoc, Ramat Yishai, Israel) was used to measure CPT and HPT. The baseline

temperature was set at 32°C and increased or decreased at a ramp rate of 1°C/s until participants pressed a button to indicate that their threshold had been reached. Three consecutive measurements were performed and used in the analysis.

2.4.2. Wind-up ratio

The perceived magnitude of pain from a single pinprick stimulus (256 mN; MRC Systems GmbH, Heidelberg, Germany) on a 101-point numeric rating scale (NRS101) was compared with that of a series of 10 pinprick stimuli of the same force to measure WUR. The repeated stimuli were delivered at a rate of 1/s within an area of 1 cm^2. Wind-up ratio was calculated as the mean pain rating from the 5 series of 10 repeated stimuli, divided by the mean pain rating from the 5 single stimuli.

2.4.3. Pressure pain threshold

A pressure algometer (FDK40; Wagner Instrument, Greenwich, CT) was used to measure PPT. The pressure was increased at a ramp rate of 50 kPa/s until participants verbally indicated that their threshold had been reached. Three consecutive measurements were performed and used in the analysis.

2.4.4. Two-point discrimination

A stainless steel calliper ruler (150 mm vernier calliper; Kincrome, Australia) was applied bilaterally and perpendicularly to the back at the level of L3 for all participants until the first blanching of the skin to measure TPD threshold. The distance between the 2 tips of the calliper was increased from 0 mm (ascending series) or decreased from 100 mm (descending series) by 2 mm until participants were able to perceive or no longer perceive 2 points, respectively. Two ascending and 2 descending measurements were performed and used in the analysis.

2.4.5. Conditioned pain modulation

2.4.5.1. Heat pain—test stimulus

A 30-second thermal heat contact (ATS thermode 30 × 30 mm, PATHWAY; Medoc) inducing a pain score of 60 on an NRS101 (*pain60*) was used as the test stimulus at the volar aspect of the nondominant forearm. A series of increasing or decreasing heat stimuli, starting at a temperature of 45°C, with 30 seconds' interstimulus interval, was used to individually identify the intensity of the heat stimulus to induce *pain60*.

2.4.5.2. Cold pressor test—conditioning stimulus

The immersion of the contralateral foot in a cold water bath maintained at a temperature of 10.5 ± 1°C for 2 minutes was used as conditioning stimulus (CS). The bath was made of a container divided into 2 by a perforated perspex sheet with one chamber filled with ice. The water was stirred to maintain the other chamber at a constant temperature which was continuously monitored by a digital thermometer. Participants could withdraw the foot from the cold bath if they were no longer able to tolerate the stimulus.

2.4.5.3. Conditioned pain modulation procedure

Participants were asked to rate the pain intensity of the CS at 30, 60, and 90 seconds from foot immersion on an NRS101 pain scale. The 30-second heat stimulus was applied again during the last 30 seconds of CS. The final CPM scores were calculated as the difference in test stimulus pain rating before and after the CS. A negative value was considered an inhibitory response and a positive value was considered a facilitatory response.

2.5. Data analysis

This study reports on pilot data to investigate longitudinal changes in somatosensory function in acute LBP. No previous studies were available on longitudinal analysis of QST variables in people with acute LBP and comparison of their responses with controls; therefore, an a priori calculation was not possible.

2.5.1. Statistical analysis

There is no standardised approach for measuring recovery from LBP.[26] In this exploratory study, people with LBP were classified into 2 groups based on their average pain intensity score over the previous week (NRS11) at 4 months: people reporting an NRS $\leq$ 1 were classified as recovered LBP and those reporting NRS $\geq$ 2 as persistent LBP, as reported previously.[17,33] Group differences in continuous variables (demographic and clinical) at baseline between recovered and persistent LBP and pain-free controls were compared using nonparametric one-way analysis of variance Kruskal–Wallis tests. Categorical variables were compared using χ^2 tests of association. For the QST variables tested at the back, it was decided a priori that only the values of the affected side of people reporting unilateral LBP would be used in the analysis, whereas for people with bilateral (or central) LBP and for pain-free controls, the values of the left and right sides would be averaged. Two QST variables (WUR and PPT) were highly skewed; so, a log transformation was used to avoid potential issues with modelling assumptions.

Linear mixed-effects models were used to model the change over time in QST variables and clinical and psychological variables (RMDQ, FRI, PSEQ, PCS, and DASS-21) between groups, with a random intercept used to control for the repeated measures for each individual within a time point and over time. Results were adjusted for sex differences.[19] Use of a random slope to control for an individual's change over time was also explored but did not improve the model fit and was not retained. Time was treated as categorical to model possible nonlinear changes and because it produced the best model fit compared with continuous time. The initial model looked for the presence of a significant interaction between time and groups. Because multiple testing was performed on related outcome variables, a Bonferroni type correction was used to adjust the significance level for the 11 QST outcome measures and the 5 clinical and psychological variables, and was set at $\alpha = 0.003$ (0.05/16). If the interaction was significant, the groups were compared at specific time points using Tukey pairwise multiple comparisons (corrected $\alpha = 0.05$). If there was no significant interaction, then the interaction term was removed and the main effects model was retained to determine whether there was a significant change over time after adjusting for groups or a significant difference between groups after adjusting for time. All available data were used in the analysis with the linear mixed-effects model providing unbiased mean effect estimates under the assumption that any missing values were missing at random.[23]

To further illustrate sensory profiles of the LBP groups across the 3 time points, QST data were z-transformed using values of pain-free controls as reference data using the following expression, *z*-scores: $(\text{mean}_{\text{single individual}} - \text{mean}_{\text{controls}})/\text{SD}_{\text{controls}}$.[45] For clarity of data presentation, the algebraic sign of *z*-scores for each

QST variables was adjusted so that z-values above 0 indicated a gain of function (ie, higher sensitivity compared with controls) and z-values below 0 indicated a loss of function (ie, reduced sensitivity compared with controls). These z-plots were presented only for QST variables from the DFNS protocol.

All the analyses were performed using R statistical software.

3. Results

3.1. Study participation

Figure 1 shows the flow chart of recruitment and screening of participants. A total of 246 individuals were screened for the study. Of 98 potentially eligible participants, 73 (25 people with LBP and 48 controls) provided consent to participate and were enrolled in the study. Two people with LBP and 4 pain-free controls withdrew after the baseline assessment; 1 control did not attend the first follow-up, and 1 person with LBP and 1 control did not attend the second follow-up session.

3.2. Participants

Twenty-two people with LBP completed the study and were therefore included in the analysis. Fifteen people were classified as recovered LBP (NRS $\leq$ 1 at 4 months) and 7 people were classified as persistent LBP (NRS $\geq$ 2 at 4 months). This classification was consistent with a significantly higher level of functional pain interference (assessed with the FRI) reported in the persistent LBP group compared with the recovered LBP group at 4 months ($P = 0.003$). Although recruitment targeted both primary care clinics and the community, the majority of LBP participants (88%) who were enrolled in the study were from the community and not actively seeking health care.

Demographic and clinical features at baseline are reported in **Table 1**. The recovered and the persistent LBP were assessed, on average, as early as 10 and 13 days from onset of LBP, respectively. There were no statistically significant differences between the LBP groups and the pain-free controls in demographic variables with the exception of body mass index, which was higher in the LBP groups ($P = 0.04$). Among the LBP groups, those with persistent LBP had significantly higher pain intensity (NRS11) compared with the recovered LBP group, at baseline ($P = 0.03$) and at 2 months ($P = 0.002$). Medication intake and treatments received during the 4-month period in both LBP groups are reported in **Table 2**.

3.3. Clinical and psychological variables

Longitudinal data for clinical and psychological variables are reported in **Table 3**. For disability levels measured by the RMDQ, no significant interaction between time and group was found. After adjusting for groups, the RMDQ scores significantly decreased over time ($P < 0.001$). For the level of functional pain interference measured by the FRI, a significant interaction between time and group was observed ($P < 0.001$). Post hoc

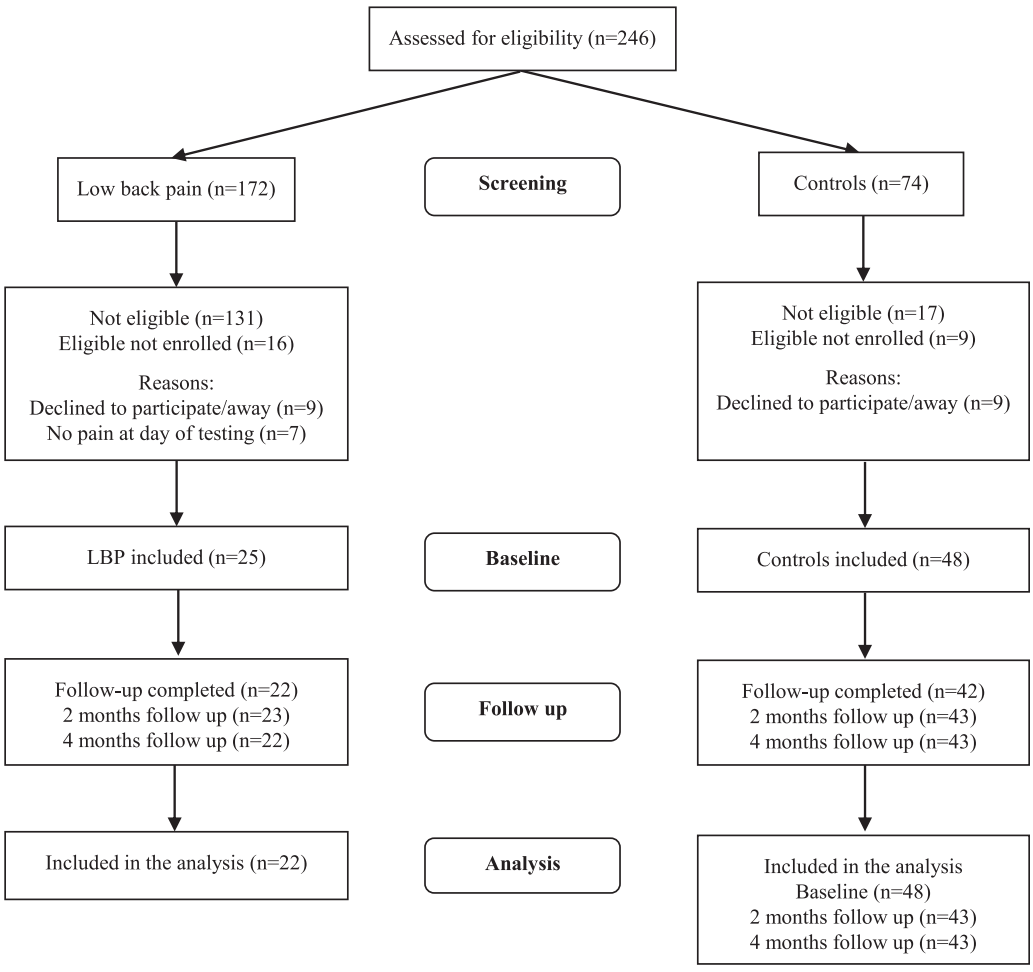

Figure 1. Screening and study participation flow diagram adapted from Consort Transparent Reporting of Trials.

Table 1

Demographic and clinical characteristics of recovered and persistent low back pain groups and pain-free controls at baseline.

	Recovered LBP, N = 15	Persistent LBP, N = 7	Pain-free controls, N = 48
Female, n (%)	8 (53.3)	3 (42.9)	25 (52.1)
Age, y	32.5 (13.2)	30.6 (11.9)	30.0 (9.8)
BMI, kg/m^2	24.8 (3.2)*	24.3 (2.7)*	23.2 (5.9)
Race, n (%)			
White/Caucasian	9 (60.0)	4 (57.1)	28 (58.3)
Asian	4 (26.7)	1 (14.3)	15 (31.3)
Other	2 (13.3)	2 (28.6)	5 (10.4)
Current work status, n (%)			
Student	9 (60.0)	3 (42.9)	29 (60.4)
Employed	6 (40.0)	3 (42.9)	17 (35.4)
Unemployed/retired	0 (0.0)	1 (14.3)	2 (4.2)
Pain duration, d	9.9 (6.4)	13.1 (3.2)	NA
Average pain intensity, NRS11	3.8 (1.4)*	5.4 (1.5)*	NA
Neuropathic screening, PainDETECT, n (%)			
Nociceptive (0–12 score)	15 (100)	5 (71.4)	NA
Unclear (13–18 score)	0 (0.0)	2 (28.6)	NA
Neuropathic (19–38 score)	0 (0.0)	0 (0.0)	NA
Pain descriptors, SF-MPQ			
Sensory (0–33)	7.7 (4.2)	10.9 (5.7)	NA
Affective/emotional (0–12)	1.0 (1.0)	2.7 (2.6)	NA

Data are presented as mean (SD) unless otherwise specified.

* $P < 0.05$.

BMI, body mass index; LBP, low back pain; NRS11, numeric rating scale (0–10); SF-MPQ, Short-Form McGill Pain Questionnaire.

tests showed that in both LBP groups, the level of functional pain interference significantly decreased from baseline to 2 months ($P < 0.004$) and in the recovered LBP group, further decreased from 2 to 4 months ($P = 0.008$). No differences in FRI scores were found at baseline between LBP groups ($P = 0.509$); however, the persistent LBP group had significantly higher levels of functional pain interference at 2 and 4 months compared with the recovered LBP ($P < 0.001$).

A significant interaction between time and group was observed for all 3 psychological variables assessed ($P < 0.001$). Post hoc tests showed that pain self-efficacy and pain catastrophising significantly improved (ie, PSEQ increased and PCS decreased) in both LBP groups from baseline to 2 months ($P < 0.001$) and, in the persistent LBP group, further improvement was shown from 2 to 4 months ($P = 0.043$). However, the persistent LBP group had significantly lower levels of pain self-efficacy and higher levels of pain catastrophising compared with the recovered LBP at all time points ($P < 0.047$) (**Fig. 2**). Depression, anxiety and stress (DASS-21) scores were low and in the normal range in all 3 groups. Post hoc tests showed that DASS-21 scores significantly decreased in recovered LBP from baseline to 2 and 4 months ($P < 0.004$) and in persistent from baseline to 2 months ($P = 0.011$). A significant difference was observed between the LBP groups and the pain-free controls at baseline ($P < 0.044$), but no significant differences were observed between groups at 2 and 4 months.

3.4. Quantitative sensory testing

Longitudinal data for QST variables at 3 time points and linear mixed-effect model analyses are reported in **Table 4**.

3.4.1. Thermal pain threshold

There was a significant interaction between time and group for CPT at the hand ($P < 0.001$) (**Table 4**). Post hoc tests showed that in the recovered LBP group, CPT at the hand significantly increased from baseline to 2 months ($P < 0.001$) and normalised by 4 months, as also illustrated in the *z*-score plot (**Fig. 3**), whereas in the persistent LBP group and in the pain-free controls, CPT at the hand remained unchanged over the 4 months. For

Table 2

Use of medications and treatments in the 24 hours before QST assessment in people with low back pain at 3 time points.

	Recovered LBP, N = 15			Persistent LBP, N = 7		
	Baseline	2 mo	4 mo	Baseline	2 mo	4 mo
Participant taking medications, n (%)	4 (26.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)
Medication type	Simple analgesic (acetaminophen, NSAIDs)	NA	NA	NA	Simple analgesic (NSAIDs)	NA
Participant receiving treatments, n (%)	5 (33.3)	4 (26.7)	2 (13.3)	3 (43.0)	2 (28.6)	0 (0.0)
Treatment type	Physiotherapy, chiropractic, massage	Physiotherapy, chiropractic, massage	Physiotherapy, chiropractic	Physiotherapy	Physiotherapy	NA

LBP, low back pain; NA, not applicable; NSAIDs, nonsteroidal anti-inflammatory drug.

Table 3

Clinical and psychological variables in people with low back pain at 3 time points.

	Recovered LBP, N = 15			Persistent LBP, N = 7		
	Baseline	2 mo	4 mo	Baseline	2 mo	4 mo
Clinical variables						
Pain intensity (average previous week), NRS11	3.8 (1.4)	1.3 (1.3)	0.3 (0.6)	5.4 (1.5)	3.3 (0.8)	3.3 (1.4)
Disability, RMDQ (0–24)	4.9 (1.1)	2.2 (0.8)	1.1 (0.3)	6.7 (2.0)	3.1 (1.0)	2.4 (1.0)
Function, FRI (0–40)*	13.3 (1.7)	6.0 (1.7)	2.9 (0.8)	14.7 (2.2)	11.4 (2.0)	10.9 (1.4)
Psychological variables						
Pain self-efficacy, PSEQ (0–60)*	52.3 (3.0)	58.1 (1.1)	59.1 (0.4)	32.2 (5.8)	45.0 (6.8)	48.7 (2.4)
Pain catastrophizing, PCS (0–52)*	7.0 (2.0)	3.7 (0.7)	2.5 (0.8)	17.0 (2.8)	11.9 (3.1)	6.9 (1.8)
DASS-21 total score (0–126)*	19.3 (3.7)	13.5 (3.5)	9.8 (2.5)	23.1 (7.6)	18.3 (7.7)	19.7 (8.9)
Depression (0–42)	5.3 (1.8)	3.2 (1.1)	2.9 (1.2)	5.7 (2.3)	4.3 (2.4)	7.1 (4.0)
Anxiety (0–42)	3.9 (0.9)	3.2 (1.0)	1.7 (0.5)	7.7 (2.8)	6.6 (2.5)	4.6 (1.9)
Stress (0–42)	10.1 (1.9)	7.1 (1.8)	4.3 (1.5)	9.7 (3.1)	7.4 (3.1)	8.0 (3.1)

Values are reported as mean (SE).

* Significant interaction time × group: $P < 0.001$.

DASS-21, Depression, Anxiety and Stress Scale; FRI, Functional Rating Index; LBP, low back pain; NRS, numeric rating scale; PCS, Pain Catastrophizing Scale; PSEQ, Pain Self-Efficacy Questionnaire; RMDQ, Roland-Morris Disability Questionnaire.

CPT at the back and HPT at both sites, no significant interactions between time and group were observed, and no significant main effects for time and for group were observed after removing the interaction term.

3.4.2. Wind-up ratio

No significant interaction between time and group was found for WUR at both sites ($P > 0.05$). No significant main effects for time and for group were observed ($P > 0.02$) after removing the interaction term. The *z*-score plots (**Fig. 3**) illustrate that compared with the recovered LBP group, the persistent LBP group shows a trend towards an increase in WUR at the hand between baseline and 2 months, with a further increase at 4 months, then reaching a difference of 2 SDs from controls.

3.4.3. Pressure pain threshold

There was a significant interaction between time and group for PPT at the hand ($P = 0.003$) and at the back ($P < 0.001$). Post hoc tests showed a significant decrease in PPT at both sites in pain-free controls from baseline to 2 months ($P < 0.014$) and in the persistent LBP group from 2 to 4 months ($P = 0.013$), whereas in the recovered LBP group PPT remained unchanged ($P > 0.05$). No significant differences were observed between groups at any time points for PPT at the hand ($P > 0.05$). For PPT at the back, the persistent LBP group had significantly lower PPT compared with the recovered LBP group at 4 months ($P < 0.001$) as illustrated in the *z*-score plots (**Fig. 3**).

3.4.4. Two-point discrimination threshold

There was no significant interaction between time and group for TPD ($P = 0.088$). A significant main effect for time was observed after removing the interaction term. After adjusting for groups, TPD showed a significant decrease from baseline to 4 months ($P < 0.001$).

3.4.5. Cold pressor test

There was no significant interaction between time and group for the cold pressor test ($P = 0.017$). No significant main effects for time and for group were observed ($P > 0.05$) after removing the interaction term.

3.4.6. Conditioned pain modulation

There was no significant interaction between time and group for the CPM response ($P = 0.251$). No significant main effects for time and for group were observed ($P > 0.05$) after removing the interaction term (**Fig. 4**).

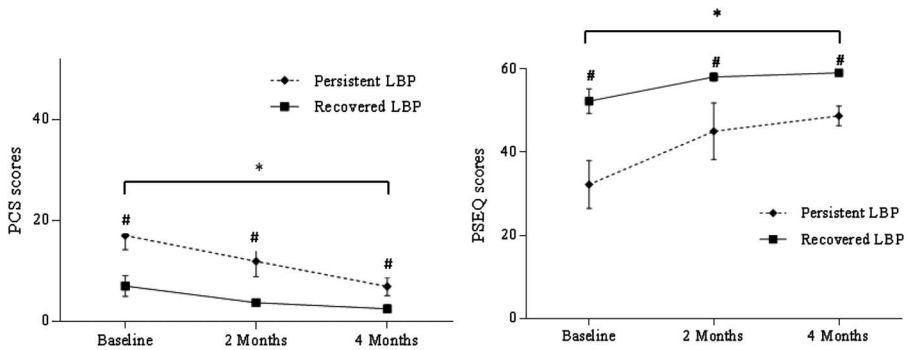

Figure 2. Mean (SE) pain catastrophising (PCS) and pain self efficacy (PSEQ) scores in persistent and recovered LBP groups at 3 time points. #Significant difference between groups $P < 0.05$; *Significant change over time $P < 0.001$. LBP, low back pain; PCS, Pain Catastrophizing Scale; PSEQ, Pain Self-Efficacy Questionnaire.

Table 4

Descriptive statistics of QST variables of recovered and persistent low back pain groups and pain-free controls at 3 time points and linear mixed effect model analyses.

	Recovered LBP			Persistent LBP			Pain-free controls			Interaction time × group	Main effect†, *P*	
	Baseline	2 mo	4 mo	Baseline	2 mo	4 mo	Baseline	2 mo	4 mo	*P*	Time	Group
CPT, °C												
Hand	8.1 (2.0)	13.5 (2.0)	11.6 (2.0)	12.5 (3.0)	13.1 (3.0)	14.7 (3.0)	10.9 (1.2)	11.3 (1.2)	11.2 (1.2)	<0.001‡		
Back	15.7 (2.6)	13.6 (2.6)	13.3 (2.6)	15.8 (3.8)	17.2 (3.8)	16.8 (3.8)	11.4 (1.6)	11.6 (1.6)	11.7 (1.6)	0.126	0.985	0.304
HPT, °C												
Hand	43.6 (0.8)	42.1 (0.8)	43.6 (0.8)	42.0 (1.1)	42.6 (1.1)	42.4 (1.1)	43.3 (0.4)	43.1 (0.4)	43.6 (0.4)	0.731	0.218	0.506
Back	42.4 (0.8)	42.5 (0.8)	43.1 (0.8)	42.0 (1.1)	42.0 (1.1)	41.6 (1.1)	42.7 (0.5)	42.3 (0.5)	42.7 (0.5)	0.215	0.038	0.715
WUR*, ratio												
Hand	2.1 (0.4)	2.0 (0.4)	2.3 (0.6)	2.1 (0.6)	3.6 (1.3)	4.2 (1.6)	1.7 (0.1)	1.9 (0.2)	1.9 (0.1)	0.155	0.023	0.072
Back	2.6 (0.4)	2.4 (0.4)	2.3 (0.4)	2.7 (0.7)	2.4 (0.7)	3.9 (0.7)	2.2 (0.3)	2.3 (0.3)	2.1 (0.3)	0.371	0.954	0.671
PPT*, kPa												
Hand	451 (39)	464 (39)	485 (39)	373 (57)	399 (57)	345 (57)	409 (22)	383 (22)	384 (22)	0.003‡		
Back	604 (46)	624 (46)	645 (46)	441 (66)	436 (66)	374 (66)	505 (26)	452 (26)	457 (26)	<0.001‡		
TPD, mm Back	62.3 (3.0)	60.8 (3.0)	59.1 (3.0)	66.0 (4.3)	59.7 (4.3)	59.0 (4.3)	61.5 (1.7)	60.1 (1.7)	58.8 (1.7)	0.088	<0.001‡	0.949
Cold pressor test, NRS101	54.9 (6.0)	53.8 (6.0)	49.3 (6.0)	71.2 (8.7)	63.3 (8.7)	63.8 (8.8)	55.7 (3.4)	57.9 (3.4)	56.7 (3.4)	0.017	0.280	0.423
CPM heat, NRS101	−16.3 (3.7)	−16.0 (3.7)	−17.5 (3.7)	−21.8 (5.5)	−26.4 (5.5)	−14.2 (5.8)	−20.0 (2.1)	−15.8 (2.2)	−13.4 (2.3)	0.251	0.276	0.348

Values are reported as mean (SE) unless otherwise specified.

* Analysis performed on log-transformed variables.

† *P* values of main effects after removing the interaction term.

‡ Bonferroni-corrected significance level: $\alpha < 0.003$.

CPM, conditioned pain modulation; CPT, cold pain threshold; HPT, heat pain threshold; LBP, low back pain; NRS, numeric rating scale; PPT, pressure pain threshold; QST, quantitative sensory testing; TPD, two-point discrimination; WUR, wind-up ratio.

4. Discussion

This exploratory study is the first to report the time course of somatosensory function in an inception cohort of acute LBP followed up until 4 months. A comprehensive QST protocol encompassing static and dynamic tests was used, and longitudinal changes in pain-related psychological factors were concurrently evaluated.

The main finding of this study was that an increase in mechanical pain sensitivity was observed in the persistent LBP group, suggesting potential underlying changes in the nervous system sensitivity occurring in the subacute stage. Specifically, an increase in pressure pain sensitivity was seen between 2 and 4 months; and an earlier trend towards increased temporal summation was identified between baseline and 2 months, and 2 to 4 months, at which point it exceeded 2 SDs beyond the pain-free control reference value (although not reaching statistical significance). In addition to the temporal changes in mechanical sensitivity in the persistent LBP group, a gain in cold pain sensation was observed in the recovered LBP group from

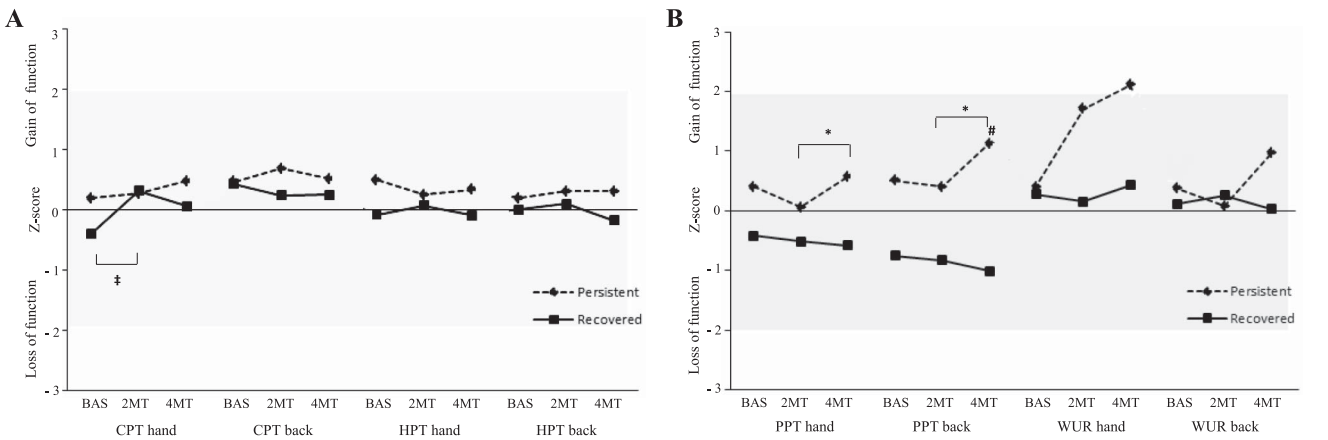

Figure 3. Sensory profiles of LBP groups for QST variables of the DFNS protocol at 3 time points. (A) Thermal QST variables and (B) Mechanical QST variables. Shaded area represents 95% confidence interval of reference values from controls. ‡Significant change over time in recovered LBP, $P < 0.001$; *Significant change over time in persistent LBP, $P < 0.001$; #Significant difference between LBP groups, $P < 0.001$. 2 MT, 2 months; 4 MT, 4 months; BAS, baseline; CPT, cold pain threshold; HPT, heat pain threshold; LBP, low back pain; PPT, pressure pain threshold; QST, quantitative sensory testing; WUR, wind-up ratio.

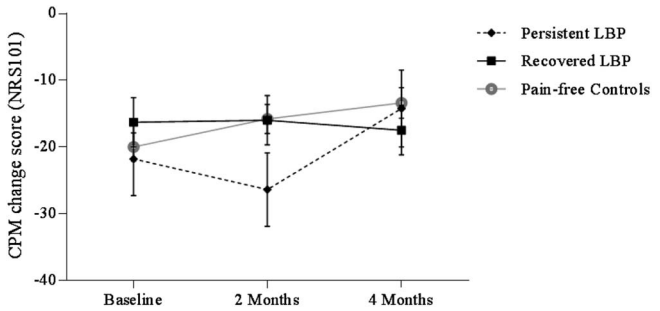

Figure 4. Mean (SE) CPM scores in persistent and recovered LBP groups and pain-free controls at 3 time points. CPM, conditioned pain modulation; LBP, low back pain; NRS, numeric rating scale.

baseline to 2 months, which normalised from hypoesthetic to the pain-free values by 2 months.

4.1. Pressure pain testing

At baseline, pressure pain tests were similar between groups, which aligns with results from a previous prospective study in acute LBP[48] and other studies that reported no differences in PPT between acute LBP and healthy controls.[38,39] When the *z*-score plots (**Fig. 3B**) are examined, it is evident that the pressure pain sensitivity of the 2 LBP groups diverges, with the persistent LBP group significantly increasing over time (particularly at the back). By 4 months, these differences between persistent and recovered groups are significant. A similar increase in pressure pain sensitivity at the back has been reported in cross-sectional studies in subacute LBP.[10,11] Enhanced responses to localised pressure pain testing may reflect underlying sensitisation of primary afferent nociceptors through the release of neuromediators such as neurotrophins and cytokines[18] as well as the recruitment of silent nociceptors after persisting stimulation.[54] Reduced PPT has been associated with functional disturbances in lumbar spine muscle activity in people with LBP,[9] which may contribute to ongoing pain.

A significant decrease in PPT was also detected at the remote site at the hand in the persistent LBP group, although this was within 1 SD of the healthy control values and the differences between the LBP groups were not statistically significant. It is possible that widespread changes in pressure pain sensitivity become more evident in people with longer LBP duration[1,5,15,16,37] whereby increases in central nervous system excitability are more likely to have been established. However, it has been recently shown that generalised changes in pressure sensitivity do not occur uniformly in chronic LBP, but are selectively associated with LBP subgroups[14,43,53] which, interestingly, report more disturbed clinical and psychological profiles.

Nonetheless, it is important to note the tendency for PPT to significantly decrease over time (ie, control values reduce from baseline to 2 months, $P < 0.02$). This phenomenon of a systematic decrease in PPT in pain-free controls has previously been reported, particularly between the first and the second measurements.[24] This emphasises the importance of longitudinal comparative analyses with pain-free controls to identify potential clinically meaningful differences.

4.2. Temporal summation

The increase in temporal summation (WUR) at the hand in the persistent LBP group during the 4-month period is noteworthy, given that it was 2 SDs higher than the mean control value. The failure to reach statistical significance may be due to the relatively large variance, particularly in the persistent LBP group.

To the best of our knowledge, only one published study has reported on a range of QST variables in acute LBP (≤4 weeks from onset) using a prospective study design[48] with QST performed at baseline. These authors reported that generalised hyposensitivity to thermal (non-noxious) stimuli, as well as enhanced temporal summation at the hand (but not at the back) measured in acute LBP, differentiated people who had not recovered at 6 months from those who had. Unlike in the study by Starkweather et al.,[48] we did not find any differences in temporal summation (WUR) between the LBP groups at baseline; however, we identified a trend towards an increase in WUR amplitude in the persistent LBP group at the subacute stage. Two other cross-sectional studies have shown early enhancement of temporal summation in people with acute LBP (<4 weeks duration) compared with healthy controls,[31,49] demonstrating that, in some subgroups of people with LBP, central hyperexcitability may be detected in the very early stages of LBP.

4.3. Thermal pain testing

Among the thermal pain tests (cold and heat) including the cold pressor test, only the CPT showed a differential change over time (**Fig. 3A**) with CPT at the hand significantly increasing (return to normal) in the recovered LBP group from baseline to 2 months. However, although this change was statistically significant, the magnitude of CPT change (within 1 SD of pain-free controls) is unlikely to be clinically meaningful.

4.4. Tactile acuity

This study provides the first data on tactile acuity in acute LBP as well as serial measures over time, until the onset of chronic LBP. The results showed no differences in TPD threshold between the 2 LBP groups and the controls, suggesting that in this cohort tactile acuity was not impaired in the acute, subacute, or early chronic LBP phases. However, there was a small, but significant decrease in TPD threshold over time, indicating an improvement in tactile acuity, although these changes were within the measurement error range.[4] The significance of this change is unclear, although a learning effect may have contributed. A previous systematic review has demonstrated a relatively consistent presence of altered tactile acuity in chronic LBP, particularly when measured at the area of greatest pain.[3] Studies included in the review investigated people with longstanding chronic LBP (eg, from 30 to 108 months) and may reflect functional changes that develop over longer periods, compared with the maximum 4-month duration of LBP in our study. The lack of changes in tactile acuity in our study may also be due to the fact that the measurement was performed at a standardised site at the back (L3), rather than the most painful site, due to the need to maintain blinding of assessor.

4.5. Conditioned pain modulation

Our result that those with acute LBP had a significant CPM effect that did not differ from pain-free controls adds to the limited literature on this topic. Two previous reports of CPM in acute LBP (<6 weeks' duration) also found no significant differences in CPM effect from controls.[35,59] It has been suggested that ongoing persistent pain may impair the balance in descending spinal cord modulation reducing CPM inhibition and/or increasing facilitation.[41] However, the literature reporting changes in CPM in

chronic LBP is sparse and somewhat conflicting with some studies reporting altered pain inhibition[5,42] and others showing no difference in CPM effect[25,35,58] compared with controls. In other chronic pain conditions such a fibromyalgia or headache, CPM dysfunction has been more consistently documented.[28] The current longitudinal analysis did not find changes in descending pain inhibition with LBP persistence, at least in the early months in this study sample. However, in light of the methodological variability of CPM testing,[41] it is also not possible to exclude that the test was unable to detect changes if they did exist.

4.6. Psychological factors

Of interest was that the only measures that differentiated the persistent from recovered LBP groups at baseline were psychological measures of self-efficacy (PSEQ) and pain catastrophising (PCS). Clinically significant lower self-efficacy scores were noted at baseline for the persistent LBP compared with the recovered LBP group (baseline PSEQ [SD] = 32.2 [5.8] mild impairment and 52.3 [3.0] minimal impairment, respectively [Electronic Persistent Pain Outcomes Collaboration, https://ahsri.uow.edu.au/eppoc/resources/index.html]). This would suggest that even mild PSEQ impairment may be noteworthy at baseline in acute LBP.

Psychological distress and pain-related cognitions both reduced over time in both LBP groups, although significant differences between the 2 groups were maintained at all time points. The improvements in pain-related psychological variables, particularly in the persistent LBP group align with the concurrent reduction of pain severity and disability levels (measured by RMDQ) observed at all 3 time points assessed (**Table 3**). This may reflect the fact that our sample was primarily community-based with relatively low initial levels of psychological distress and inherently greater capacity to cope with, and adapt to, pain over time.

4.7. Strengths and limitations

The strengths of this study are that established protocols were used for multimodal QST testing by a single DFNS-trained assessor; that we were able to assemble and follow-up an inception cohort of people at as early as 3 weeks from onset of LBP; and that we reduced bias by blinding the investigator to participants' condition.

The following limitations of the study are acknowledged: first, the sample size was relatively small; so, we may have been underpowered to detect statistically significant differences between groups at different time points, particularly for some QST measures. Nonetheless, the results from this novel time series provide insights into longitudinal changes, which will be valuable for the design and conduct of future research. Second, although the recruitment strategy aimed to target both primary care clinics and the community, most of the people were recruited from the community. Therefore, these results are most relevant to people not seeking care for LBP.

5. Conclusions

The results of this exploratory study suggest that to understand the role of somatosensory changes in the development of acute to persistent LBP, mechanical pain tests (ie, PPT and temporal summation) are variables of potential significance to further investigate. The fact that higher levels of pain-related cognitions at baseline distinguish persistent LBP from the recovered LBP groups emphasizes the importance of concurrent evaluation of psychological contributors, in particular confidence to manage pain (self-efficacy) and pain-related worries (catastrophizing). In future studies of samples seeking care for LBP, psychological factors such as depression and anxiety (which were not observed at clinical levels in this community sample) would also be important to assess. Although changes in endogenous pain modulation continue to be of great interest, efforts need to first focus on the standardisation of a CPM protocol to improve the reliability and interpretability of the test.

Disclosures

The authors have no conflict of interest to declare.

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