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ORIGINAL ARTICLE

Pain and Disability in Low Back Pain Can be Reduced Despite No Significant Improvements in Mechanistic Pain Biomarkers

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Objective: Altered balance in nociception in response to noxious stimuli is commonly reported in chronic low back pain (LBP). However, it is unclear whether an improvement in the clinical presentation is contingent on a reduction in pain sensitivity. This study investigated whether the quantitative sensory testing (QST) profile changes in people undergoing rehabilitation for LBP.

Design: A prospective, observational case-control study.

Methods: Forty males and females, 18 to 40 years' old (20 with LBP) participated in 2 sessions. QST was performed at baseline and after discharge from rehabilitation (LBP) or after 3 to 8 weeks (controls). The QST battery consisted of determining pressure-pain thresholds at the low back and shoulder, temporal summation of pain and conditioned pain modulation. Questionnaire data was used to determine pain (Numeric Rating Scale [NRS]), disability (Roland-Morris Questionnaire [RMQ]), Fear Avoidance Beliefs (FABQ) and The Örebro Musculoskeletal Pain Screening Questionnaire (ÖMPSQ) at baseline and discharge. The treatment effect was determined by calculating the Cohen *d*.

Results: No significant group×time interactions or main factor effect was found for any of the QST measures. The LBP group reported a significant reduction in NRS ($P < 0.0002$, $d = 1.23$), RMQ ($P < 0.0001$, $d = 1.58$), FABQ ($P < 0.001$, $d = 0.87$), and in the ÖMPSQ ($P < 0.00001$, $d = 1.44$).

Conclusions: The results indicate that an improvement of clinical LBP is not contingent upon changes in the pain sensory profile. The value of screening pain sensitivity in LBP patients in primary care, needs to be investigated further, due to the patient population heterogeneity and the sensitivity of assessment methods.

Key Words: conditioned pain modulation, pressure pain threshold, temporal summation, rehabilitation, pain questionnaires

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Low back pain (LBP) is common in modern day society[1] where in the majority of cases, the symptoms cannot be related to any specific underlying cause and are therefore described as nonspecific LBP.[2] One common feature in chronic nonspecific LBP is that the mechanistic pain biomarkers, such as mechanical and thermal pain sensitivity, seem to be facilitated when compared with healthy, asymptomatic controls.[3–5] Interestingly, this is also seen in other nonspecific musculoskeletal pain conditions, such as neck pain,[6,7] shoulder pain,[8] and tendinopathy.[9] Collectively, those findings suggest that increased pain sensitivity is part of a transition from acute pain, toward ongoing symptoms and that recovery may perhaps be contingent on the normalization of the pain sensory profile.

Pain sensitivity can be assessed in different ways, e.g. by assessing pressure pain thresholds (PPTs), as well as general pain detection and tolerance thresholds.[10] Moreover, it is possible to determine the function of pronociceptive and anti-nociceptive mechanisms by way of assessing the response to repeated painful stimuli (temporal summation of pain, TSP) and conditioned pain modulation.[11] Previously, it has been demonstrated that by surgically removing or reducing nociceptive activity in peripheral structures, positive changes of the mechanistic pain biomarkers are found (eg, normalization of widespread hypersensitivity, TSP, and conditioned pain modulation).[12] An important factor is, however, that the pain hypersensitivity (extent and distribution) seems to increase with longer duration and higher pain intensity in the area of the original painful area.[10] Removing the locus of nociceptive activity in chronic LBP, may be challenging, considering the nonspecific nature of the condition. Moreover, such an approach would not account for the multidimensional nature of chronic pain where, for example, emotional, psychological, and social aspects also play an important role in the pathogenesis.[13]

It is recommended that interventions, aimed at reducing pain and improving function in chronic LBP, are patient-centered and focus on advice, exercise and addressing the patient's thought processes, related to the pain condition.[14] This can be puzzling, as the management

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strategies need to be individually tailored to the patient, and address factors that may be difficult to quantify such as unhelpful thoughts and beliefs, as well as identifying movement patterns and postures that aggravate pain. A part of the management will then often consist of functionally challenging and individually tailored activities. It has been demonstrated that implementing such a multifaceted intervention, has a superior effect when compared to standard care in the short-term and long-term.[15]

The aim of the study was to evaluate how and if the mechanistic pain profile changes in relation to rehabilitation. The overall hypotheses were that (1) increased pain sensitivity seen in participants with chronic LBP would be reduced/reversed with successful rehabilitation, as measured in reduced pain and improved function. Moreover, (2) an association between the change in pain sensitivity and changes in pain and function was expected.

METHODS

Participants

Individuals, in the age range 18 to 40 years, were recruited through social media, as well as through fliers at the university campus. People, with a current, chronic, non-specific LBP, lasting more than 12 weeks, were included.[16] Previous history of treatment for the pain condition was not an exclusion criterion but any previous treatment and effect hereof was noted at baseline. A maximum length of 60 months (5 y) with pain was set to limit the potential spread in pain duration, which may increase the sensitivity of mechanistic pain biomarkers.[17] Healthy people, whose age and sex matched to the LBP group, were recruited as controls. Participants were recruited into the LBP group if their pain was limited to the area between the posterior superior iliac spine and the thoracolumbal junction. Participants were excluded from the study if their pain was caused by a confirmed, specific pathology (eg, spinal stenosis, fracture or cancer), had signs of nerve root compression causing radicular pain, had multiple pain sites in areas unrelated to the back (eg, chronic headache, shoulder or knee pain), any previous spinal surgery, were pregnant or had any systemic diseases. Any habitual use of over-the-counter pain medication for the participants in the LBP group was noted at inclusion, but not used as an exclusion criterion. The healthy control participants were recruited on the premise that they were free from any pain, specific to the back and/or in general, and had no history of any on-going pain defined as pain lasting more than 3 months. For both groups, participants were only included if they were naïve to the testing procedure.

The group size was estimated with Gpower 3.1.9.4 (Kiel University, Germany), by using data from Blumenstiel et al,[5] who achieved an effect size of 0.81 when comparing low back pressure-pain thresholds (PPTs) between chronic back pain patients and controls. To acquire the desired power of 0.8 and an α level of 0.05, 20 people were required for each group (LBP and control). To account for potential dropouts and missing data, additional 5 individuals were recruited for each group. Participants received a written and oral description of the study, before giving their informed consent. The protocol was registered on clinicaltrials.gov (NCT03748849), conducted in accordance with the Helsinki Declaration and approved by the regional Ethics Committee (N-20150048).

Experimental Protocol

The study was single blinded, and had a prospective, case-control design. All participants went through 2 experimental sessions, where the pressure pain sensitivity, TSP, and conditioning pain modulation (CPM) were assessed. The assessor (E.D.M.) was blinded to group allocation. For the LBP group, sessions were at baseline and after discharge from treatment. For the control group, the period between the 2 sessions was randomized with a roll of a dice (3 to 8 wk) to maintain the blinding of the assessor. First, the sensitivity to pressure was assessed at 3 body sites, by PPTs. Next, cuff pressure algometry was used to determine cuff pressure pain sensitivity, TSP, and to assess the effectiveness of endogenous pain inhibition by a CPM paradigm. The study's hypotheses were not revealed to any of the participants until all data had been collected.

Following measurements at baseline and at discharge, participants were asked to fill out questionnaires regarding the levels of disability, fear avoidance behavior, and psychosocial aspects related to pain (LBP group only). These were completed at baseline and then again at discharge from the study. Furthermore, all participants were sent an automated text message once a week, where they were asked to indicate their average back pain intensity for that week using a numeric rating scale (NRS, 0 to 10, with 0 defining no pain and 10 indicated worst pain imaginable). This was done for monitoring purposes (LBP group) and for screening purposes (control group) to ensure that participants in the control group did not develop LBP after inclusion. All questionnaire data and text messages were automatically sent to the participants once they were enrolled in the study using SmartTrial (SmartTrial, Version 2.6, Medei ApS, Aalborg, Denmark). In case a participant did not respond to these messages, computer generated reminders were sent until the questionnaires had been completed. If the participant did not respond to the reminders, the clinicians could contact the respective individual and ask him/her to fill out the questionnaires. For blinding purposes, all questionnaire data and text messages were kept concealed to the research group until all participants in both groups had been through the 2 experimental sessions.

Questionnaire Data

The Fear Avoidance Beliefs Questionnaire (FABQ) aims to assess how beliefs about how physical activity and work may affect symptoms amongst LBP patient.[18] The questionnaire consists of 16 items, each with the option of scoring between 0 and 6 where higher scores will indicate greater levels of fear and avoidance beliefs.

The Roland Morris Disability Questionnaire (RMDQ) is designed to assess self-perceived physical disability related to LBP.[19] The questionnaire consists of 24 statements relating to functional limitations the respondent has on the day of filling out the questionnaire. It works by binary responses as the respondent marks only the statements that apply. The total number of marked statements can range from 0 to 24, where greater levels of disability are reflected by higher scores.

The Örebro Musculoskeletal Pain Screening Questionnaire (ÖMPSQ) consists of 20 questions answered by providing a Likert scale score (0 to 10). The questionnaire has been used to screen for the risk of future sick-leave as a result of an acute soft tissue injury.[20,21] A score over 130 has been shown to predict for a high-risk of future disability,

while moderate to low risk is reflected in scores 105 to 130 and below 105, respectively.[22]

Pressure Pain Sensitivity

Assessment of PPTs was done at 5 sites on the back and marked for multiple assessments: (1) 2 cm lateral to the spinous process of L5 (bilateral), (2) 2 cm lateral to the spinous process of L1 (bilateral), and (3) at the infraspinatus muscle (dominant side). The test side was the pain dominant side in CLBP group. In case both sides were affected or unaffected (control group), the dominant side was defined as the test side. The infraspinatus site was identified by locating the intersection between a line lying perpendicular from the medial border of the scapula and a line connecting the middle part of the spine of scapula with the inferior angle of scapula. A handheld pressure algometer (Algometer, Somedic, Sweden) with a 1 cm^2 probe (covered by a disposable latex sheath) was used to apply increasing pressure with a ramp of 30 kPa/s. The PPT was defined to each participant as the moment where the pressure first became painful. Here, the participant pressed a button that stopped the pressure stimulation. Three individual PPTs were acquired at each site with a minimum 30 seconds between assessments. The average of measurements on each side (low back sites) as well as across repetitions at the infraspinatus site, were extracted for statistical analysis.

Cuff Pain Detection and Tolerance Thresholds

A cuff algometer (NociTech, Aalborg, Denmark and Aalborg University, Aalborg, Denmark) was used to assess the cuff-pressure pain sensitivity.[11,23,24] A double-chamber cuff (VBM, Sulz, Germany) was placed on the lower leg, with the upper rim of the cuff level with the upper border of the tibialis anterior muscle. Firstly, the cuff-pressure pain sensitivity was determined on the test leg and subsequently on the contralateral leg, using 2 separate pressure cuffs. During the assessment of cuff-pressure pain sensitivity, both chambers of the cuff were inflated gradually at a rate of 1 kPa/s. Participants were instructed to continuously rate the pressure-evoked pain intensity until it became intolerable, at which point they were instructed to press a stop button. This stopped the stimulation and the cuff was deflated immediately. The participant used an electronic visual analogue scale (VAS) to indicate the intensity of pressure-induced pain where 0 cm was defined as "no pain" and 10 cm was anchored with "maximal pain." The pain detection threshold (PDT) was defined as the cuff pressure where the VAS score exceeded 1 cm the first time. The pain tolerance threshold (PTT) was the cuff pressure, where the participant stopped cuff inflation. The PDT and PTT were recorded twice for each leg and the average value used for further analysis. In case the PTT was not reached before reaching the safety limit (100 kPa) of the cuff algometer, the PTT was defined as 100 kPa. The values from the test leg were used to evaluate group differences, changes within session (CPM response) and changes between sessions.

TSP and CPM

TSP was assessed by applying a series of 1-seconf long cuff pressure stimuli with a 1-second break in between (10 stimuli in total) to the test leg. Between each stimulus, a pressure of 5 kPa was kept to maintain cuff position. For standardizing the target stimulation intensity for the TSP paradigm, each individual's PTT was used. The participant was asked to rate the pain intensity from each stimuli during the repeated stimulations, using the electronic VAS scale, without returning to 0 between stimulations. For data analysis, the VAS data was normalized to the first stimulus and then the ratio of mean VAS score of the first 4 (VAS-I) and the last 3 (VAS-III) stimuli was calculated as the temporal summation index (TSP-effect).[11] The repeated stimulation protocol was administered once on the test leg only.

For assessment of the CPM, a tonic painful stimulus was applied by inflating the double cuff on the nontest leg to 80% of PTT for that leg, in the respective sessions.[25] Tonic pressure was maintained while the PDT and PTT were determined on the test leg. The CPM-effect was determined by subtracting unconditioned PDT and PTT values from the PDT and PTT recorded during conditioning in the same session and comparing between groups.

The Rehabilitation Program

Following baseline assessments, participants in the LBP group entered the rehabilitation program under the guidance of 2 clinicians (T.S.P. or S.W.M.C.). Both clinicians had postgraduate training in musculoskeletal physiotherapy and several years' experience with managing musculoskeletal pain within the primary sector. The clinicians were blinded to the outcome of the baseline experimental session and questionnaire data. All rehabilitation sessions were free of charge and lasted between 45 and 60 minutes. In the beginning, the clinical sessions were held weekly. Later in the program, the intervals between sessions increased depending on how the participants responded to the intervention. The intervention followed contemporary guidelines.[26,27] It was individualized and pragmatic, following the subjective and objective assessment. The findings were explained to the participant and plan for the program was designed, together with the participant. The program plan consisted of exercises, selected on the basis of the functional limitations and personal preferences identified during the assessment. These could be, for example, exercises in bending forwards, functional tasks, such as lifting, or ways of altering sitting positions, in order to reduce perceived pain. Attention was paid to the participants' thoughts and beliefs related to performing the task, as these may otherwise limit the effect of the intervention.[28,29] Although most focus was on individualized exercises, manual therapy was provided if it was considered relevant and was delivered with a contemporary explanation of its effect.[30,31] The relevance and progression of the chosen intervention was re-evaluated and modified during each follow-up session as needed. The program was stopped when (1) the participant had recovered, (2) no more recovery was expected by the clinician, or (3) when the participant wanted to stop. The decision to stop was always made in consensus between the clinician and the patient. In a previous study, using a similar approach,[15] participants got 8 sessions during the rehabilitation period. In this study, however, no upper limit was set for number of consultations as long as further improvements were to be expected by continuing.

Statistics

Parametric data are presented as mean and SD and nonparametric data as median and interquartile range [IQR, 0.25 to 0.75]. Normality of data was assessed by the Shapiro-Wilk test.

The questionnaire data (NRS, RMDQ, Örebro, and FABQ) were only administered to the LBP group. Paired

samples tests (*t* test or Wilcoxon, pending normality) were used to compare baseline and discharge scores. In case of incomplete or missing questionnaire data at discharge, the baseline score from the respective questionnaire was carried over to the score at discharge. To determine a potential treatment effect, the effect size for all questionnaire data was calculated.

Pressure pain thresholds were analyzed, using a mixed model analysis of variance (ANOVA) with *time* (baseline and discharge)×*sites* (low back and shoulder), set as repeated factors while *group* (LBP and controls) were set as a between-group factor. For PDT, PTT, TSP-effect, and CPM-effect a mixed model ANOVA was used, with *time* as a repeated factor and *group* as a between-group factor.

Associations between significant group differences were assessed by calculating the Pearson correlation coefficient or Spearman rank correlation coefficient. Considering that sex differences exist in healthy populations, for measures of peripheral and central pain sensitivity,[32] additional analyses were performed, where an adjustment was made for sex. All analyses were corrected for multiple post-hoc comparisons using either the Newman-Keuls test (parametric data) or a Bonferroni correction (nonparametric data). A *P*-value below 0.05 was considered to reflect a significant difference or association.

RESULTS

Participants

Eighty potential participants with LBP were screened for eligibility, of which 55 were excluded as they failed to meet the inclusion criteria. The main reasons for exclusion were age (above 40 y) and too long duration of pain (more than 5 y). Additional 5 participants (all females) were excluded, after they had started in the study (see Fig. 1 for further details). Data from the 5 women were removed before data analysis. For the control group, there were no drop-outs and a full data set was available from all participants. Therefore, a full data set (baseline and discharge) from 20 participants with LBP and 20 controls was available for data analysis. For a demographic description of the participants, see Table 1. Out of the 20 participants in the LBP group, only 4 had not sought any care for their condition (Supplementary material, Appendix i, Supplemental Digital Content 1, http://links.lww.com/CJP/A736). Two of the participants took prescription medication (paracetamol 500 mg) on a regular basis (4× 1 g/d) at inclusion; 1 male and 1 female. Inspection of their QST measures showed that the data were comparable with the group mean at both baseline and discharge and were therefore included in all

TABLE 1. Demographic Description of the Study Participants and the Mean (±SD) of All Psychometric Variables Measured at Baseline and Discharge Sessions in the Low Back Pain Group (N = 20) and the Control Group (N = 20)

	Control Group (N = 20)	Low Back Pain Group (N = 20)
Age (y)	27.9 ± 5.9	27.4 ± 6.5
Sex (male/females)	10/10	12/8
Occupation	University student (n = 13) IT support (n = 1) Social worker (n = 1) Daycare institution (n = 1) Registered nurse (n = 1) University lecturer (n = 2) Physiotherapist (n = 1)	University student (n = 9) Office worker (n = 3) Daycare institution (n = 1) School teacher (n = 1) Sales and marketing (n = 3) Warehouse (n = 2) Unemployed (n = 1)
Duration of back pain (y)	NA	2.1 ± 1.5
Pain intensity (NRS, 0-10)	NA	4.5 ± 2.3
RMDQ (0-24)	NA	6.8 ± 3.7
ÖMPQ (0-210)	NA	88.4 ± 23.0
FABQ (0-42)	NA	27.2 ± 15.0

Values for low back pain intensity (NRS), RMDQ, FABQ, and ÖMPSQ are shown for the low back pain group only.
*Indicates a change > 0.05.
FABQ indicates Fear-Avoidance Beliefs Questionnaire; NA, not applicable; NRS, Numeric Rating Scale; ÖMPSQ, Örebro Musculoskeletal Pain Questionnaire; RMDQ, Roland-Morris Disability Questionnaire.

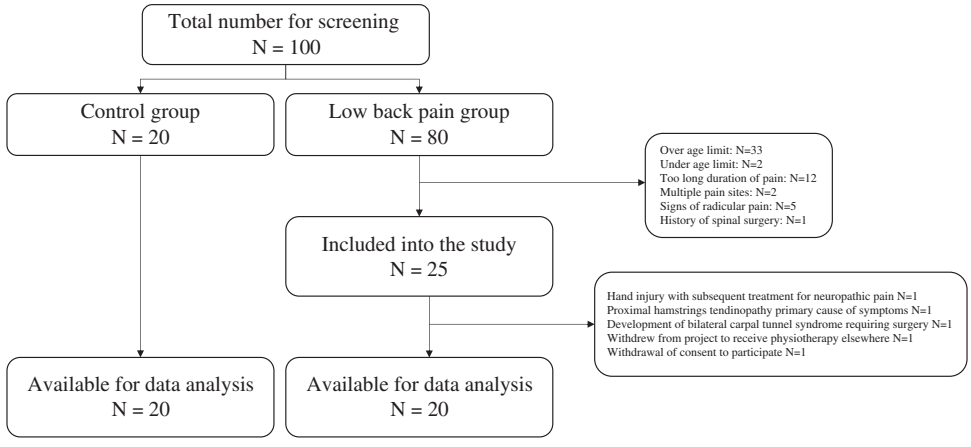

FIGURE 1. A Consort flow diagram demonstrating the screening process for the low back pain (LBP) group. A hundred individuals were screened for eligibility; 20 in the control group and 80 in the LBP group. Twenty-five participants were finally included in the LBP. Five female participants dropped out of the study before finishing the rehabilitation program leaving 20 participants that were included in the LBP group. The 20 matched participants were recruited for the control group.

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TABLE 2. The Effect of Treatment in the LBP Group (N = 20), Mean (± SD), Percentage (%) Change and Effect Size of All Psychometric Variables Measured at Baseline and at Discharge

	Low Back Pain Group (N = 20)			
	Baseline Value	Discharge Value	Percentage Change	Effect Size (Cohen *d*)
Pain intensity (NRS, 0-10)	4.5 ± 2.3	1.8 ± 1.8*	62	1.23
RMDQ (0-24)	6.8 ± 3.7	1.7 ± 2.3*	76	1.61
ÖMPQ (0-210)	88.4 ± 23.0	56.9 ± 30.7*	38	1.44
FABQ (0-42)	27.2 ± 15.0	17.3 ± 14.5*	31	0.87

Values for low back pain intensity (NRS), RMDQ, FABQ and ÖMPSQ.
*Indicates a change > 0.05.
FABQ indicates Fear-Avoidance Beliefs Questionnaire; NRS, Numeric Rating Scale; ÖMPSQ, Örebro Musculoskeletal Pain Questionnaire; RMDQ, Roland-Morris Disability Questionnaire.

data analyses. The remaining participants used over-the-counter pain medication as needed (paracetamol: n = 4), in combination with ibuprofen (combination of paracetamol and ibuprofen: n = 7). The remaining participants (n = 7) took no pain medication for their back pain. The participants in the LBP group had 5 clinical sessions [IQR 4 to 8] spread over a median of 100.5 days [IQR 82.5 to 119]. The interventions consisted mainly of patient education and home exercises that were adapted to functional limitations, physical capacity and personal preferences. In some cases, manual therapy was used as part of the management strategy.

Questionnaire Data

For the LBP group, a significant improvement (Table 2) was found in pain NRS scores (Wilcoxon: $Z = 3.72$, $P < 0.0002$), disability (Wilcoxon: $Z = 3.8$, $P < 0.0001$), FABQ (*t* test: $t_{(18)} = 4.0$, $P < 0.001$), and ÖMPSQ (*t* test: $t_{(18)} = 6.2$, $P < 0.00001$).

Pressure Pain Sensitivity, PDT and PTT

The mixed model ANOVA on PPTs demonstrated no *group*×*time*×*sites* interactions (ANOVA: $F_{2,76} = 1.90$, $P < 0.16$, Table 3). No significant main factor effects were seen.

For cuff PDT, the mixed model ANOVA demonstrated no *group*×*time* interaction (ANOVA: $F_{1,76} = 5.70$, $P < 0.31$, Table 3) or a main factor effect. Similarly, no *group*×*time* interaction was found for PTT (ANOVA: $F_{1,37} = 0.01$, $P < 0.78$, Table 3) or a main factor effect.

A post-hoc power calculation showed that the achieved power was considerably lower (6.6%) than the expected 80% power we had anticipated in our a priori power calculations for PPT values at the low back.

TSP and CPM

For the TSP-effect, the mixed model ANOVA showed no *group*×*time* interaction (ANOVA: $F_{1,34} = 0.80$, $P < 0.39$, Table 3) or a main factor effect.

For the CPM-effect, the mixed model ANOVA showed no indication of *group*×*time* interactions for PDT (ANOVA: $F_{1,36} = 0.41$, $P < 0.6$) or PTT (ANOVA: $F_{1,36} = 0.68$, $P < 0.2$, Table 3). Likewise, no main factor effect was found for the CPM-effect for PDT or PTT.

TABLE 3. Mean (± SD) Baseline and Discharge Measures for Pressure Pain Thresholds (PPT), the Effect of Conditioned Pain Modulation (CPM-effect) on Pain Detection Thresholds (PDT), Pain Tolerance Thresholds (PTT), and Temporal Summation of Pain Effect (TSP-effect)

	Low Back Pain Group (N = 20)	Control Group (N = 20)	Analysis of Variance, *P*
PPT (kPa) baseline			
L5	527.6 ± 276.0	522.4 ± 254.4	< 0.2
L1	563.3 ± 234.0	560.9 ± 252.5	
Infraspinatus	412.2 ± 185.1	392.8 ± 149.3	
PPT (kPa) discharge			
L5	562.4 ± 294.4	535.5 ± 226.2	
L1	601.8 ± 304.7	555.5 ± 258.4	
Infraspinatus	374.1 ± 189.9	388.4 ± 200.2	
Cuff pressure (kPa) baseline			
PDT	28.9 ± 9.4	31.9 ± 16.8	< 0.3
PTT	79.5 ± 22.8	71.0 ± 24.1	< 0.8
Cuff pressure (kPa) discharge			
PDT	33.6 ± 13.5	33.26 ± 17.1	
PTT	77.4 ± 22.5	70.1 ± 23.0	
% change in cuff pressure at baseline CPM response			
PDT	45.5 ± 75.3	31.0 ± 31.5	< 0.4
PTT	11.1 ± 19.7	11.04 ± 10.8	< 0.3
% change in cuff pressure at discharge CPM response			
PDT	16.8 ± 30.7	20.4 ± 32.3	
PTT	9.7 ± 15.2	16.4 ± 19.3	
Temporal summation index baseline (cm)	1.90 ± 1.60	1.20 ± 1.62	< 0.4
Temporal summation index discharge (cm)	1.87 ± 1.61	1.18 ± 1.61	

Correlation

A correlation analysis showed no significant associations between changes in any of the variables (Table 4).

DISCUSSION

This is the first study to investigate whether pain sensitivity in people with chronic LBP changes with reduced pain and disability in primary care. Although a significant

TABLE 4. Correlation Analysis (Spearman ρ [*S*] or Pearson Correlation Coefficient [*P*]) Showing Associations Between the Variables Pain (Numeric Rating Scale [NRS]), Disability (Roland-Morris Disability Questionnaire [RMQD]), Fear Avoidance Beliefs (FABQ), and Signs of Yellow Flags (Örebro Musculoskeletal Pain Questionnaire, [ÖMPSQ])

	NRS	RMDQ	FABQ	ÖMPSQ
NRS		0.112^P $P < 0.65$	0.004^S $P < 0.99$	0.241^P $P < 0.32$
RMDQ	0.112^P $P < 0.65$		0.525^S $P < 0.84$	0.074^P $P < 0.76$
FABQ	0.004^S $P < 0.99$	0.525^S $P < 0.84$		0.302^S $P < 0.21$
ÖMPSQ	0.241^P $P < 0.32$	0.074^P $P < 0.76$	0.302^S $P < 0.21$	

The strength of the association between each variable is shown along with the *P*-value (shown below the correlation).

reduction in pain and disability were demonstrated, the pain sensitivity and central pain mechanisms were not different at baseline and did not change after completing rehabilitation.

A Successful Rehabilitation Strategy

A significant improvement was found in pain and function in the LBP group with large effect sizes similar to what has been demonstrated previously when employing a patient-centered approach to managing LBP.[15,33] Moreover, the improvement in pain and disability were noticeably better than what is considered clinically meaningful.[34,35] However, these improvements were not aligned with changes in pain sensitivity similar to recent findings by Vaegter et al.[36]

Arguably, the initial symptoms, experienced immediately after the onset of clinical LBP, could reflect tissue injury. However, recovery is not contingent upon the injured structures, reverting to normal or in fact being fully intact.[37,38] The clinical trajectories of LBP after the initial onset vary from "full recovery" to "fluctuating" to "persistent,"[39] where participants entering this study seemingly belonged to either of the last 2 categories. Acute back pain is known to result in transient changes in motor control, often manifested as increased trunk stiffness.[40] Despite the protective benefits of decreased movement in the short-term, this may in the long-run become the main catalyst to the pain condition, when tissue recovery has run its course.[41,42] Based on the inclusion criteria in this study, the assessment methods used and the fact that changes in motor strategies, in response to back pain, vary between individuals,[43] it is not possible to determine whether the functional improvements, seen here, can be attributed to changes in tissue loading. Nevertheless, employing a strategy aimed at modifying the patients' current movement strategy, may be sufficient to change spinal loading and thereby reducing pain.

Chronic LBP manifests itself in numerous ways, where patients demonstrate both pro-nociceptive and anti-nociceptive characteristics, as well as psychometric variables and movement patterns being affected in various ways.[44,45] In that regard, cognitive and emotional factors seem to have a mediating role in the clinical course of LBP.[37,46,47] This is supported by qualitative findings that indicate, that a successful outcome in back pain rehabilitation, is related to changes in pain-related beliefs and achieving more independence in terms of self-managing the pain condition.[28] In the present study, the participants reported a significant reduction in fear-avoidance behavior and psychosocial factors, related to their pain condition, in parallel with improvements in pain and function. Nevertheless, no associations were found between any of the factors where significant improvements occurred, indicating that although these factors are present, an improvement in one is not contingent on an improvement in the other. The current findings likely reflect the complicated nature of LBP, where multiple domains may contribute to the pain experience to various degrees across patients.

Pain Sensitivity in Chronic LBP

Interestingly, no baseline differences were found between the groups. Although this has been described before,[48] it contrasts the findings of many other studies that have compared people with chronic LBP and controls,[3,5,49,50] where both local and widespread hyperalgesia was demonstrated. These discrepancies in localized and widespread pain hyperalgesia, may be due to several factors. The pain-related functional interference demonstrated in the present study (6.8/24) could be considered moderate[51,52] and was lower than reported by, for example, Imamura et al[53] (12.4/24) in chronic LBP. Even though patients in the current study reported average pain levels above what is considered clinically meaningful to patients (4.5/10),[54] the pain was lower than what has been seen in other studies assessing pain sensitivity in LBP populations, for example, Vaegter et al (7.7/10),[36] Giesecke et al (6.2/10),[4] Imamura et al (6.8/10),[53] Mlekusch et al (5.1/10).[50]

In the recent findings of Vaegter et al,[36] who included people with chronic musculoskeletal pain, with back pain being their main complaint, the PPTs at the low back were considerably lower (221 ± 109.4 kPa) than reported here (527.6 ± 276.0 kPa). Moreover, Blumenstiel et al[5] (3/10) also demonstrated significantly lower PPTs compared with controls. In these 2 studies, it is important to note that the participants were older than here (52.4 and 43.4 y, respectively) and had lived with their pain for longer than the participants in this study (14.5 and 15.9 y, respectively). Previously, a conceptual model has been suggested, where an extended duration of pain results in increased sensitivity of central pain mechanisms.[10] Likewise, pain sensitivity increases with age.[55] It is therefore possible, that baseline differences could not be identified due to the relatively young age (27.4 y) and short duration of pain (2.1 y) of participants in this study.

TSP was not different between the groups in the present study at baseline, in contrast to previous findings.[56–58] In line with the current findings, Mlekusch et al[50] found no significant differences in the magnitude of the CPM-effect between their chronic LBP patients and controls. In fact, it has been suggested that endogenous pain inhibition is not deficient in chronic LBP.[59] A recent large systematic review[17] demonstrated that there is facilitated response to repeated nociceptive stimuli and a reduced efficiency of the CPM response in chronic LBP, and that these changes in pro-nociceptive and anti-nociceptive processing were dependent upon the severity and duration of the pain condition. Although the participants in the LBP group fulfilled all the criteria for the diagnosis of chronic LBP,[16] an upper limit of 5 years was set as inclusion criteria to reduce the heterogeneity in the LBP group. This may have resulted in the participants in this study having shorter average duration of pain (average of 2.1 y) compared with, for example, Imamura et al[53] (4.1 y), Giesecke et al[4] (4.5 y), Mlekusch et al[50] (7 y), and Blumenstiel et al[5] (15.9 y). Taken together, the difference in duration of symptoms and the age of participants between the different studies, may have contributed to the lack of baseline differences in the current study.

Potential Implications

The management strategy used in this study is in line with recent recommendations[26,27] and it is positive that the intervention significantly improved pain, disability, and pain-related cognitive factors. It is, however, not possible to determine the lasting effect of the intervention, even though long-lasting positive effects have been noted from a comparable intervention elsewhere.[15,36,60]

The participants in this study reported lower pain and disability levels and shorter duration of pain than many other studies. Nevertheless, the majority of participants (16/20) had previously sought treatment for their condition, with little or no success. Therefore, although the severity profile might indicate that many of the participants only had mild to moderate pain, it seemed to be meaningful enough for them to seek treatment.

The small sample size makes it difficult to fully evaluate how and if an assessment of pain sensitivity in clinical practice is relevant for the target group in this study. This is especially important to consider, as it is likely that individuals comparable to those included in the LBP group had pro-nociceptive characteristics.[17,61] A larger sample could potentially have revealed clusters with some patient characteristics demonstrating pro-nociceptive mechanisms in the pain system. An investigation of whether such information can inform the clinical decision-making and improve the outcome, is clearly warranted. However, considering the large individual variability as demonstrated in this study (Table 3) and elsewhere (see McPhee et al[17] for an overview), it is questionable whether screening for pain hypersensitivity can be used to guide treatment.

Limitations and Methodological Considerations

The management strategy used here, was not standardized, but instead focused on what was considered the underlying driver for each individual's pain condition. Although this approach mimics standard procedures in clinical practice, and has been used in previous studies,[36,62] it introduces a risk of improvement being related with the dosage of attention the participants got. The study, however, aimed at investigating potential relationships between the subjective experience of pain and disability on one side and pain sensitivity on the other. Addressing individual characteristics, including functional limitations, unhelpful thought processes and movement strategies is considered important in the management of chronic LBP.[14] For this reason, the management approach was adapted to the individual patient rather than using a standardized intervention.

In previous studies, targeted and efficient management of the nociceptive drive (e.g. total knee replacement in osteoarthritis) resulted in improved anti-nociceptive and pro-nociceptive mechanisms.[63] The relative proportion of attention-related improvement in this current study is unknown, but it may affect the actual peripheral nociceptive drive via, for example, changes in tonic muscle activity. This is, however, only speculative and needs to be investigated further.

The clinicians in this study (T.S.P. and S.W.M.C.) were blinded to all outcome measures (questionnaire data, QST measures and pain data) until end of data collection. Likewise, participants were instructed not to reveal their group allocation to the assessor (E.D.M.) in the experimental session. Despite these preventative measures, it was not possible to eliminate the potential source of bias. For example, the intervention was individually tailored and thereby the clinicians addressed the functional limitations the patient reported. Thereby, the clinicians got an insight into the patient's functional capacity at baseline and over time, even though they were blind to the questionnaire scores. Likewise, for the experimental sessions, it cannot be excluded that the assessor discovered which group they belonged to because of pain-related grimacing or pain when moving around in the laboratory (eg, moving from standing to lying down on the plinth). Nevertheless, as all the QST measurements were controlled by the participants (who pressed indicated pain severity and stop stimulation by the control of a button) who all got the same standardized participant information, this is unlikely to have affected the outcome of the measurements.

Socioeconomic factors, such as level of education, work situation and income, are known to be associated with a greater risk of suffering from long-lasting LBP,[64,65] whereas the participants in this study seemingly belonged to the upper end of the socio-economic spectrum, considering their educational status and work situation. For this reason, the relatively low age and short duration of pain, compared with other studies, the participants here might have had a greater chance of experiencing improvement than a cohort with a different composition.

Surprisingly, we did not see a baseline difference between the 2 groups similar to what other studies have shown, where patients with chronic LBP appear to be more sensitive than controls.[3,5,49,50] However, these findings may relate to the methodological approach where a series of paired tests were run, comparing different sites instead of using a repeated measures ANOVA as done here. A post-hoc power calculation of our study sample showed that the achieved power was considerably lower (6.6%) than the expected 80% power we had anticipated in our a priori power calculations. Based on this calculation, a considerably larger cohort (N = 1184) would have been needed to detect a statistically significant difference in PPT's at the shoulder, to demonstrate signs of widespread hyperalgesia. A post-hoc analysis was likewise run to investigate any potential associations between the changes seen in self-reported outcomes with QST data at baseline. In line with the previous findings of Mlekusch et al,[66] no such relationships were evident. Another potential reason may relate to the upper limit of pain duration which was set to 5 years. This was done to avoid potential inflation of study findings as a longer duration of back pain is known to be associated with higher levels pain sensitivity.[17] It is, therefore, likely that the low levels of sensitization seen in the LBP group can be attributed to the short duration of symptoms.

It is possible that over-the-counter pain medication may affect the sensitivity of pain mechanisms and thereby the QST measurements performed. For blinding purposes, however, it was neither possible to register whether the participants had taken pain medication on the day of QST measurements, nor whether this affected the outcome.

CONCLUSION

The observed positive effect the individually tailored rehabilitation approach had on pain and disability in people with mild to moderate back pain, did not occur in parallel with changes in the pain sensory profile. A larger sample from a population including people with more severe and longer lasting back pain, is needed to qualify the value of screening for pain hypersensitivity in primary care due to the patient heterogeneity and possible sensitivity of assessment methods.

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