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ORIGINAL RESEARCH

Quantitative sensory testing in physically active individuals and patients who underwent multidisciplinary pain therapy in the longitudinal course

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Objective: The aim of this study was to evaluate possible differences of quantitative sensory testing (QST) results in healthy individuals (group control, n=20), physically active individuals (group sport, n=30) and in patients suffering from chronic musculoskeletal pain (group pain, n=30).

Methods: Thermal detection thresholds, thermal pain thresholds and blunt pressure pain thresholds were measured at various sites (T0). Additionally, group pain was treated in multidisciplinary pain therapy for 4 weeks. All groups were retested after 4 weeks to evaluate the reliability of QST measurements and to investigate possible early changes following treatment (T1).

Results: Importantly, QST-measurements showed stable test results for group sport and group control at both time points. Athletes demonstrated the highest pain thresholds in general (cold pain threshold mean in degree Celsius for the hand: 5.76, lower back right: 7.25, lower back left: 7.53; heat pain threshold mean in degree Celsius for the hand: 46.08, lower back right: 45.77, lower back left: 45.70; and blunt pressure pain mean in kilograms for the hand: 3.54, lower back right: 5.26, lower back left: 5.46). Patients who underwent therapy demonstrated significant differences at T1 (cold pain threshold hand mean in degree Celsius for the hand: 11.12 [T0], 15.12 [T1]; and blunt pressure pain mean in kilograms for the lower back right: 2.87 [T0], 3.56 [T1]). They were capable of enduring higher blunt pressure, but on the other hand cold pain tolerance had decreased (P=0.045 and P=0.019, respectively).

Conclusions: In conclusion, we were able to demonstrate significant differences of QST results among the three groups and we detected early changes following multidisciplinary pain therapy, which will be discussed.

Keywords: quantitative sensory testing, chronic musculoskeletal pain, multidisciplinary pain therapy

Introduction

Chronic pain is a widespread disability affecting about 8.85% of the population in the European Union on a daily basis.[1] In Germany specifically, about 17% of the inhabitants are dealing with chronic pain; among those, approximately 5.1% (4.5 million people) suffer from severe pain.[2–4]

Patients suffering from chronic pain syndrome have been shown to exhibit widespread enhanced sensitivity to noxious stimuli, which has been mainly attributed to central sensitization.[5–8] A peripheral and/or central change of pain sensitivity could play a significant role not only in patients suffering from chronic pain syndromes but also

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in athletes. Recently it has been demonstrated that athletes indeed show differing sensitivity to non-noxious stimuli and pain thresholds, which might be explained by the fact that pain represents an essential controlling tool in physical training.[9]

Furthermore, an association between chronic pain and lack of physical activity, mostly caused by fear of movement, has been established, as well as positive effects of exercise on physical and mental health.[10] In this context, it has also been shown that patients suffering from depression benefit from regular physical exercise.[11,12]

To evaluate pain thresholds in a standardized fashion, quantitative sensory testing (QST) has been introduced. The latter represents a subjective psychophysical method to quantify functions of the somatosensory system. By means of thermal and mechanical stimuli, not merely loss of function, but also gain of sensory functions can be evaluated, along with hyperalgesia, allodynia and hyperpathia.[13–15]

Quantitative sensory testing therefore provides an ideal opportunity to gain further understanding about the symptom "pain" by defining pain thresholds in the normal population and comparing with other test groups, that is, athletes or patients suffering from neuropathic pain conditions.[16–20]

The aim of this study was to evaluate QST in healthy test persons, who were not regularly physically active, and compare the results with physically active individuals and with patients suffering from chronic musculoskeletal pain. We hypothesized that physically active participants demonstrate lower detection rates to non-noxious stimuli and higher pain thresholds compared with healthy, non-active individuals and that patients suffering from chronic musculoskeletal pain show reversed test results, high detection rates to non-noxious stimuli and low pain thresholds.

Furthermore, we were interested in evaluating reliability and stability of QST.

Therefore, all participants were re-tested after 4 weeks. We hypothesized that test results would be unchanged in athletes and healthy test persons, whereas treatment would have an effect on detection and/or pain thresholds of patients with chronic musculoskeletal pain who underwent 4 weeks of multidisciplinary pain therapy. The latter treatment consists of somatic and psychotherapeutic procedures in combination with physical and psychological training programs (100 hours of therapy, 50% physical exercise and 50% cognitive behavioral therapy).

Methods

Test persons

A total of 80 test persons were included in this study. The study was approved by the local ethics committee of Heidelberg University (S-413/2013). Written and informed consent was obtained from all participants.

The following three groups were examined (all test persons and patients were right-handed):

Group control (n=20)

Participants who were not continually physically active and who did not suffer from acute or chronic pain were recruited from the staff of Heidelberg University.

Group sport (n=30)

Physically active test persons (2–4 hours of running per week on a regular basis) who did not suffer from acute or chronic pain were recruited at sports clubs and running groups.

Group pain (n=30)

This group comprised patients who suffered from chronic musculoskeletal pain (Korff III and IV[21]) and were treated according to multidisciplinary pain therapy (combined physical and psychological training programs[22]) at the outpatient Pain Management of the Clinic for Orthopedics and Trauma Surgery of Heidelberg University Hospital. All patients were diagnosed with chronic medically unexplained musculoskeletal pain. Pain levels were measured in group pain before and after treatment using a visual acuity numeric scale (0–10). Patients were also asked to rate an improvement of their subjective well-being following 4 weeks of therapy (0% no improvement to 100% maximum improvement). All the patients included in this study complained of persistent back pain in particular, and four patients described chronic pain of the entire body.

Exclusion criteria were the following: acute or chronic pain syndrome (except for group pain), chronic inflammatory disease of the musculoskeletal system, history of cancer, any acute illness (associated with elevated body temperature, sickness, muscle and joint pain), severe mental disorder, regular treatment with opioid analgesics, previous surgical intervention at the tested area, epilepsy, cardiac pacemaker, any metal implants within 20 cm of the tested area, any acute injuries to the tested area, any known dysfunction of the afferent nervous system (ie, polyneuropathy), anticoagulants, dementia or other factors affecting cooperation and/or consent of the test person, current pregnancy and left handedness.

Quantitative Sensory Testing

Thermal detection thresholds, thermal pain thresholds and mechanical pain sensitivity to blunt pressure were tested according to a standardized protocol published by Rolke et al.[23] The aforementioned parameters were tested on the right hand and on the lower back (right side and left side).

First, thermal detection thresholds were evaluated using the TSA II (MEDOC Inc., Ramat Ishai, Israel), followed by thermal pain thresholds. The contact area of the thermode was 9 cm^2 and the baseline temperature was 32°C. Temperature was raised or lowered by 1°C/s until thermal detection was indicated by the test person. The mean value of four consecutive measurements was evaluated. Afterward, thermal pain thresholds were examined accordingly. Cutoff values for thermal pain were 0°C and 50°C, respectively.

Additionally, mechanical pain sensitivity to blunt pressure was measured using a pressure algometer (FPK Algometer, Wagner Instruments, Greenwich, CT, USA). Contact area was 1 cm^2 and stimuli were gradually increased by 50 kPa/s. Mean pressure pain thresholds were calculated using three consecutive measurements.

All tests were carried out by one trained, blinded examiner only. Each session took about 45 minutes and the tests were always performed in the same order. First, thermal detection thresholds were evaluated followed by thermal pain thresholds. Finally, mechanical pain sensitivity to blunt pressure was measured. Room temperature was constantly between 20°C and 24°C and the test persons were seated comfortably on a chair.

Quantitative sensory testing was repeated after 4 weeks. During this time, group control and group sport had not undergone any intervention, but patients from group pain had undergone multidisciplinary pain therapy for a month (Figure 1).

Statistical analysis

Test results were evaluated using SPSS 20.0. Data were evaluated using descriptives like mean and SD. Differences among groups as well as differences between the first and the second examination were calculated by non-parametric tests (Kruskal–Wallis test with post hoc Mann–Whitney *U* test and Friedmann test with post hoc Wilcoxon test). Non-parametric statistical tests were used because single comparisons were evaluated and there was no statistical normal distribution. To counteract the problem of multiple comparisons, Bonferroni correction was used. The significance level was determined as $P<0.05$. The study was registered in the Study Registry of Heidelberg University and the German Registry for Clinical Studies (http://www.drks.de).

Results

Clinical data

The mean age of patients was 33.65 years in group control, 47.41 years in group sport and 48.43 years in group pain. There were 5 male and 15 female test persons in group control, 9 male and 21 female in group sport and 13 male and 17 female in group pain (Table 1).

Temperature detection threshold, temperature pain threshold, and blunt pressure pain threshold

The mean values for cold/warm detection threshold, cold/heat pain detection threshold and blunt pressure pain threshold for the three groups are depicted in Table 2.

Differences between groups

Cold detection threshold (hand) was significantly higher in group control than in group sport and group pain ($P=0.022$ and $P=0.031$*, respectively). When cold detection threshold

Table 1 Clinical data

	Mean age, years (SD)	Gender	
		Male	Female
Group control	33.65 (10.18)*	5	15
Group sport	47.41 (11.38)	9	21
Group pain	48.43 (6.53)	13	17

Note: * indicates a significant difference of age between group control and the other groups. Significance level was determined as $P<0.05$

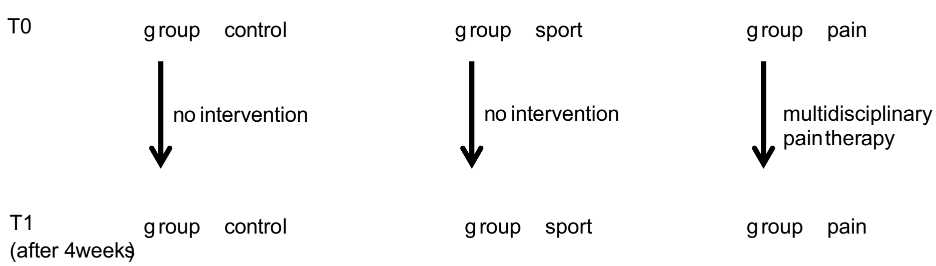

Figure 1 QST was performed at two time points, at T0 and after 4 weeks (T1).
Notes: Healthy control test persons (group control) and physically active test persons (group sport) did not receive any intervention during the two time points. Patients suffering from chronic musculoskeletal pain (group pain) were treated with multidisciplinary pain therapy (combined physical and psychological training programs) for 4 weeks before QST was repeated.

Table 2 Mean values and standard deviations of cold/warm detection thresholds, cold/heat pain thresholds and blunt pressure pain thresholds of group control, group sport and group pain. The parameters were measured on the hand, the lower back right (LB right) and the lower back left (LB left)

	Cold detection threshold mean in °C (SD)			Warm detection threshold mean in °C (SD)		
	Hand	LB right	LB left	Hand	LB right	LB left
Group control	31.095 (0.47)	30.545 (0.98)	30.74 (1.3)	33.29 (0.54)	34.675 (1.09)	34.02 (2.7)
Group sport	30.46 (1.15)	29.977 (1.46)	30.347 (0.94)	33.73 (0.74)	34.883 (1.45)	35.063 (1.45)
Group pain	30.5 (0.93)	30.143 (1.32)	29.933 (1.23)	33.967 (1.2)	35.003 (1.36)	35.353 (1.87)

was measured on the lower back left, group control showed significant higher test results than group pain (P=0.017*). Warm detection threshold (hand) was lower in group control compared with group pain (P=0.011) (Figure 2A and B).

Cold pain threshold of the hand was significantly lower in group sport than in group pain and group control (P=0.005* and P=0.024, respectively). Additionally, on the lower back left (LB left), cold pain threshold of group control and group sport was lower than that of group pain (P=0.017* and 0.003, respectively). On the lower back right (LB right), test results for group control and group sport were also significantly lower than for group pain (P=0.002* and P<0.001*, respectively) (Figure 2C).

Heat pain threshold of group sport was significantly higher compared to group pain (P=0.013*) on the LB right and higher compared to group control on both, LB right and left (LB right P=0.013* and LB left P=0.016*, respectively) (Figure 2D).

Furthermore, the levels of blunt pressure pain (LB right and left) were significantly higher in group sport than in group pain (P<0.001*), as well as group control (P=0.02*, P<0.001*) (Figure 2E). The *-marked significances are also stable to Bonferroni correction.

Differences at T1

Measurements were repeated after 4 weeks without any intervention for group control and group sport. Patients (group pain) were treated in multidisciplinary pain therapy for 4 weeks before quantitative sensory testing was repeated.

At the second examination, no differences were detected in group sport compared with the first. In group control, values for heat pain threshold (hand and LB right) were significantly different (P=0.034 and P=0.014*, respectively). All other measurements remained unchanged (data not shown).

Following 4 weeks of therapy, there were significant differences between the two time-points for cold pain threshold (hand) and blunt pressure pain (LB right) in group pain (cold pain threshold mean in degree Celsius for the hand: 11.12 [T0], 15.12 [T1]; and blunt pressure pain mean in kilograms for the lower back right: 2.87 [T0], 3.56 [T1]). Patients were capable of enduring higher blunt pressure, but on the other hand, cold pain tolerance had decreased (P=0.045 and P=0.019, respectively) (Figure 3A and B).

Pain level

The mean pain levels in group pain were 6.82 before treatment (SD 1.72, range 3–10) and 4.38 after treatment (SD 2.39, range 0–9). Following 4 weeks of therapy, the mean improvement of subjective well-being was 43.5% (SD 33.76, range 0–100). Four of 30 patients included in this study reported an increase of pain following therapy.

Discussion

Quantitative sensory testing represents a diagnostic method to investigate functions of the somatosensory system and has been evaluated for a number of neurological diseases.[24] Previous findings indicate that patients suffering from chronic pain conditions show a differing perception of noxious stimuli compared with healthy individuals.[7] Furthermore, a beneficial effect of physical activity on chronic pain has been proposed.[10]

The aim of this study was to examine QST results in physically active individuals, in healthy but not physically active individuals and in patients suffering from chronic musculoskeletal pain over time. We evaluated for the first time the effect of 4 weeks of pain treatment on somatosensory functions.

Concerning the three examined groups, differences in thermal detection thresholds could only be detected between the control group and the other two groups. This phenomenon might be explained by the fact that individuals in group control were significantly younger than in the other two groups and, although not statistically significant, there were relatively more women included in group control. Younger

Cold pain threshold mean in °C (SD)			Heat pain threshold mean in °C (SD)			Blunt pressure pain threshold mean in kg (SD)		
Hand	**LB right**	**LB left**	**Hand**	**LB right**	**LB left**	**Hand**	**LB right**	**LB left**
10.755 (7.49)	10.51 (9.7)	10.665 (13.8)	43.975 (4.0)	42.65 (4.29)	41.605 (9.6)	4.06 (2.43)	4.02 (2.67)	3.87 (2.66)
5.76 (6.2)	7.25 (8.49)	7.527 (9.49)	46.077 (3.44)	45.773 (3.14)	45.697 (3.3)	3.54 (1.39)	5.26 (2.68)	5.46 (2.65)
11.4 (8.8)	19.447 (10.84)	16.897 (12.44)	44.7 (4.64)	42.987 (5.08)	42.967 (4.11)	3.54 (1.61)	2.87 (1.38)	3.16 (2.03)

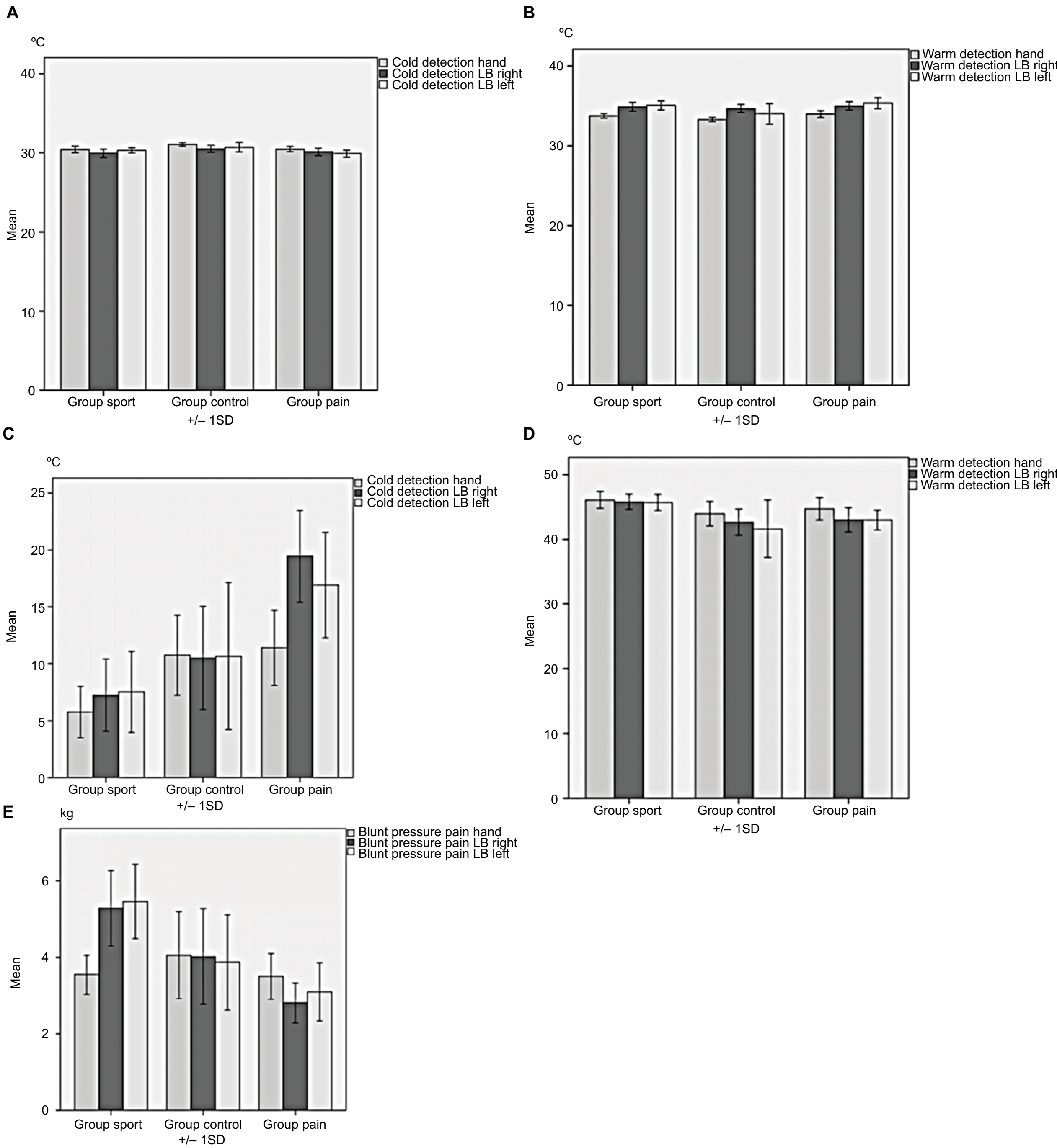

Figure 2 Evaluation of thermal detection thresholds, thermal pain thresholds and blunt pressure pain thresholds.

Notes: Cold (**A**) and warm (**B**) detection thresholds, cold (**C**) and warm (**D**) pain detection thresholds, as well as blunt pressure pain thresholds (**E**) were measured on the hand, the lower back left (LB left) and the lower back right LB (LB right).

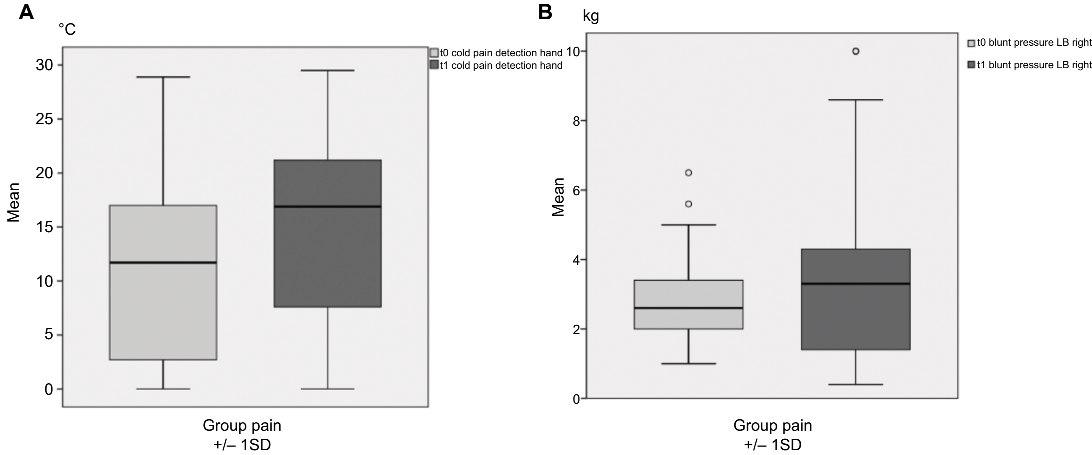

Figure 3 Differences in group pain after 4 weeks of therapy.
Notes: Cold pain threshold (**A**) on the hand and blunt pressure pain threshold (**B**) on the lower back right (LB right) differed significantly between the two time-points.

age in particular has been previously associated with higher sensitivity to thermal stimuli, which might in part explain differing test results in this group.[23] On the other hand, it has been recently proposed that age differences might not play a significant role in some pain regulatory processes.[25] Differences among gender have been mostly documented in the context of sensitivity to noxious stimuli[26] and not with regard to thermal detection thresholds. Furthermore, difficulties in defining a truly "healthy" test group for pain studies have been recently reported and a thorough screening of this particular group has been proposed to avoid a possible bias.[27]

Of note, in our study, there were no differences between group pain and group sport, meaning that athletes and patients suffering from chronic musculoskeletal pain had the same thermal detection thresholds. Compared with the reference data published by Rolke et al,[23] thermal detection thresholds were within the normal range.

When thermal pain thresholds were evaluated, athletes showed the highest tolerance to pain with significant differences compared with group control and group pain. Cold pain threshold, when measured on the lower back in particular, was lowest in group sport and differed statistically significantly from group pain. Additionally, cold pain threshold in group control was also lower than in group pain.

Importantly, patients with chronic musculoskeletal pain also showed region-specific differences in cold pain threshold of the hand when compared with the lower back. Of note, the majority of 30 patients included in this study stated chronic pain of the lower back and therefore perception of cold pain seems to be enhanced in the affected area.

Normal, regional differences of QST values have been previously described;[23] however, in our study, enhanced sensitivity to cold pain on the lower back affected only patients suffering from chronic musculoskeletal pain, thus indicating cold pain hyperalgesia at the affected area in this particular group.

Cold pain hyperalgesia has been previously reported as a typical feature of neuropathic pain[28] and two mechanisms have been proposed. First, it has been suggested that a central suppression of C-nociceptors by A delta fibers is disturbed, resulting in cold pain hyperalgesia combined with cold hypoesthesia. Secondly, a peripheral sensitization of C-nociceptors has been proposed, which presents without concomitant cold hypoesthesia.[29,30,13]

Since thermal detection thresholds were not affected in group pain, our data rather support the second theory – a peripheral sensitization of nociceptors – in patients suffering from chronic musculoskeletal pain at the affected area.

Among the three groups, group sport showed the highest pain tolerance in some test areas when heat pain thresholds were evaluated. Moreover, physically active individuals showed the highest values for blunt pressure pain compared to group control and group pain.

Overall, athletes demonstrated the highest pain tolerance compared with the other groups and also when compared with the reference data in the literature.[23] This finding is in line with the data by others.[9]

We were also interested in evaluating QST results after the course of 4 weeks. Changes in QST results were reported as early as 1 week following oral surgery.[31] In group sport, there were no differences between the first and the second examination, therefore advocating QST as a stable and reliable testing device. In group control, all parameters remained equally stable with the exception of heat pain threshold even though no form of treatment or intervention had been introduced.

When patients suffering from chronic pain syndrome were re-evaluated 4 weeks after multidisciplinary pain therapy, we found that pain tolerance for blunt pressure on the lower back had improved significantly. Blunt pressure pain, which is said to be transmitted via type III and IV axons,[13] has been controversially discussed in the context of acute or chronic pain. Some studies provide proof of widespread hyperalgesia, others of region-specific hyperalgesia and one study even found higher pressure tolerance in patients with chronic pain.[6,32–35]

Furthermore, our data show that cold pain sensitivity on the hand was significantly higher than before treatment. According to Rebbeck et al,[6] patients with chronic neck pain showed a significant widespread increase of cold pain sensitivity when compared to healthy controls, and Marcuzzi et al[34] describe early (within 6 weeks) hypersensitivity to painful cold stimuli in patients who suffered whiplash injury. According to our results, patients with chronic back pain showed similar cold pain hyperalgesia, but only at the affected region, and following 4 weeks of therapy, cold pain threshold had increased at a non-affected region (hand). When patients undergo multidisciplinary pain therapy, they receive a challenging training program covering elements of psychotherapy and physical therapy. Frequently, patients first report an increase of symptoms during the first two weeks of therapy, and increased cold pain sensitivity might reflect an acute reaction to physical training which patients are not accustomed to (similar to the patients who suffered an acute injury).

Overall, our QST results on the effects of 4 weeks of therapy on somatosensory function showed improved blunt pressure pain thresholds, but on the other hand also increased cold pain thresholds. These results might seem conflicting, but it has been argued that peripheral sensitization might play a major role in thermal pain sensitivity but not in mechanical sensitivity, which is considered a characteristic of central sensitization.[7] These different underlying mechanisms of pain generation thus explain the early changes we detected in patients following multidisciplinary pain therapy.

In conclusion, we were able to show that quantitative sensory testing is a reliable and stable method. Physically active individuals showed the highest pain tolerance among the tested groups. Furthermore, we examined the effects of 4 weeks of multidisciplinary pain therapy on QST results in patients suffering from chronic musculoskeletal pain and detected early changes of improved blunt pressure pain threshold, as well as increased cold pain threshold at a distant region.

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Disclosure

The authors report no conflicts of interest in this work

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