

Self-reported sensory descriptors are associated with quantitative sensory testing parameters in patients with cervical radiculopathy, but not in patients with fibromyalgia

Brigitte Tampin^{1,2,3}, Noelle K. Briffa¹, Helen Slater^{1,4}

¹School of Physiotherapy, Curtin Health Innovation Research Institute, Curtin University, Perth, Western Australia

²Department of Physiotherapy, Sir Charles Gairdner Hospital, Perth, Western Australia

³Department of Neurosurgery, Sir Charles Gairdner Hospital, Perth, Western Australia

⁴Pain Medicine Unit, Fremantle Hospital and Health Service, Fremantle, Western Australia

Author responsible for correspondence:

Brigitte Tampin

School of Physiotherapy, Building 408, Level 3

Curtin University, GPO Box U1987

Perth, Western Australia 6845, Australia

Tel: +61 8 9266 4644

Fax: +61 8 9266 3699

Email: brigitte.tampin@postgrad.curtin.edu.au

Category: original article

Keywords (5): Somatosensory profile, painDETECT, quantitative sensory testing, cervical radiculopathy, fibromyalgia

Abstract

Background: The painDETECT questionnaire (PD-Q) has been used as a tool to characterize sensory abnormalities in patients with persistent pain. This study investigated whether the self-reported sensory descriptors of patients with painful cervical radiculopathy (CxRAD) and patients with fibromyalgia (FM), as characterized by responses to verbal sensory descriptors from PD-Q (sensitivity to light touch, cold, heat, slight pressure, feeling of numbness in the main area of pain), were associated with the corresponding sensory parameters as demonstrated by quantitative sensory testing (QST).

Methods: Twenty-three patients with CxRAD (eight women, 46.3 ± 9.6 years) and 22 patients with FM (20 women, 46.1 ± 11.5 years) completed the PD-Q. Standardized QST of dynamic mechanical allodynia, cold and heat pain thresholds, pressure pain thresholds, mechanical and vibration detection thresholds was recorded from the maximal pain area. Comparative QST data from 31 age-matched healthy controls (HCs; 15 women) were obtained.

Results: Patients with CxRAD demonstrated a match between their self-reported descriptors and QST parameters for all sensory parameters except for sensitivity to light touch, and these matches were statistically significant compared to HC data ($p \leq 0.006$). The FM group demonstrated discrepancies between the PD-Q and QST sensory phenotypes for all sensory descriptors, indicating that the self-reported sensory descriptors did not consistently match the QST parameters ($p = \leq 0.017$).

Conclusion: Clinicians and researchers should be cautious about relying on PD-Q as a stand-alone screening tool to determine sensory abnormalities in patients with FM.

1. Introduction

The traditional approach to classification and management of musculoskeletal and neuropathic pain (NeP) according to the aetiological condition has its limitations (Jensen and Baron, 2003; Baron, 2006). A mechanism, or symptom based classification approach, (Jensen and Baron, 2003; Baron, 2006) has been proposed. This approach is based on the hypothesis that different clinical signs and symptoms reflect different underlying pathophysiological mechanisms of pain generation (Hansson, 2002; Jensen and Baron, 2003), with the ultimate aim to target treatment to the underlying pain mechanisms. The assessment of symptoms can be attained by means of questionnaires such as the Neuropathic Pain Symptom Inventory (NPSI) (Bouhassira et al., 2004; Attal et al., 2008) and the painDETECT questionnaire (PD-Q) (Freynhagen et al., 2006; Baron et al., 2009; Mahn et al., 2011) and signs by quantitative sensory testing (QST) (Haanpää et al., 2011).

The PD-Q was originally developed and validated as a screening tool to identify patients with likely NeP (Freynhagen et al., 2006), and has been employed in this capacity in various patient populations (Stegers et al., 2008; Gwilym et al., 2009; Jespersen et al., 2010). Recently it has also been used in large surveys, as a tool to identify somatosensory profiles in patients with lumbar radiculopathy/radicular pain (Mahn et al., 2011), in patients with diabetic neuropathy and postherpetic neuralgia (Baron et al., 2009) and in patients with fibromyalgia (FM) (Rehm et al., 2010; Koroschetz et al., 2011). Based on the responses to verbal sensory descriptors in PD-Q and results of cluster analyses, these latter four studies were able to demonstrate sub-groups of patients with distinct symptom profiles. No study to date has shown symptom profiles for patients with CxRAD, using the PD-Q.

The PD-Q contains questions relating to evoked pain (light touch, pressure, cold/heat) and numbness. Whilst a correlation between self-reported responses to evoked pain (brushing, pressure, cold) and clinical sensory testing has been demonstrated for the NPSI questionnaire (Attal et al., 2008), no study to date has assessed the criterion-related validity for such parameters of PD-Q. A comparison of responses to PD-Q with more objective measurements like standardised QST may substantiate the validity of the questionnaire. QST is a valuable tool to obtain reliable quantitative measures of the presence of positive sensory signs such as allodynia and mechanical and thermal hyperalgesia as well as negative signs (sensory loss) (Rolke et al., 2006a; Rolke et al., 2006b; Hansson et al., 2007; Cruccu et al., 2010; Maier et al., 2010).

The aim of our study was to investigate whether the self-reported sensory descriptors for evoked pain and numbness of patients with painful CxRAD and of patients with FM, as indicated by responses to verbal sensory descriptors items of PD-Q, were associated with their corresponding sensory parameter as demonstrated by QST, using QST data from healthy control subjects as reference criteria.

2. Methods

2.1. Study population

This study included patients with painful CxRAD (n = 23), patients with FM (n = 22) and age matched healthy controls (HC) (n = 31) (Table 1). Patients were recruited from general private physiotherapy, medical, and neurosurgery practices; physiotherapy and pain management departments at five local hospitals; a neurosurgery outpatient department; a neurosurgery triage clinic at a large metropolitan hospital; from the local community via radio and newspaper advertising and from FM support groups. The study protocol and recruitment procedures were approved by the local Ethics Committee of all participating institutions and adhered to the ethical guidelines of the Declaration of Helsinki. Informed consent was obtained from each subject prior to participation.

The inclusion criteria for patients with CxRAD were: unilateral pain distribution consistent with specific radicular distributions (C6/C7), symptom duration of 3 to 18 months, pain intensity ≥ 2 on a visual analogue scale (VAS), signs of C6 or C7 nerve root dysfunction such as sensory impairment and motor impairment (either myotomal weakness and/or absent or diminished reflexes) and a demonstrable clinically relevant abnormality on imaging studies (Treede et al., 2008; Bono et al., 2011) indicating compromise of the exiting nerve root at the relevant spinal level. Exclusion criteria were: evidence of medical or metabolic disease, a history of cardiovascular disease, neurological or psychiatric disease and an insufficient level of English. Depending on the mode of recruitment, some of the potential subjects underwent an initial phone screening examination to ascertain they satisfied the inclusion and exclusion criteria. Prior to inclusion into the study, all patients underwent a comprehensive clinical

examination in order to ascertain they met the inclusion criteria. As no gold standard exists for the diagnosis of painful cervical radiculopathy, the consensus of two clinical experts (a Fellow-trained Neurosurgeon and a Fellow-qualified Specialist in Musculoskeletal Physiotherapy) was used to verify the diagnosis, as consistent with a previous study (Freynhagen et al., 2008). Using a blinded design, both experts reviewed the patient's clinical records, including the findings of the clinical examination and available investigations. Where there was not consensus between the experts and clinical examiner, subjects were excluded from the data analyses.

Patients with FM underwent an initial phone screening examination to ascertain they fulfilled the inclusion and exclusion criteria. The diagnostic criteria for FM according to the 1990 American College of Rheumatology (ACR) (Wolfe et al., 1990) were used as inclusion criteria and were current at the time of recruitment. These criteria include widespread pain of at least 3 months duration in combination with tenderness at 11 or more of 18 specific anatomical sites. Although new diagnostic criteria now exist (Wolfe et al., 2010), the clinical profile of our FM group appears to also correspond with these new guidelines (Table 1). The exclusion criteria were the same as for the radiculopathy group. Of the participating 22 patients, 9 patients had been diagnosed with FM by a rheumatologist, 4 patients by a medical specialist (the patient could not remember what type of specialist), 8 patients by their general practitioner by exclusion (negative blood tests) and positive tender point count, and in one patient the origin of the diagnosis was not recorded. Prior to participation, tender point count was verified by means of a pressure algometer (probe size 1cm²) (Somedic AB, Farsta, Sweden), and assessing nine paired points as defined by the ACR Criteria (Wolfe et al., 1990) and two control points (at the centre of the right forearm and the

right thumb nail). The algometer was placed on the examination site, and pressure was gradually increased by 1 kg/s. The participants were asked to press a button when the sensation at the examination site changed from pressure to pain. Pressure testing was stopped at that moment and the result recorded as positive if maximal pressure was ≤ 4 kg. If no pain was elicited at ≤ 4 kg, the test results were recorded as negative. The average number of tender point ratings of pain was 19 (+/- 0.9) from the possible 22. The patient's clinical history was taken, including pain location on a body chart and identification of the main pain area nominated as the site to be tested by QST. All patients were requested to refrain from non-steroidal anti-inflammatory drugs and analgesics on the day of examination.

HC were recruited from the local community and were excluded if they had a history of current pain or a chronic pain condition or fulfilled any of the exclusion criteria for the patients, including taking medications which influence pain perception.

2.2. Questionnaires

All patients completed the PD-Q. The PD-Q is a self-reported tool consisting of seven weighted sensory descriptor items, plus one item relating to temporal pain characteristics and one item relating to spatial pain characteristics. The questionnaire was originally designed to identify NeP components specifically in low back pain patients with and without referred pain (Freynhagen et al., 2006). The PD-Q was developed and validated in 392 German patients with clinically diagnosed pain of predominantly either nociceptive or neuropathic origin and demonstrated a sensitivity of 85% and specificity of 80%. The Cronbach's alpha as measure of internal consistency of the seven weighted sensory descriptors was 0.83 (Freynhagen et al.,

2006). Reliability was not assessed in that study as the authors considered this ethically and scientifically unjustifiable (Freyenhagen et al., 2006). Reliability of the Swedish versions of PD-Q assessed in 40 patients with spinal cord injury was moderate (kappa coefficient 0.59) and sensitivity to identify NeP was 68% and specificity 83% (Hallström and Norrbrink, 2011). A validation study of the Spanish PD-Q in 221 patients with various etiologies (peripheral and central NeP and nociceptive pain disorders) demonstrated 81.2% sensitivity and specificity with an intraclass correlation coefficient of 0.934 for reliability measured over 1-2 days (De Andrés et al., 2012). To our knowledge, no reliability and validity data exist on the English version of PD-Q.

The following questionnaires were employed in order to characterise the patients and HC group and to capture the multidimensional aspects of pain as recommended by the IMMPACT guidelines (Dworkin et al., 2012). Patients and HC subjects completed the short form-36 health questionnaire (SF-36) to assess quality of life (Ware, 2000) and the Hospital Anxiety and Depression Scale (HADS) to screen for the presence of psychological factors (Zigmond and Snaith, 1983). Individual scores for anxiety and depression are generated with a maximum score of 21 for each parameter. Scores of ≤ 10 for each are considered within normal range. In addition, sleep quality over the last week was rated by all subjects on a 100-cm VAS with the end points 0 cm (good sleep) and 10 cm (bad sleep) (Hurtig et al., 2001). Sleep disturbance was assessed by asking whether the subject awakened tired or non-refreshed; fatigue was assessed by asking: “Are you fatigued?” (Wolfe et al., 1990). Both questions allowed for answers: “never”, “seldom”, “often or usually”, “always”. “Often or usually” or “always” was scored as positive, and other replies as negative. In all patients, average pain intensity

over the last week was determined with a VAS with the end points 0 cm (no pain) and 10 cm (maximum tolerable pain) (Jensen et al., 1989). The strongest and average pain intensity over the last four weeks were documented on a numeric rating scale (NRS) as part of the PD-Q (0 = no pain, 10 = maximum pain). All questionnaires were administered before the QST testing was performed.

2.3. Quantitative sensory testing

Standardised QST measures were recorded according to the QST protocol of the German Research Network on Neuropathic Pain (DFNS) (Rolke et al., 2006a; Rolke et al., 2006b). This protocol comprises a battery of standardised tests in the following order: thermal detection thresholds for the perception of cold and warm and paradoxical heat sensation, cold and heat pain thresholds (CPT, HPT), mechanical detection threshold for touch (MDT), mechanical pain threshold for pinprick, a stimulus-response-function for pinprick sensitivity and dynamic mechanical allodynia (DMA), wind-up ratio to repetitive pinprick stimuli, mechanical detection thresholds for vibration (VDT) and pain thresholds to blunt pressure (PPT). Good test/retest- and inter-observer-reliability of this protocol has been demonstrated (Geber et al., 2011). In our laboratory the Intraclass-Correlation Coefficients (ICC) for triplicate measurements on the same day for all measurements of interest were > 0.9 (ICC [95% CI] for CPT 0.94 [0.85 - 0.98]; HPT 0.94, [0.85 - 0.98]; VDT 0.93 [0.84 - 0.98]; PPT 0.92 [0.80 - 0.97]). Measurements were taken from the main pain area, as nominated by the patients (upper trapezius muscle $n = 18$; paravertebral cervical spine $n = 4$, paravertebral thoracic spine $n = 11$; above and below spine scapula $n = 3$; upper arm $n = 6$; forearm $n = 2$, just above the elbow $n = 1$). HC reference data from a parallel study of ours were used for comparison. Measurements in the upper trapezius muscle

had been obtained in 26 HC and measurements in all other pain areas in 8 HC, the latter including 3 HC in the upper trapezius group, consistent with established methodology in a previous QST study (Blankenburg et al., 2010). QST was conducted on each subject by the same investigator in a laboratory with a constant room temperature. The investigator was not aware of the patient's responses to the PD-Q. The full QST protocol as outlined above was performed on all subjects as part of another concurrent study. However, for the purpose of this study, only the following recordings were used to assess the patient's responses to the PD-Q.

PainDETECT question: Is light touching (clothing, a blanket) in this area painful?

QST test: Pain in response to stroking light touch (DMA) was assessed using a cotton wisp (3 mN), a cotton wool tip fixed to an elastic strip (100 mN) and a brush exerting a force of 200-400 mN. Subjects were asked to give a pain rating for each stimulus on a NRS (0 = no pain, 100 = most intense pain imaginable). This assessment forms part of the stimulus-response-function for pinprick sensitivity and DMA. Pinprick and light stroking applications were performed five times in a randomised sequence. DMA was calculated as the geometric mean of all numerical ratings across all three different types of light touch stimuli.

PainDETECT question: Is cold or heat (bath water) in this area occasionally painful?

QST test: CPT and HPT were measured using the MSA Thermotest system (Somedic AB, Farsta, Sweden). All thresholds were obtained with ramped stimuli (1° C/s) which were terminated when the subject pressed a button. The baseline temperature was set at 32°C; cut-off temperatures were 5°C and 50°C. The mean threshold temperature of three consecutive measurements was calculated.

PainDETECT question: Do you suffer from a sensation of numbness in the areas that you marked?

QST test: The MDT was measured with a standardised set of modified von Frey hairs (Optihari2-Set, Marstock Nervtest, Germany) that exert forces upon bending between 0.25 and 512 mN. The final threshold was the geometric mean of five series of ascending and descending stimulus intensities (Rolke et al., 2006b). A Rydel-Seiffer tuning fork (64Hz, 8/8 scale) was used to obtain the vibration detection threshold (VDT). VDT was measured over bony prominences unless the maximal pain area did not exhibit a bony surface (n = 11), in which case, measurements were taken over adjacent soft tissue. The threshold was determined as a disappearance threshold with three stimulus repetitions (Rolke et al., 2006b).

PainDETECT question: Does slight pressure in this area, e.g., with a finger, trigger pain?

QST test: PPTs were recorded using a pressure algometer with a probe size of 1cm² and application rate of 50 kPa/s (Somedic AB, Farsta, Sweden). The subjects were asked to push a button when the sensation changed from one of pressure alone to one of pressure and pain. Triplicate recordings were taken and the mean values used for analysis.

2.4. Statistical analysis

Data were analysed using the statistical package SPSS vs 17. Each question of the PD-Q has five possible scores listed as: never = 0; hardly noticed = 1; slightly = 2; moderately = 3; strongly = 4; very strongly = 5 (Freynhagen et al., 2006). As no criteria are currently available to indicate validated cut-offs defining what constitutes

a clinically relevant sensory disturbance, we chose the score “moderately” (≥ 3) as our cut-off score and defined this as a positive response and scores of < 3 as a negative response. Other researchers defined a clinically relevant sensory disturbance if patients marked a score > 3 (strongly and very strongly) (Baron et al., 2009; Amris et al., 2010; Rehm et al., 2010; Koroschetz et al., 2011; Mahn et al., 2011).

Consequently, we re-analysed our data using the cut-off scores >3 . Results are reported as supplementary material (Table S4, S5).

QST data were log-transformed prior to statistical analysis except HPT and VDT which were normally distributed as raw data (Rolke et al., 2006a; Rolke et al., 2006b). To compare and illustrate the patients’ QST data with control data, independently of the different units of measurement, the log data of CPT, MDT and PPT and raw data of HPT and VDT were z-transformed using the following expression: $Z\text{-score} = (\text{Mean}_{\text{single proband}} - \text{Mean}_{\text{healthy controls}}) / \text{SD}_{\text{healthy controls}}$ (Rolke et al., 2006b). Z-values were calculated based on the included HC group data. To assess any difference in z-score QST parameters between positive and negative responders compared to healthy control data, a univariate analysis was performed for each patient group. Post hoc comparisons were calculated using Bonferroni-post hoc tests for

- (i) all patients giving positive responses and matched HC,
- (ii) all patients giving negative responses and HC
- (iii) patients giving positive responses and patients giving negative responses.

Patient subgroups with less than 4 patients were not included in the univariate analysis. In this case, an independent T-test was used to analyse differences between the HC group and the remaining larger patient subgroup. The measurements of CPT, HPT and PPT in our patients were significantly lower in females than males (p

<0.001), consistent with previous reports (Rolke et al., 2006a), hence gender was included in the model for analyses of these QST parameters. Measurements of MDT and VDT were not affected by gender in our study.

Data are presented as mean and standard deviation (SD). Age and sleep quality were compared between groups using one-way ANOVA. Post hoc comparisons were calculated using LSD-post hoc tests. The frequency of sleep disturbances was determined using Fisher's exact test. Anxiety and depression scores and the physical and mental components of the SF-36 were compared between groups using the Kruskal-Wallis Test. If there was a difference between groups, further pairwise analyses were performed using the Mann-Whitney-U Test. Symptom duration and pain intensity were compared between patient groups using an independent-samples T-Test. Significance was accepted at $p < 0.05$ for all analyses.

3. Results

3.1. Clinical profiles

A summary of the demographics is presented for each group in Table 1. Both patient groups had significantly poorer sleep quality compared to HC and more frequently reported signs of increased sleep disturbance and fatigue. Patient groups also had significantly higher anxiety and depression scores on the HADS than HC.

Nonetheless, depression scores were within the normal range for over 85% of patients in both groups. Anxiety scores were within the normal range in 91% of patients with CxRAD, but in only 32% of patients with FM. SF-36 physical and mental component summary scores were significantly lower than in HC.

3.2. Sensory phenotypes

The z-score QST sensory profiles for CPT, HPT, MDT, VDT and PPT in patients with CxRAD are illustrated in Figure 1. There was a significant gain in cold, heat and pressure sensitivity in those patients with CxRAD who indicated being sensitive to these QST parameters and a sensory loss in patients who indicated feeling numbness. QST parameters of patients responding negative to the PD-Q questions were within one SD of the HC data.

Figures 1 and 2 to be inserted here or after next sentence

The z-score QST sensory profiles of patients with FM are illustrated in Figure 2. All patients with FM demonstrated a significant gain in cold, heat and pressure sensitivity, irrespective of their responses to PD-Q.

3.2.1. Patients with cervical radiculopathy

Sensitivity to light touch

The PD-Q report indicated sensitivity to light touch in four patients with CxRAD (Table 2), and one of these patients demonstrated DMA on QST testing. Nineteen patients reported not being sensitive to light touch on PD-Q. None of these demonstrated DMA and no HC demonstrated DMA.

Sensitivity to cold/heat

Patients responding being sensitive to cold or heat demonstrated a significantly increased sensitivity to cold and heat (CPT: $p = 0.001$; HPT: $p = 0.006$) compared to HC subjects (Table 2). Patients who indicated not being sensitive to cold/heat did not differ in their pain thresholds when compared to HC. Patients indicating being sensitive to heat demonstrated a lowered HPT compared to patients not being sensitive to heat ($p = 0.018$).

Sensation of numbness

Patients who indicated feeling numbness in the area of pain demonstrated a loss of sensation, manifesting as a significantly elevated MDT ($p = 0.004$) and VDT ($p < 0.001$) compared to HC data (Table 2). Patients who responded as not feeling numbness, did not differ in their mechanical detection sensitivity compared to HC data.

Sensitivity to slight pressure

Patients responding being sensitive to pressure demonstrated significantly increased pressure sensitivity compared to HC ($p = 0.004$) and to patients responding not being

sensitive to pressure ($p < 0.001$) (Table 2). Patients reporting not being sensitive did not differ compared to HC.

3.2.2. Patients with fibromyalgia

Sensitivity to light touch

The PD-Q report indicated sensitivity to light touch in four patients with FM (Table 3), and none of these patients demonstrated DMA on QST testing. Eighteen patients reported not being sensitive to light touch on PD-Q. Three of these patients demonstrated DMA on QST testing.

Sensitivity to cold/heat

Regardless of PD-Q responses to cold/heat sensitivity, all patients with FM demonstrated a significantly increased sensitivity to both thermal stimuli ($p < 0.001$) (Table 3). There was no significant difference in CPT and HPT between patients responding on PD-Q as being sensitive to these thermal stimuli and those responding as not being sensitive.

Sensation of numbness

Patients responding as feeling numbness in their maximal pain area did not demonstrate a significant difference in MDT or VDT compared to HC (Table 3). Patients responding as not feeling numbness, demonstrated a loss of sensation with a significant difference in VDT ($p = 0.008$) compared to HC, but not in MDT (Table 3).

Sensitivity to slight pressure

All patients with FM demonstrated a significantly increased sensitivity to pressure compared to HC, regardless of a positive or negative PD-Q response (positive responders: $p < 0.001$; negative responders: $p = 0.017$) (Table 3).

3.3. Analyses using a cut-off score > 3

While the number of patients with CxRAD and patients with FM responding positive or negative to the PD-Q differed compared to the analyses using a cut-off score (≥ 3), (i.e. less patients responded positive to the item descriptors), the results remain mostly consistent with our previous analyses (supplementary material Tables S4, S5).

Compared to HC, patients with CxRAD who indicated being sensitive to a parameter demonstrated the sensory alteration (MDT: $p = 0.043$; VDT: $p = 0.013$; PPT: $p = 0.001$) (Table S4). Although patients who did not indicate being sensitive to cold or feeling numbness also demonstrated the sensory alteration (CPT: $p = 0.015$; VDT: $p = 0.004$) (Table S4), the difference in CPT between these patients and HC was not clinically significant. All patients with FM, irrespective of their answers to PD-Q, demonstrated increased sensitivity to both thermal and pressure stimuli (positive responders: CPT, HPT: $p < 0.001$; PPT: $p = 0.002$, negative responders: CPT, HPT, PPT: $p < 0.001$) and patients who did not indicate feeling numbness in their main area of pain, also demonstrated a loss of sensation compared to HC (VDT: $p = 0.003$) (Table S5).

4. Discussion

We investigated whether the self-reported sensory descriptors of patients with CxRAD and patients with FM, obtained through the PD-Q, were associated with the corresponding QST parameters, using HC QST data as reference criteria. Patients with CxRAD demonstrated a match between their self-reported sensory phenotype and their QST sensory phenotype for all sensory descriptors except for sensitivity to light touch. In contrast self-reported sensory descriptors did not consistently match the QST parameters in patients with FM.

Clinical and QST somatosensory profiles of study groups

Our patient cohort of CxRAD was characterised predominantly by mechanical hypoesthesia with 83% reporting the presence of numbness and demonstrating elevated MDT and VDT. Negative sensory signs are core signs of NeP due to the reduction of afferent input caused by a nerve lesion (Hansson, 2002; Jensen and Baron, 2003). In contrast only 16% of patients with painful lumbar radiculopathy/radicular pain (Mahn et al., 2011) reported numbness. While this difference is partly related to using different cut-off scores for PD-Q, the latter study did not employ specific inclusion criteria of nerve root dysfunction, hence it is possible that patients may have presented with radicular pain, but without any associated nerve damage (Merskey and Bogduk, 1994).

Thermal and mechanical hyperalgesia were present only in a minority of patients with CxRAD. Five patients demonstrated cold hyperalgesia defined as $\geq 15^\circ$ (Bennett, 2006) which is a common sequel of peripheral nerve injury (de Medinaceli et al., 1997; Kleggetveit and Jørum, 2010; Landerholm et al., 2010; Taylor et al., 2010) and

has been previously demonstrated in patients with CxRAD using QST (Chien et al., 2008). According to PD-Q results, thermal hyperalgesia was uncommon in patients with lumbar radiculopathy/radicular pain (8%) (Mahn et al., 2011). The percentage of our patients reporting increased pressure and light touch sensitivity was consistent with findings by Mahn et al (2011). Our patients' somatosensory profile corresponded with that of a subset of patients with lumbar radiculopathy/radicular pain (Mahn et al., 2011), characterised by mainly numbness together with burning pain and paraesthesia, indicating deafferentation of the affected skin. Similarly, Maier et al (2010) documented in 1236 patients with NeP that for some patients a sensory loss was the only presenting sensory abnormality.

The heterogeneity seen in our patient cohort, as indicated by positive or negative responders to the PD-Q, may be related to multiple factors, such as the mechanisms and magnitude of nerve root compression (e.g. compression due to osteophytic stenosis or disc herniation) and symptom duration, and may also reflect the mixed pain types (nociceptive/neuropathic) evident in radiculopathies (Baron and Binder, 2004; Pérez et al., 2007). It has to be mentioned that while the z-score QST profile of the CxRAD negative responders did not differ from the HC data and was within one standard deviation of the reference data, this does not imply the absence of NeP as patients may have responded in the negative for one parameter, but in the positive for another.

The demographic features of our FM cohort was consistent with previous data (Gormsen et al., 2010). All patients, irrespective of their answers to PD-Q, demonstrated increased pressure sensitivity in their maximal pain area, as documented

previously using QST (Kosek et al., 1996; Klauenberg et al., 2008; Pfau et al., 2009; Blumenstiel et al., 2011) and increased cold/ heat sensitivity, corresponding with some QST findings (Kosek et al., 1996; Hurtig et al., 2001; Berglund et al., 2002; Blumenstiel et al., 2011), but not with others (Klauenberg et al., 2008; Pfau et al., 2009). The differences in findings between studies are probably indicative of the heterogeneity of FM as sub-groups of patients demonstrating increased thermal sensitivity have been identified (Hurtig et al., 2001; Rehm et al., 2010; Koroschetz et al., 2011). Our patient cohort might have incorporated a larger proportion of patients characterised by increased thermal sensitivity (Rehm et al., 2010; Koroschetz et al., 2011) which may also explain the observed magnitude of thermal sensitivity (z-scores outside 95% confidence interval of HC data). Despite similarities in symptomatology between patients with FM and patients with NeP, such as a gain of function in thermal and pressure sensitivity, FM cannot be viewed as a neuropathic pain state according to the new definition of neuropathic pain (Jensen et al., 2011).

There was a trend to increased MDT in all patients with FM, but this did not reach statistical significance. In comparison to other QST studies, Pfau et al (2009) found significantly increased MDT in patients with FM compared to HC, but others did not (Kosek et al., 1996; Blumenstiel et al., 2011). In this regard, tactile hypoesthesia does not necessarily indicate structural damage to tactile pathways (Geber et al., 2008) and can be present in clinical pain disorders possibly consistent with changes in central nervous system plasticity. Hypoesthesia was also documented by an increased VDT in patients who indicated not feeling numbness. It is unclear why this was observed only in these patients and not in patients who reported feeling numbness.

The percentage of our patients indicating numbness (14%), pressure (50%) and thermal sensitivity (23%) was lower compared to other studies (numbness 20%-22%, pressure sensitivity 50%-83%, thermal sensitivity 26%-54%) (Amris et al., 2010; Rehm et al., 2010; Koroschetz et al., 2011). Similarly, a small proportion of our patients demonstrated DMA (14%), consistent with findings in another QST study (Pfau et al., 2009), but differing to others (20%-28%) (Amris et al., 2010; Rehm et al., 2010; Blumenstiel et al., 2011; Koroschetz et al., 2011). These differences, together with the above mentioned differences in QST findings in patients with FM, may provide further support for the presence of sub-groups in this population.

Correspondence between PD-Q sensory descriptors and QST parameters

The self-reported sensory descriptors of patients with CxRAD corresponded with the QST parameters for all sensory descriptors, except for DMA. Compared to HC, patients who indicated sensitivity to a specific sensory parameter also demonstrated the corresponding sensory alteration. Patients who did not indicate being sensitive to a parameter did not demonstrate a sensory alteration. In contrast, self-reported sensory descriptors in the FM group did not consistently match the QST parameters. Although all patients who indicated sensitivity to heat/cold and pressure demonstrated increased sensitivity for these parameters, those who responded as not being sensitive also showed these sensory alterations. Furthermore, compared to HC, patients with FM who indicated numbness in the area of their pain did not demonstrate significant hypoaesthesia. Patients who reported not feeling numbness had a significantly elevated VDT, again demonstrating a discrepancy between patients' self-reported profile and the associated QST sensory profile. Our data suggest that there is potential

for misclassification if only patient reported outcomes are used for sub-grouping of the FM population.

It is unclear why the multiple discrepancies between self-reported and QST parameters were observed in patients with FM, but not in patients with CxRAD. The observation may suggest a more globally impaired sensory discriminative function in the FM cohort. In interpreting our findings, consideration should be given to the fact that PD-Q has never been validated for use in the FM population. It is also possible that psychological factors (Giesecke et al., 2003) or altered cognitive function (Dick et al., 2008) may have influenced patients' responses to PD-Q. In addition, it is open to debate if the PD-Q is suitable for people with widespread pain (Bouhassira and Attal, 2011; Mulvey and McBeth, 2011). Although the main pain area was identified prior to completing the PD-Q, most of the patients with FM (n = 20) drew their main pain area, plus additional pain areas on the PD-Q body chart. It is therefore possible that patients answered the questions of verbal descriptors for all their pain areas. It is unclear if the indication of multiple pain areas on the body chart could explain the discrepancy between patients' perception of sensory stimuli and the associated QST findings, as QST parameters were only measured in the maximal pain area. In contrast, all patients with CxRAD indicated correctly the area of their neck-arm pain/paraesthesia and also demonstrated good agreement between self-reported and QST sensory parameters.

The sample size of our cohorts was small, hence limiting the generalisability of our results. However, the recruitment of patients with CxRAD proved to be extremely difficult with only 23 fulfilling the inclusion criteria for CxRAD out of 464 clinically

examined patients with neck-arm pain. Furthermore, we were not able to gender match HC and patient data, however our results were controlled for gender. Our preliminary data provide valuable information into the criterion validity of specific sensory descriptors of the PD-Q and may direct future research in this field.

In conclusion, the data from our study demonstrate correspondence between the self-reported sensory descriptors of patients with CxRAD and their associated QST parameter. The QST sensory phenotype of patients with FM was not consistently reflected by responses to verbal descriptors from the PD-Q. Clinicians and researchers should be cautious about relying on PD-Q as a stand-alone screening tool to determine sensory abnormalities in FM.

Acknowledgement

This study was supported by the National Health and Medical Research Council (Grant 425560), Arthritis Australia (Victorian Ladies' Bowls Association Grant) and the Physiotherapy Research Foundation (seeding grant). We would like to thank Toby Hall and Gabriel Lee for their assistance in validation of patients' diagnosis of cervical radiculopathy. We thank Walter Magerl, Thomas Klein and Doreen Pfau from the DFNS group for their assistance with implementation of and valuable advice on QST. We are grateful to all patients participating in this research and to all colleagues assisting us in recruitment of patients. The authors report no conflict of interest.

Author contributions

Brigitte Tampin takes responsibility for the integrity of the work as a whole, from inception to published article. Each author contributed to the conception and design of the study and analysis and interpretation of data. All authors were involved in the drafting and revision of the article, discussed the results and gave final approval of the version to be published.

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Table 1

Demographics and profiles of healthy control (HC) subjects, patients with cervical radiculopathy (CxRAD) and patients with fibromyalgia (FM)

	HC (n = 31)	CxRAD (n = 23)	FM (n = 22)	p-value
Age (years) ^f	45.6 (12.5)	46.3 (9.6)	46.1 (11.5)	0.968
Gender (female, n)	15	8	20	
Symptom duration (months) ^f		7.6 (4.1)	124.9 (83.1)	<0.001
Average pain intensity during last week (VAS) ^f		5.2 (2.0)	7.3 (1.2)	<0.001
Maximal pain intensity during last 4 weeks (NRS 0-10) ^f		7.2 (2.2)	8.3 (1.2)	0.054
Average pain intensity during last 4 weeks (NRS 0-10) ^f		5.0 (2.1)	6.2 (1.3)	0.025
Sleep quality during last week (VAS) ^f	2.9 (2.6)	5.3 (2.7) ^b	6.8 (2.3) ^a	<0.001
Sleep disturbance (n)				<0.001
Negative	26	11	1	
Positive	5	12	21	
Fatigue (n)				<0.001
Negative	25	9	2	
Positive	6	14	20	
Hospital Anxiety and Depression Scale				
Anxiety score (HADS) ^g	3.0 (5.0)	6.0 (5.0) ^b	12.0 (6.2) ^{a, c}	<0.001

Within normal range (≤ 10), n	29 (93%)	21(91%)	7 (32%)	
Depression score (HADS) ^g	1.0 (1.0)	3.0 (4.0) ^a	6.0 (4.2) ^{a, d}	<0.001
Within normal range (≤ 10), n	31 (100%)	21 (91%)	19 (86%)	
SF-36				
Physical Component ^g	57.7 (3.7)	40.6 (12.6) ^a	36.4 (11.9) ^{a,}	<0.001
Mental Component ^g	56.0 (7.6)	52.3 (17.4) ^b	30.8 (21.5) ^{a, d}	<0.001
Patients with medication, n		15 (65.2%)	12 (54.5%)	
Current medication ^e				
Selective serotonin reuptake inhibitor, n		1 (4.3%)	7 (31.8%)	
Serotonin-norepinephrine reuptake inhibitor, n		2 (8.7%)	2 (9.1%)	
Tricyclic antidepressant, n		1 (4.3%)	3 (13.6%)	
Tetracyclic antidepressant, n			1 (4.5%)	
Antiepileptics, n		2 (8.7%)		
Opioids, n		4 (17.4%)	1 (4.5%)	
Benzodiazepine, n		2 (8.7%)		
Analgesics, n		7 (30.4%)	3 (13.6%)	
Non-steroidal anti-inflammatories, n		7 (30.4%)		

^aSignificantly different to HC ($p < 0.001$).

^bSignificantly different to HC ($p < 0.05$).

^cSignificantly different to CxRAD ($p < 0.001$).

^dSignificantly different to CxRAD ($p < 0.05$).

^eMultiple answers possible.

^fData are mean (SD)

^gData are median (IQR)

Table 2

Comparison of each QST parameter between healthy controls (HC), patients with cervical radiculopathy (CxRAD) who responded on painDETECT as being sensitive to a QST parameter (positive), and patients who responded on painDETECT as being not sensitive to a QST parameter (negative). The score “moderate” was used as the cut-off score for answers on the painDETECT. Data are shown as mean (SD) for untransformed data and retransformed mean for log-normally distributed data (CPT, MDT, PPT).

	HC (n = 31)	CxRAD positive	CxRAD negative	p-value
<i>Is light touching in this area painful?</i>		n = 4	n = 19	
DMA	0 had DMA	1 had DMA	0 had DMA	
<i>Is cold or heat in this area occasionally painful?</i>		n = 5	n = 18	
CPT (°C)	7.0	18.8 ^a	9.6	0.001
HPT (°C)	46.7 (1.9)	41.2 (5.6) ^{a, b}	46.5 (3.3)	0.003
<i>Do you suffer from a sensation of numbness in the area that you marked?</i>		n = 19	n = 4	
MDT (mN)	1.9	4.5 ^a	1.7	0.006
VDT (x/8)	6.1 (0.9)	5.3 (1.2) ^a	5.8 (0.2)	0.002
<i>Does slight pressure in this area trigger pain?</i>		n = 7	n = 16	
PPT (kPa)	439	303 ^{a, c}	457	0.001

DMA: dynamic mechanical allodynia, CPT: cold pain threshold, HPT: heat pain threshold, MDT: mechanical detection threshold, VDT: vibration threshold, PPT: pressure pain threshold.

^aSignificantly different to HC ($p < 0.05$).

^bSignificantly different to CxRAD negative ($p < 0.05$).

^cSignificantly different to CxRAD negative ($p < 0.001$).

Table 3

Comparison of each QST parameter between healthy controls (HC), patients with fibromyalgia (FM) who responded on painDETECT as being sensitive to a QST parameter (positive), and patients who responded on painDETECT as being not sensitive to a QST parameter (negative). The score “moderate” was used as the cut-off score for answers on the painDETECT. Data are shown as mean (SD) for untransformed data and retransformed mean for log-normally distributed data (CPT, MDT, PPT).

	HC (n = 31)	FM positive	FM negative	<i>p</i> -value
<i>Is light touching in this area painful?</i>		n = 4	n = 18	
DMA	0 had DMA	0 had DMA	3 had DMA	
<i>Is cold or heat in this area occasionally painful?</i>		n = 10	n = 12	
CPT (°C)	7.0	21.9 ^a	26.3 ^a	<0.001
HPT (°C)	46.7 (1.9)	39.2 (3.2) ^a	39.8 (3.5) ^a	<0.001
<i>Do you suffer from a sensation of numbness in the area that you marked?</i>		n = 7	n = 15	
MDT (mN)	1.9	2.9	3.2	0.208
VDT (x/8)	6.1 (0.9)	6.1 (1.1)	5.2 (1.0) ^b	0.010
<i>Does slight pressure in this area trigger pain?</i>		n = 18	n = 4	
PPT (kPa)	439	182 ^a	186 ^b	<0.001

DMA: dynamic mechanical allodynia, CPT: cold pain threshold, HPT: heat pain threshold, MDT: mechanical detection threshold, VDT: vibration threshold, PPT: pressure pain threshold.

^aSignificantly different to HC ($p < 0.001$).

^bSignificantly different to HC ($p < 0.05$).

Table S4

Comparison of each QST parameter between healthy controls (HC), patients with cervical radiculopathy (CxRAD) who responded on painDETECT as being sensitive to a QST parameter (positive), and patients who responded on painDETECT as being not sensitive to a QST parameter (negative). The score “strongly” was used as the cut-off score for answers on the painDETECT. Data are shown as mean (SD) for untransformed data and retransformed mean for log-normally distributed data (CPT, MDT, PPT).

	HC (n = 31)	CxRAD positive	CxRAD negative	p-value
<i>Is light touching in this area painful?</i>		n = 0	n = 23	
DMA	0 had DMA	0 had DMA	1 had DMA	
<i>Is cold or heat in this area occasionally painful?</i>		n = 1	n = 22	
CPT (°C)	7.0	26.2	10.7 ^{bd}	
HPT (°C)	46.7 (1.9)	36.6	45.8 (4.0) ^d	
<i>Do you suffer from a sensation of numbness in the area that you marked?</i>		n = 11	n = 12	
MDT (mN)	1.9	4.5 ^b	3.3	0.012
VDT (x/8)	6.1 (0.9)	5.4 (1.2) ^b	5.4 (1.1) ^b	0.004
<i>Does slight pressure in this area trigger pain?</i>		n = 5	n = 18	
PPT (kPa)	439	335 ^{b, c}	424	<0.001

DMA: dynamic mechanical allodynia, CPT: cold pain threshold, HPT: heat pain threshold, MDT: mechanical detection threshold, VDT: vibration threshold, PPT: pressure pain threshold.

^aSignificantly different to HC (p < 0.001).

^bSignificantly different to HC (p < 0.05).

^cSignificantly different to CxRAD negative (p < 0.001).

^dIndependent T-test

Table S5

Comparison of each QST parameter between healthy controls (HC), patients with fibromyalgia (FM) who responded on painDETECT as being sensitive to a QST parameter (positive), and patients who responded on painDETECT as being not sensitive to a QST parameter (negative). The score “strongly” was used as the cut-off score for answers on the painDETECT. Data are shown as mean (SD) for untransformed data and retransformed mean for log-normally distributed data (CPT, MDT, PPT).

	HC (n = 31)	FM positive	FM negative	<i>p</i> -value
<i>Is light touching in this area painful?</i>		n = 1	n = 21	
DMA	0 had DMA	0 had DMA	3 had DMA	
<i>Is cold or heat in this area occasionally painful?</i>		n = 5	n = 17	
CPT (°C)	7.0	17.4 ^a	29.0 ^{a, c}	< 0.001
HPT (°C)	46.7 (1.9)	40.5 (3.6) ^a	39.2 (3.3) ^a	< 0.001
<i>Do you suffer from a sensation of numbness in the area that you marked?</i>		n = 3	n = 19	
MDT (mN)	1.9	7.1	2.7 ^d	
VDT (x/8)	6.1 (0.9)	6.6 (0.8)	5.3 (1.1) ^{b, d}	
<i>Does slight pressure in this area trigger pain?</i>		n = 11	n = 11	
PPT (kPa)	439	201 ^b	167 ^a	< 0.001

DMA: dynamic mechanical allodynia, CPT: cold pain threshold, HPT: heat pain threshold, MDT: mechanical detection threshold, VDT: vibration threshold, PPT: pressure pain threshold.

^aSignificantly different to HC ($p < 0.001$).

^bSignificantly different to HC ($p < 0.05$).

^dIndependent T-test

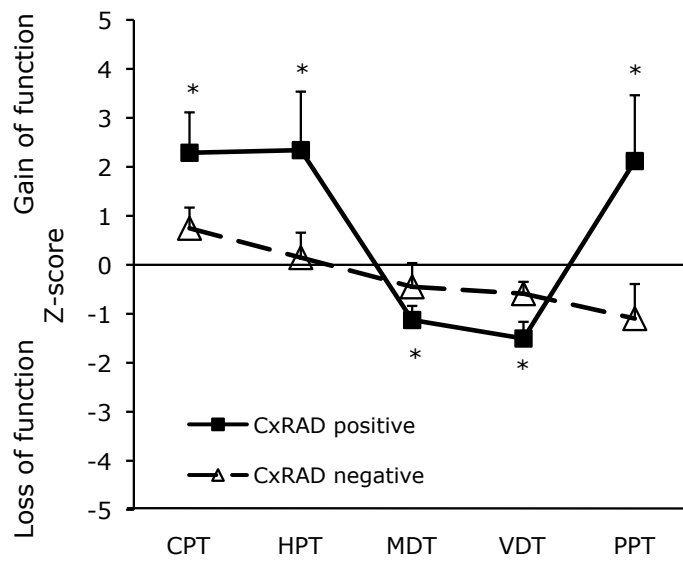


Fig. 1. Sensory profiling of patients with cervical radiculopathy (CxRAD). The z-score sensory profiles are shown for cold pain threshold (CPT), heat pain thresholds (HPT), mechanical detection threshold (MDT), vibration detection threshold (VDT), pressure pain threshold (PPT) in patients responding positive (filled square) and negative to verbal descriptors (empty triangle). Data are shown as the mean. The score “moderate” was used as the cut-off score for answers on the painDETECT.

*Significantly different from HC ($p < 0.05$).

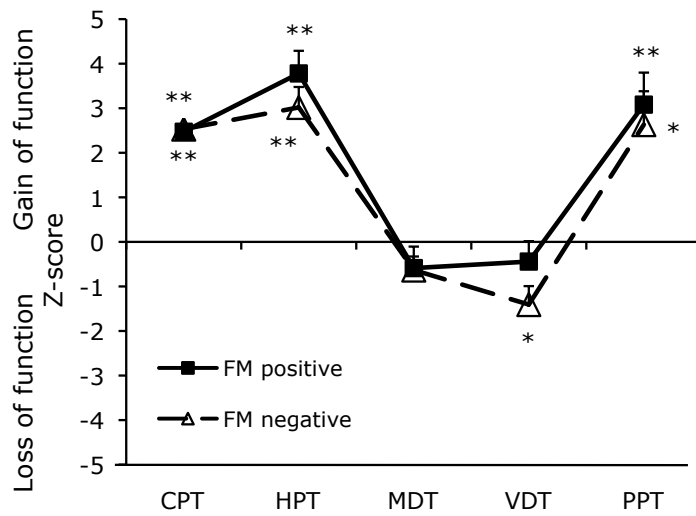


Fig. 2. Sensory profiling of patients with fibromyalgia (FM). The z-score sensory profiles are shown for cold pain threshold (CPT), heat pain thresholds (HPT), mechanical detection threshold (MDT), vibration detection threshold (VDT), pressure pain threshold (PPT) in patients responding positive (filled square) and negative to verbal descriptors (empty triangle). Data are shown as the mean. The score “moderate” was used as the cut-off score for answers on the painDETECT.

*Significantly different from HC ($p < 0.05$).

**Significantly different from HC ($p < 0.001$).