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Neuropathic pain components are common in subjects with painful cervical radiculopathy, but not in subjects with non-specific neck-arm pain

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Abstract

Objectives: The aim of this study was to investigate, using quantitative sensory testing (QST) parameters and the painDETECT (PD-Q) screening questionnaire, the presence of neuropathic pain (NeP) in subjects with unilateral painful cervical radiculopathy (CxRAD) and in subjects with unilateral non-specific neck-arm pain associated with heightened nerve mechanosensitivity (NSNAP). **Methods:** All subjects completed the PD-Q prior to QST. QST was performed bilaterally in the maximal pain area and the affected dermatome in 23 subjects with painful C6 or C7 radiculopathy and 8 subjects with NSNAP following a C6/7 dermatomal pain distribution. **Results:** Subjects with CxRAD demonstrated a significant loss of sensory function in mechanical ($p \leq 0.021$) and vibration sense ($p \leq 0.003$) on the symptomatic side compared to the asymptomatic side in both tested body regions and in the dermatome reduced cold detection ($p = 0.021$) and pressure pain sensitivity ($p = 0.005$), findings consistent with nerve root damage. These sensory alterations in the maximal pain area/symptomatic side are confirmative for the presence of NeP. In contrast to these QST data, only 30% of subjects with CxRAD demonstrated a NeP component according to the PD-Q score. In subjects with NSNAP, a significant side-to-side difference was demonstrated for warm detection threshold in the dermatome ($p = 0.030$). The PD-Q score indicated that NeP components were unlikely in this group. **Discussion:** QST data suggest that NeP is likely to be observed in subjects with painful CxRAD, but not in subjects with NSNAP.

Keywords (3-5): Neuropathic pain; quantitative sensory testing; neck-arm pain; cervical radiculopathy; painDETECT

INTRODUCTION

Nerve-related neck-arm pain disorders are heterogeneous with clinical signs and symptoms and pattern of pain and sensory abnormalities varying widely between individuals. While a neuropathic mechanism is commonly implied in disorders such as painful cervical radiculopathy (CxRAD)[1], patients are likely to present with a mix of nociceptive and neuropathic pain (NeP), more commonly referred to as a mixed pain syndrome[2-7]. Both NeP and mixed pain sydnromes can be intense forms of pain, and patients with these disorders are characterised by impaired physical and mental quality of life and a substantial level of disability, leading to increased health care costs compared to patients with nociceptive pain[5,6,8]. Characterisation of these patients with respect to the 'pain mix', and the possible dominance of one pain type in mixed pain syndromes is of therapeutic relevance[9], as NeP in particular requires targeted management.

This study investigated two samples of subjects with nerve-related neck-arm pain: subjects with painful CxRAD and subjects with non-specific neck-arm pain (no clinical signs of radiculopathy) associated with heightened nerve mechanosensitivity (NSNAP). Heightened nerve mechanosensitivity is defined as pain in response to upper limb movement that causes nerve elongation[10]. This condition can present as a discrete disorder without any signs of nerve damage such as sensory or motor loss[10,11]. Subjects with CxRAD and NSNAP may demonstrate similar pain characteristics such as pain with or without negative/positive sensory symptoms, however the mix of NeP and nociceptive pain may vary and has not yet been defined in these groups.

Quantitative sensory testing (QST) has been recommended for accurate sensory profiling in the assessment of patients with NeP[12]. A side-to-side comparison of QST data within patient groups is recommended[13,14], as patients may present with subtle sensory alterations not identifiable by comparison to reference data. To date, only one study investigated sensory abnormalities in patients with CxRAD[15], however QST measurements were not taken from the patient's maximal pain area, as is required for the assessment of NeP components[12,16]. No study, to our knowledge, has established the QST profile of patients with NSNAP comparable to our cohort.

Further, the use of NeP screening tools for identification of NeP components has been recommended[12]. The painDETECT (PD-Q)[17], a validated self reported NeP screening tool, has increasingly been employed for the identification of NeP in patients with low back and leg pain[17-20], however, its usefulness in the screening of NeP in patients with neck-arm pain has not been reported.

The purpose of this study was to investigate, using QST and the PD-Q, the presence of NeP components in subjects with CxRAD and subjects with NSNAP. We hypothesized that:

1. For subjects with CxRAD, there would be a significant side-to-side difference in QST parameters between the symptomatic and asymptomatic side.
2. For subjects with NSNAP, there would be no significant side-to-side difference in QST parameters between the symptomatic and asymptomatic side.

3. There would be no difference in the PD-Q score between subjects with CxRAD and subjects with NSNAP.

MATERIALS AND METHODS

Subjects

Subjects were recruited as part of another concurrent study[21]. For inclusion into the study, all subjects were required to fulfil the inclusion criteria of unilateral neck pain and arm pain/paraesthesia in a C6/7 distribution, symptom duration of 3 to 18 months and current pain intensity ≥ 2 on a visual analogue scale (VAS). Subjects with CxRAD were required to demonstrate signs of either C6 or C7 nerve root dysfunction with neurological deficits consistent with the affected nerve root level and with compressive radiculopathy (either absent or diminished reflexes and/or myotomal weakness and dermatomal sensory deficits of light touch and/or vibration sense). Additionally, subjects were required to have a demonstrable clinically relevant abnormality on imaging studies[16,22] that indicated compromise of the exiting nerve root at the relevant spinal level. Inclusion criteria for subjects with NSNAP were no clinical signs of radiculopathy and evidence of increased peripheral nerve sensitivity to mechanical stimuli[10], including pain in response to a nerve provocation test in the upper limb (NPT_{MEDIAN})[10]. Exclusion criteria for both groups were: evidence of a metabolic or a medical disease; other neurological or psychiatric disease; a history of cardiovascular disease; and an insufficient level of English. Subjects had to be able to understand the PD-Q questions and independently complete the PD-Q. Specifically, subjects had to be able to understand the instructions and requirements for the QST procedures and be able to give a reliable response that did not depend on translation. Subjects were not screened for the presence of depression or anxiety.

Prior to participation, all subjects were examined by a highly qualified Musculoskeletal Physiotherapist (Master qualification) who had extensive clinical experience within a tertiary pain medicine unit in triaging patients with suspected nerve lesions and associated NeP to ascertain they met the inclusion criteria (BT). The assessment included the subject's history, pain drawings, pain description for their neck and for their arm pain and pain behaviours, musculoskeletal and neurological examination and review of reports of diagnostic tests (imaging, nerve conduction studies). The diagnostic classification of both participating groups was verified by a Fellowship-trained spinal Neurosurgeon (GL) and a Fellowship–qualified (Fellow of the Australian College of Physiotherapists) Specialist in Musculoskeletal Physiotherapy (TH), both of whom were blinded to the clinician's subject classification. Each Fellow independently reviewed the subjects' notes and the results of any medical investigations. Only subjects whose clinical presentation was confirmed by all three examiners were included in the data analyses (see Fig. 1).

Subjects were recruited from private clinics and physiotherapy, pain management and neurosurgery departments at five local metropolitan hospitals in Perth, Western Australia, and from the local community via radio and newspaper advertising (see flow chart of recruitment Fig.1). All referrals of patients with neck/upper limb symptoms to the neurosurgery triage clinic received between September 2007 and November 2010 were reviewed by the investigator (author BT). Patients in whom the referral indicated the possible presence of a unilateral nerve lesion/disease were selected and were clinically examined. The study protocol and recruitment procedures were approved by the local Ethics Committees of all participating institutions and adhered to the ethical guidelines of

the Declaration of Helsinki. All subjects were asked to sign an informed consent form prior to participation.

Questionnaire

A battery of questionnaires was used to clinically characterise the subject groups and to incorporate the multidimensional aspects of pain as proposed by the IMMPACT guidelines[23]. This battery was administered immediately before the QST. The instructions given on the questionnaires were the instructions consistent with the standardized instruments. All subjects completed the short form-36 health questionnaire (SF-36v2®)[24] to assess health-related quality of life. The Hospital Anxiety and Depression Scale (HADS)[25] was used to screen for anxiety and depression, with two outcome scores generated, each with a maximum score of 21 for each parameter. Scores of ≤ 10 for each are considered within normal range. Sleep quality over the last week was recorded on a 100-cm VAS with the end points 0 cm (good sleep) and 10 cm (bad sleep)[26]. In addition, to assess fear avoidance behaviours, subjects completed the Tampa Scale of Kinesiophobia (TSK)[27]. This questionnaire contains 17 items that relate to fear of movement and fear of (re) injury. A score ≥ 40 is considered to indicate significant kinesiophobia[28]. The Neck Disability Index (NDI)[29] was used to assess the level of subject disability. It is a well-validated ten-item questionnaire[30,31]. Scores of < 4 indicate no disability, 5 – 14 mild disability, 15 – 25 moderate disability, 25 – 34 severe disability, and > 35 complete disability[29].

The PD-Q[17] consists of one descriptor relating to temporal and one to spatial pain

characteristics and of seven weighted sensory descriptors. These sensory descriptors relate to the main pain area that a person records on the body chart of PD-Q[17]. The lowest weight for each descriptor is 0, indicating that the person does not experience the relevant sensation, and the highest weight is 5, indicating the sensation is felt very strongly. PD-Q classifies patients into three groups, defined by Freynhagen et al[17] as follow: the result is negative = a NeP component is unlikely (score 0 – 12), the result is unclear = the result is ambiguous, however a NeP component can be present (score 13 – 18), or the result is positive = a NeP is likely (score 19 – 38). The strongest and average pain intensity over the last four weeks was recorded on a numeric rating scale (NRS) (0 = no pain, 10 = maximum pain) as part of the PD-Q[17]. Subjects were not given any specific instructions on how to complete the PD-Q other than the instructions given on the questionnaire.

Quantitative sensory testing

The standardised QST protocol of the German Research Network on Neuropathic Pain (DFNS) was employed using the same equipment and standardised instructions as outlined by Rolke et al.[14,32] The test battery comprised the following assessments: cold and warm detection thresholds (CDT, WDT); the number of paradoxical heat sensations (PHS) during the procedure of alternating warm and cold stimuli (thermal sensory limen (TSL)); cold and heat pain thresholds (CPT, HPT); mechanical detection threshold (MDT); mechanical pain threshold (MPT); stimulus-response functions: mechanical pain sensitivity (MPS) and dynamic mechanical allodynia (DMA); wind-up ratio (WUR); vibration detection threshold (VDT) and pressure pain threshold (PPT).

QST was performed over the maximal pain area, as indicated by the subjects and the corresponding contralateral mirror side. In subjects with CxRAD, additional testing was conducted in the exact dermatomal area of sensory loss as determined during clinical examination, and for subjects with NSNAP in the area of distal paraesthesia or pain, plus in the contralateral side for both groups. While the QST in the dermatome does not give information about the presence of NeP components[16], it does assist to further characterise each subject group and to detect possible sensory alterations that may be indicative of a nerve root lesion. Testing was conducted by one investigator (BT) in a laboratory with a constant room temperature. The investigator was blind to the results of the PD-Q as the questionnaire was scored after the QST testing. As the clinical examination of subjects and QST testing were not performed on the same day, the key inclusion criteria for each group (for CxRAD: signs of nerve root dysfunction, for NSNAP absence of nerve root dysfunction and presence of heightened nerve mechanosensitivity) were reassessed prior to QST. Subjects were asked not to take any analgesics on the day of testing. A sample size calculation, based on QST data by Rolke et al[14], estimated that a sample of 25 in each subject group was needed to detect clinically significant differences between the symptomatic and asymptomatic arm.

Nerve provocation test (NPT_{MEDIAN})

The NPT_{MEDIAN} was performed after the QST as described previously[11]. The range of elbow extension was measured with an electro-goniometer (SG110, Biometrics Ltd, United Kingdom). The subject was asked to press an external trigger at the first onset of pain or at the increase of their resting pain (P1) if present, and at a second time point

when the subject reached their pain tolerance (P2) for this movement. Elbow extension was performed to the end of joint range or to P2, whichever occurred first. The NPT_{MEDIAN} was performed three times on each side and the mean value of three recordings of P1 and P2 was used for analysis. Subjects who did not report consistently an onset of P1 or P2 in all three trials (i.e. they reported an onset in only 1 or 2 trials) were excluded from the analysis (P1 asymptomatic side n = 3). Four subjects with CxRAD could not be tested due to high pain levels and the associated potential for exacerbation of their condition.

Statistical analysis

SPSS version 17 was used for all analyses. All data were analysed for their distribution properties (Shapiro-Wilk test). An independent T-test was used to compare symptom duration, pain intensity, sleep quality, the NDI, TSK and PD-Q scores between subject groups. Anxiety and depression scores and the physical and mental component summary scores of the SF-36 were compared using the Mann-Whitney-U Test.

The QST variables HPT and VDT were normally distributed. All other QST data were normally distributed in log-space and were log-transformed prior to statistical analysis[32]. Within each group, QST data were compared between sides using a paired T-test. For subjects with CxRAD, a side-to-side comparison was also performed for two subgroups, based on imaging results: (i) subjects with nerve root compression due to a disc protrusion/herniation (n = 14), and (ii) subjects with nerve root compression due to osteophytic stenosis (n = 7). Responses to the NPT_{MEDIAN} were compared using

Wilcoxon Signed Ranks Test, as data were not normally distributed. Significance was accepted at $p < 0.05$ for all analyses.

RESULTS

Subject characteristics

Twenty-three subjects with painful C6 or C7 CxRAD (8 female; mean age 46.3 ± 9.6 years) and 8 subjects with NSNAP following a C6/C7 dermatomal distribution (7 female; mean age 45.1 ± 14.9 years) participated in the study. Eleven subjects presented with a C6 radiculopathy and 12 subjects with a C7 radiculopathy. Their maximal pain areas were as follows: upper trapezius muscle n = 4; paravertebral cervical spine n = 2; paravertebral thoracic spine n = 7; above and below spine scapula n = 2; upper arm n = 5; forearm n = 2; just above the elbow n = 1. All subjects with CxRAD had undergone medical imaging (Computed tomography (CT) n = 1; Magnetic Resonance Imaging (MRI) n = 22). Based on the imaging findings, 7 subjects demonstrated nerve root compression due to osteophytic stenosis, 2 subjects due to a disc/osteophytic complex and 14 subjects due to a disc protrusion/herniation. One subject with NSNAP presented with pain in a C6 dermatomal distribution and 7 subjects with pain in a C7 dermatomal distribution. Six patients reported the upper trapezius muscle as their maximal pain area, and 2 patients the paravertebral thoracic spine. Only two subjects with NSNAP had medical imaging (CT) performed of the cervical spine. In these two subjects, CT did not demonstrate any abnormality indicating compromise of a nerve root at the relevant spinal level.

Table 1 presents demographic data of all subjects. The independent T-test showed no significant differences between subject groups in age, symptom duration, pain intensities, fear avoidance behaviour and scores on the NDI. NDI scores reflected moderate

disability for patients with CxRAD and mild disability for patients with NSNAP. There were no significant differences between subject groups physical and mental components of the SF-36 and anxiety and depression scores (Mann-Whitney-U Test). The anxiety scores were within the normal range in over 75% of patients and the depression scores in over 91% of patients. Subjects with CxRAD had a significantly higher score on the PD-Q compared to subjects with NSNAP (independent T-test: $p = 0.038$). Seven subjects (30%) with CxRAD reported a score of ≥ 19, indicating the 'likely' presence of NeP and one subject (12.5%) with NSNAP scored ≥ 19. A larger proportion of subjects with CxRAD were on pain medication compared to the group with NSNAP.

The subjects' self-reported pain descriptors for their neck and arm pain obtained during the clinical examination are documented in Table 2. Both groups demonstrated clinical signs of heightened nerve mechanosensitivity in the symptomatic arm, indicated by a significant side-to-side difference in the range of motion of elbow extension deficit at the onset of P1 ($p < 0.03$) and P2 ($p < 0.013$) between arms (Fig. 2) (Wilcoxon Signed Ranks Test). In both groups, the pain onsets occurred much earlier in range in the symptomatic arm compared to the asymptomatic arm.

Side-to-side comparison in subjects with CxRAD

For subjects with CxRAD, in the maximal pain area vibration and mechanical detection sense were significantly reduced on the symptomatic side compared to the asymptomatic side (paired T-test: VDT: $p = 0.003$; MDT: $p = 0.021$) (Table 3). Side-to-side comparisons of all other QST parameters in the maximal pain area were not significant.

In the dermatome, there was a loss of function on the symptomatic side in cold detection (CDT: p = 0.021), mechanical detection (MDT: p = < 0.001), vibration detection (VDT: p = 0.001) and pressure pain sensitivity (PPT: p = 0.005) (Table 4). There were no side-to-side differences in any other QST parameters. Reports of DMA and PHS were infrequent. One subject with CxRAD demonstrated DMA bilaterally in the maximal pain area and on the symptomatic side in the dermatome. PHS was reported by one subject once in the maximal pain area on the symptomatic side, and by a different subject once on the asymptomatic side. Two subjects reported PHS once on the asymptomatic side of the dermatome. Individual QST data are presented in Table 5 (Supplemental Digital Content 1). One subject appeared to present with only one sensory alteration in the maximal pain area on the symptomatic side. All other subjects seemed to demonstrate two or more sensory alterations on the symptomatic side. Eleven subjects demonstrated cold hyperalgesia (≥ 15°)[33] on the symptomatic side, and in five of these subjects cold hyperalgesia occurred bilaterally. Some subjects presented with reduced pressure sensitivity in their main pain area, while others presented with increased pressure sensitivity.

Subjects with nerve root compression due to osteophytic stenosis (n = 7) demonstrated a loss of function on the symptomatic side of the maximal pain area in warm detection (WDT: p = 0.034), TSL (p = 0.010), vibration detection (VDT: p = 0.007) and pressure sensitivity (PPT: p = 0.029), and a loss of function in the symptomatic dermatome in cold detection (CDT: p = 0.007), mechanical (MDT: p = 0.003) and vibration detection (VDT: p = 0.032) compared to the asymptomatic side (paired T-test). Subjects with nerve root

compression due to a disc protrusion/herniation (n = 14) demonstrated reduced mechanical detection sense on the symptomatic side in the maximal pain area (MDT: $p = 0.013$) and reduced mechanical and vibration sense and pressure sensitivity in the symptomatic dermatome (MDT: $p < 0.001$; VDT: $p = 0.004$; PPT: $p = 0.006$) (paired T-test).

Side-to-side comparison in subjects with NSNAP

In subjects with NSNAP, in the maximal pain area, there was no side-to-side difference in any QST parameter (Table 3; paired T-test). In the dermatome, the side-to-side comparison demonstrated a significant loss of function on the symptomatic side in WDT ($p = 0.030$) (Table 4). No other side-to-side comparisons were statistically different. No subject with NSNAP demonstrated DMA in any body region. PHS was reported by one subject twice on the symptomatic side in the maximal pain area. Individual QST data are presented in Table 6 (Supplemental Digital Content 2). Three subjects demonstrated more than one sensory alteration in their maximal pain area on the symptomatic side (subject 3, 4, 5). Three subjects (subject 1, 4, 8) demonstrated bilateral cold hyperalgesia.

DISCUSSION

This study investigated differences in QST parameters between symptomatic and asymptomatic sides and the presence of NeP components in subjects with painful CxRAD and subjects with NSNAP, using QST and the PD-Q. The subject groups demonstrated similar clinical profiles, as indicated by their psychometric data, but the dominant pain type differed between groups. In subjects with CxRAD, QST findings demonstrated a significant loss of function mediated by non-nociceptive sensory fibers in the painful innervation territory of the affected nerve root on the symptomatic side compared to the asymptomatic side, findings consistent with the characteristics of NeP[12]. The PD-Q identified 30% of subjects with CxRAD demonstrating the likely presence of NeP. In subjects with NSNAP, the absence of significant side-to-side differences in any QST parameters in the maximal pain area and the results of PD-Q suggest that NeP components were unlikely.

Subjects with CxRAD demonstrated significant side-to-side differences in mechanical and vibration detection in their maximal pain area, the symptomatic side being less sensitive to the stimuli than the control side. The hypoaesthesia on the symptomatic side is consistent with a loss of function due to nerve root damage and with the presence of NeP[16], and consistent with both findings in patients with peripheral nerve injury[34-36] and for patients with segmental post-surgical NeP[34]. Furthermore, almost all subjects with CxRAD demonstrated 2 or more sensory alterations in their maximal pain area. It has been reported that the frequency of sensory aberrations tends to increase with the likelihood of the presence of NeP[37]. The significant loss in the affected dermatome of

cold, mechanical and vibration detection and pressure sensitivity, also support the presence of a nerve root lesion. The loss of cold detection is comparable with findings in affected dermatomes of patients with cervical[15] and lumbar radiculopathy[38-42] and the loss of mechanical and vibration detection has also been reported in the affected dermatomes of patients with lumbar radiculopathy[38].

QST data in CxRAD is scarce, with only one study profiling this patient group[15], and findings demonstrated bilateral cold and pressure pain hypersensitivity in the cervical spine area. Comparison of our data to these findings is however limited, as the majority of our subjects did not have their maximal pain area in the cervical spine, furthermore the cervical spine area tested in the Chien et al study[15] did not necessarily reflect the maximal pain area of these patients. On a group level, our subjects with CxRAD did not demonstrate cold hypersensitivity compared to the asymptomatic side, however individual QST data revealed that 48% of our subjects presented with cold hyperalgesia. Cold hyperalgesia is a common sequel of peripheral nerve injury [35,43-45], but it can also occur in the absence of nerve damage and in the absence of pain, as documented in patients with painless peripheral nerve injuries[35,44] and in patients with depression without pain[46]. Bilateral cold hyperalgesia, as seen in some of our subjects with CxRAD, was also observed in individuals with painful and painless peripheral nerve injuries[44]. Mechanisms underlying cold hypersensitivity are still not fully understood and likely include both central[47-49] and peripheral nervous system mechanisms[50-52].

In contrast to patients with for example peripheral nerve injury demonstrating mechanical hyperalgesia[44,53,54], such a positive sensory sign was not a dominant feature in our subjects with CxRAD. Increased pressure sensitivity was observed in some individuals with CxRAD, however others demonstrated reduced pressure sensitivity. Similar pressure pain dichotomy has also been documented in individuals with peripheral nerve injury[44].The variances between individual subjects indicates the likely presence of sub-groups with differing somatosensory profiles within our cohort, similar to somatosensory profiles reported for patients with lumbar radiculopathy[55] and for patients with peripheral NeP [53,54]. Somatosensory heterogeneity within a clinical disorder may account for differing individual responses to pharmaceutical interventions, as seen in clinical trials of patients with lumbar and cervical radiculopathies[56,57].

Furthermore, we found differing sensory profiles between groups depending on the cervical imaging findings. The subject group with mechanical nerve root compression due to osteophytic stenosis demonstrated a loss of small and large sensory fiber function in the symptomatic maximal pain area, whereas a loss of only large sensory fiber function occurred in the disc herniation group. It is unclear why these differences in sensory phenotypes occurred, and studies with larger sample sizes are required to further attest these findings. Our data highlight the need for individual patient examination including clinical history as well as clinical examination, screening for NeP and the presence of psychological factors and imaging if appropriate. This approach is required in order to make a more fully informed clinical decision re the sensory profile and how that may link with targeted management. For example, a patient characterised by increased pain

sensitivity may require specific behavioural and cognitive management, possibly different pain medication and appropriate physical intervention such as pacing strategies compared to a patient without heightened pain sensitivity.

According to the recently proposed diagnostic grading system of certainty for the presence of NeP[16], on a group level our cohort with CxRAD demonstrated definite NeP, however this does not exclude the simultaneous presence of nociceptive pain. Other structures (e.g. joints, discs, muscles) are likely involved in contributing to nociceptive input and potentially impacting the total "pain experience". Fourteen subjects (61%) indicated the neck/trapezius/scapula/thoracic area as their main area of pain which correlates with specific cervical nerve root pain distributions[58], but is also a common area for musculoskeletal pain and referred somatic pain[59]. Coexisting musculoskeletal disorders are common in patients with suspected cervical radiculopathy[60] and nociceptive pain may be located in the same area as the innervation territory of the affected nerve structure. This consideration might complicate the interpretation of sensory aberrations, as sensory changes can be present in non-NeP conditions[61-64].

In our current study, the likely presence of mixed pain[3] is reflected in the PD-Q scores and the self-volunteered pain descriptors. Subjects used self-reported pain descriptors commonly identified for NeP[65], some of these matching the descriptors used in PD-Q, but subjects also used descriptors commonly identified for nociceptive pain[66]. The fact that 30% of our radiculopathy cohort reported a score of ≥ 19, and 65% reported a score ≥ 16, may suggest that on a theoretical continuum between 'dominantly nociceptive' and

'dominantly neuropathic' pain[67], some of these subjects' sensory profiles were characterised dominantly by NeP components compared with nociceptive pain.

Subjects with NSNAP did not demonstrate any side differences in QST parameters in their maximal pain area. Hence, based on the pain distribution and history this subject group would be classified as having 'possible' NeP[16]. However, some individuals did present with sensory alterations in their maximal pain area (bilateral cold hyperalgesia, apparent reduced vibration sense). It stands debatable if these sensory aberrations are indicative of NeP, as such sensory changes have also been reported in non-NeP conditions[61-64]. Hence, clinical judgement based on the findings of a comprehensive clinical examination, including the assessment of neural and musculoskeletal structures and other organ systems, is crucial for the determination of underlying pain types.

With the exception of reduced warm detection in the symptomatic arm, where the difference between sides was < 1° and of doubtful clinical significance, we did not find any side differences for QST parameters in the dermatome in subjects with NSNAP. The interpretation of what entails a clinically significant difference for thermal detection thresholds is inconsistent[14,36,44,68]. Based on clinical judgment, some authors consider a side difference of ≥ ± 1° as pathological[36], others argue a side difference ± 1° is within normal range[14,68]. More normative data from various body regions are required to attest these statements.

The QST findings in our subjects with NSNAP do not suggest the presence of NeP components and on the whole this is in accordance with the PD-Q score in this group, with the exception of one individual who scored >19. This person may have been an outlier with a maximum score (5) for the presence of a burning sensation and tingling and a high score (4) for the presence of numbness in her pain area. The weighing of the pain descriptor item of PD-Q may lead to skewing of the final score of PD-Q towards the presence of NeP. Apart from the descriptors for the presence of paraesthesia being used by all subjects, a minority of subjects used self-reported pain descriptors common to NeP.

The main characteristic for this group was the side-to-side difference in pain response to the NPT_{MEDIAN}, consistent with a heightened pain response in the symptomatic arm. Our results suggest that the clinical presentation of heightened nerve mechanosensitivity as a discrete disorder should not equate with the presence of a NeP component. This subject group with NSNAP did not meet the new definition of NeP, i.e. "pain caused by a lesion or disease of the somatosensory nervous system"[69] as the combination of clinical examination findings, QST data and available diagnostic tests did not provide evidence for the presence of a nerve lesion. Heightened nerve mechanosensitivity can coexist with nerve lesions and NeP, as demonstrated in our subjects with CxRAD and another patient group[15]. In fact, heightened nerve mechanosensitivity in the lower limb, as identified by the straight leg raise test, was reported to be part of a cluster of physical examination discriminative indicators for NeP in lumbar radiculopathy[70]. However the role of heightened nerve mechanosenstivity as discriminative factor for NeP in patients with CxRAD has not yet been determined.

The PD-Q[17] was specifically designed to identify NeP components in patients with low back pain with and without referred pain, and therefore it was anticipated that the questionnaire could be transferable to patients with neck-arm pain. However, the PD-Q[17] identified only 30% of subjects with cervical radiculopathy as having NeP. This seemingly lowered capability of PD-Q to identify NeP compared to the sensitivity of 85% in the original validation study[17] may be related to a mismatch between the pain descriptors reported by the subjects and the pain descriptors included in PD-Q. For example, sensitivity to light touch was not a dominant feature in our radiculopathy cohort, consistent with findings in patients with lumbar radiculopathy[55], and similarly cold and pressure sensitivity and burning pain were only present in some individuals. Using PD-Q, Mahn et al[55] identified one sub-group of patients with radicular leg pain presenting with only one dominant sensory descriptor contained in the PD-Q[55]. The PD-Q had been originally validated in a dichotomous patient sample (NeP/nociceptive pain) and patients with mixed pain presentations were excluded[17]. Splitting patients into two categories may limit the ability to generalise results to a mixed pain clinical population. It remains unclear if the discrepancy in performance of the PD-Q in our study and in the original validation study[17] relates to variations in patient cohorts, as specific patient characteristics were not reported in the original study[17].

Another possible explanation for the lowered sensitivity of PD-Q may be the weighing of the item descriptors. In a study of patients with spinal cord injuries[71], cut-off levels for discriminating NeP were low in the weighted items of PD-Q and it was suggested that the

intensity of the sensory descriptor may not be that important for discrimination, but simply its presence or absence. Summarized our findings suggest that the PD-Q may not be suitable for the identification of NeP in subjects with cervical radiculopathy and mixed pain.

The strength of our study lies in the robust methods, including a complete examination (clinical and standardized QST) of patients with CxRAD and patients with NSNAP and using tight inclusion/exclusion criteria. While the latter was chosen to ensure our groups were homogeneous, the strict inclusion criteria brought with them the compromise of obtaining smaller sample sizes than anticipated and also limit the generalisability of our findings. The sample size of our subject group with NSNAP was modest and this might limit the power to demonstrate significant side-to-side differences. Despite extensive recruitment efforts over the period of three years, we were not able to recruit more subjects fulfilling the criteria for NSNAP inclusion. Based on our recruitment strategy, and given the fact that many subjects were recruited from a neurosurgery triage clinic, the prevalence of the discrete disorder of NSNAP would appear to be low. Only anecdotal data exist on the prevalence of this condition. A further limitation of the study lies in the non-blinding of the investigator performing the QST testing and future research would be strengthened by a design that incorporated blinding.

In conclusion, although subjects with CxRAD and subjects with NSNAP had commonalities in their clinical pain pattern and clinical profile, the dominant pain type differed between subject groups, as indicated by the specific QST profiles and associated

responses to the PD-Q. NeP was more common in subjects with CxRAD, whereas subjects with NSNAP were characterised by predominantly nociceptive pain components. The variability of sensory profiles between individuals within one subject group highlights the importance of individual assessment for the identification of NeP components for patients with mixed pain syndromes. The PD-Q seemed unsuitable for the identification of NeP in our subjects with CxRAD and should not be used as a surrogate for clinical examination. Our somatosensory profiles for these clinical groups may assist clinicians in targeting more specific management for these patients and reinforces the importance of skilled clinical examination in making clinical management decisions for patients with suspected NeP.

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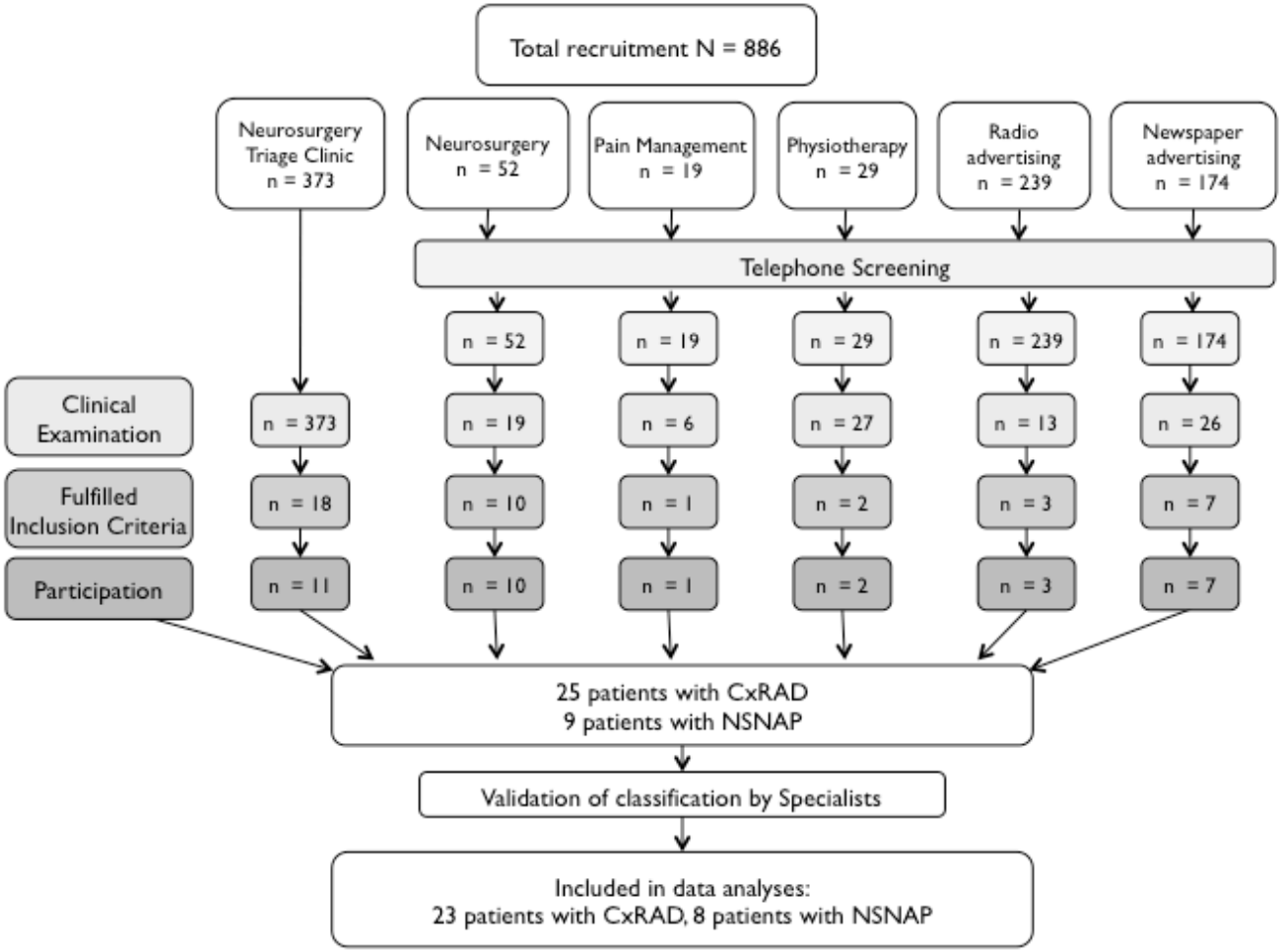

FIGURE 1. Flow chart of recruitment of subjects with cervical radiculopathy (CxRAD) and subjects with non-specific neck-arm pain associated with heightened nerve mechanosensitivity (NSNAP)

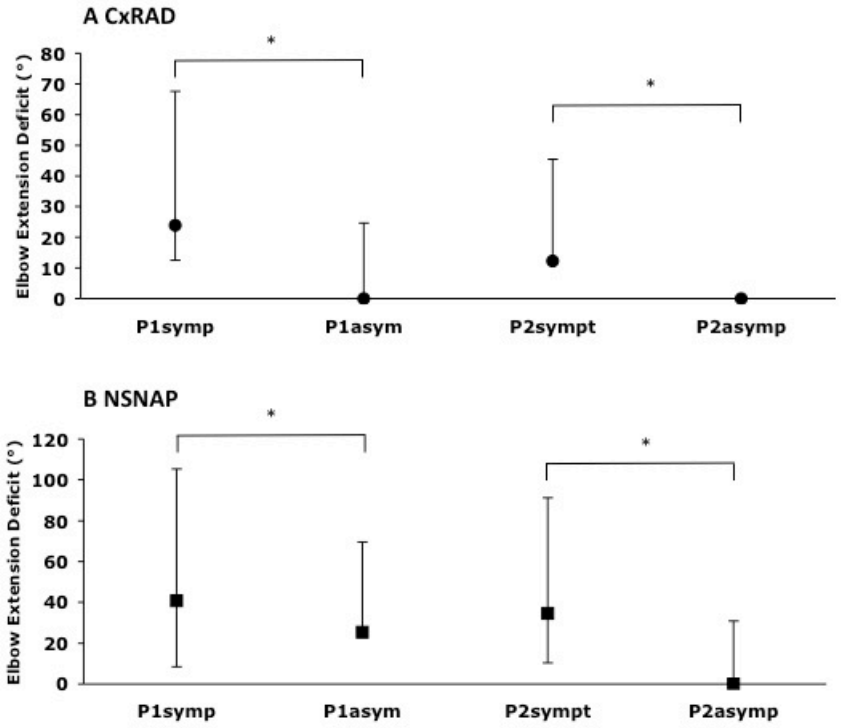

FIGURE 2. Elbow extension ROM deficit at onset of pain (P1) and at the limitation of movement due to pain (P2) in the symptomatic (sympt) and asymptomatic (asympt) arm in subjects with cervical radiculopathy (CxRAD) (A) and subjects with non-specific neck-arm pain with associated heightened nerve mechanosensitivity (NSNAP) (B). Data are presented as medians with (25^{th} and 75^{th} percentiles).

*Significant difference between sides ($p < 0.05$)

TABLE 1. Demographics and clinical profiles of subjects with cervical radiculopathy (CxRAD) and subjects with non-specific neck-arm pain associated with heightened nerve mechanosensitivity (NSNAP).

	CxRAD (n = 23)	NSNAP (n = 8)	*p*
Age (years)*	46.3 (9.6)	45.1 (14.9)	0.833
Gender (female, n)	8	7	
Symptom duration (months)*	7.6 (4.1)	8.1 (3.0)	0.766
Maximal pain intensity during last 4 weeks (NRS 0-10)*	7.2 (2.2)	7.6 (0.6)	0.686
Average pain intensity during last 4 weeks (NRS 0-10)*	5.0 (2.1)	5.1 (0.6)	0.914
Sleep quality during last week (VAS)*	5.3 (2.7)	5.9 (2.2)	0.591
Hospital Anxiety and Depression Scale			
Anxiety score (HADS)[#]	6.0 (4.0; 9.0)	8.0 (6.2; 10.5)	0.295
Within normal range (≤ 10), n	21(91%)	6 (75%)	
Depression score (HADS)[#]	3.0 (2.0; 6.0)	3.5 (1.2; 6.7)	0.982
Within normal range (≤ 10), n	21 (91%)	8 (100%)	
SF-36			
Physical Component[#]	40.6 (33.9; 46.6)	46.4 (41.2; 53.2)	0.121
Mental Component[#]	52.3 (39.1; 56.6)	48.4 (32.1; 52.7)	0.187
Neck Disability Index*	16.2 (7.7)	13.4 (5.9)	0.351

Tampa Scale of Kinesiophobia*	40.9 (8.1)	36.7 (7.5)	0.211
painDETECT*	17 (5)	12 (6)	**0.038**
Negative: NeP component unlikely, n	2 (9%)	4 (50%)	
Unclear: result ambigious, n	14 (61%)	3 (37%)	
Positive: NeP component likely, n	7 (30%)	1 (12%)	
Subjects with medication, n	15 (65.2%)	3 (37.5%)	
Current medication[◊]			
Selective serotonin reuptake inhibitor, n	1 (4.3%)	1 (12.5%)	
Serotonin-norepinephrine reuptake inhibitor, n	2 (8.7%)		
Tricyclic antidepressant, n	1 (4.3%)		
Antiepileptics, n	2 (8.7%)		
Opioids, n	4 (17.4%)		
Benzodiazepine, n	2 (8.7%)		
Analgesics, n	7 (30.4%)	1 (12.5%)	
Non-steroidal anti-inflammatories, n	7 (30.4%)	2 (25%)	

*Data are mean (SD); [#]Data are medians (25th and 75th percentile); [◊]Multiple answers possible.

TABLE 2. Distribution of pain descriptors volunteered during the clinical examination by subjects with cervical radiculopathy (CxRAD) and subjects with non-specific neck-arm pain associated with heightened nerve mechanosensitivity (NSNAP) for their neck pain and arm pain. Data are expressed in number of subjects (n) and (%)*.

	CxRAD (n = 23)		NSNAP (n = 8)	
	Neck pain	Arm pain	Neck pain	Arm pain
Constant, n	17 (74%)	11 (48%)	5 (62%)	3 (38%)
Intermittent, n	6 (26%)	12 (52%)	3 (38%)	5 (62%)
Spontaneous,◊ n	17 (74%)		3 (37%)	
Paraesthesia,◊ n		23 (100%)		8 (100%)
Numbness, n		12 (52%)		3 (38%)
Tingling, n		12 (52%)		3 (38%)
Pins and needles, n		11 (48%)		4 (50%)
Burning, n	6 (26%)	7 (30%)	5 (62%)	2 (25%)
Shooting, n		5 (22%)		2 (25%)
Electric shock, n	1 (4%)	3 (13%)		
Nerve pain, n				2 (25%)
Dead, n		3 (13%)		2 (25%)
Numbish, n	1 (4%)		1 (12%)	
Ache, n	10 (43%)	6 (26%)	3 (37%)	1 (12%)

Dull, n	7 (30%)	4 (17%)		
Sharp, n	6 (26%)	3 (13%)	1 (12%)	
Heavy, n		2 (9%)		
Deep, n	2 (9%)	2 (9%)	1 (12%)	2 (25%)
Pain, n	2 (9%)	3 (13%)		
Sore, n	1 (4%)		2 (25%)	
Muscle pain, n	1 (4%)			
Throbbing, n	1 (4%)			

*The percentages do not add to 100% as some patients used several descriptors to describe their pain.

◊Descriptor obtained through specific questioning

Common descriptors for neuropathic pain are highlighted in grey.

TABLE 3. QST parameters are shown for the maximal pain area in the asymptomatic and symptomatic sides of subjects with cervical radiculopathy (CxRAD) and subjects with non-specific neck-arm pain associated with heightened nerve mechanosensitivity (NSNAP). Data are shown as mean for untransformed data (HPT, VDT) (± standard deviation) and retransformed mean for log-normally distributed data.

		Maximal pain area		
QST Parameter	Group	Asymptomatic side	Symptomatic side	*p*
CDT (°C)	CxRAD	1.86	1.89	0.912
	NSNAP	1.12	1.16	0.787
WDT (°C)	CxRAD	3.45	3.83	0.288
	NSNAP	2.28	2.64	0.439
TSL (°C)	CxRAD	5.51	6.22	0.180
	NSNAP	3.94	4.17	0.615
CPT (°C)	CxRAD	9.10	11.16	0.084
	NSNAP	10.50	12.16	0.273

HPT (°C)	CxRAD	45.9 (± 3.7)	45.4 (± 4.4)	0.489
	NSNAP	45.3 (± 2.3)	45.1 (± 2.2)	0.801
MDT (mN)	CxRAD	2.10	3.79	**0.021**
	NSNAP	1.57	1.37	0.608
MPT (mN)	CxRAD	23.75	29.85	0.351
	NSNAP	19.87	28.10	0.351
MPS (NRS_{100})	CxRAD	0.53	0.45	0.338
	NSNAP	1.01	0.77	0.171
WUR (ratio)	CxRAD	2.68[a]	2.81[a]	0.855
	NSNAP	2.49	2.98	0.486
VDT (x/8)	CxRAD	5.9 (± 0.9)	5.4 (± 1.1)	**0.003**
	NSNAP	5.2 (± 0.4)	5.2 (± 1.0)	0.835
PPT (kPa)	CxRAD	434	403	0.346
	NSNAP	366	390	0.496

[a]n = 18

CDT: cold detection threshold; WDT: warm detection threshold; TSL: thermal sensory limen;

CPT: cold pain threshold; HPT: heat pain threshold; MDT: mechanical detection threshold;

MPT: mechanical pain threshold; MPS: mechanical pain sensitivity; WUR: wind-up ratio;

VDT: vibration detection threshold; PPT: pressure pain threshold.

TABLE 4. QST parameters are shown for the dermatome in the asymptomatic and symptomatic sides of subjects with cervical radiculopathy (CxRAD) and subjects with non-specific neck-arm pain associated with heightened nerve mechanosensitivity (NSNAP). Data are shown as mean for untransformed data (HPT, VDT) (± standard deviation) and retransformed mean for log-normally distributed data.

		Dermatome		
QST Parameter	Group	Asymptomatic side	Symptomatic side	*p*
CDT (°C)	CxRAD	2.12	2.68	**0.021**
	NSNAP	1.43	1.55	0.439
WDT (°C)	CxRAD	3.43	4.17	0.119
	NSNAP	2.25	3.14	**0.030**
TSL (°C)	CxRAD	6.15	6.87	0.258
	NSNAP	4.2	5.11	0.116
CPT (°C)	CxRAD	7.56	8.08	0.649
	NSNAP	8.4	7.80	0.721

HPT (°C)	CxRAD	45.6 (± 3.5)	46.1 (± 3.8)	0.565
	NSNAP	46.2 (± 3.1)	46.4 (± 2.2)	0.736
MDT (mN)	CxRAD	1.18	4.53	**<0.001**
	NSNAP	2.26	2.65	0.682
MPT (mN)	CxRAD	70.91	84.45	0.467
	NSNAP	36.13	34.90	0.868
MPS (NRS_{100})	CxRAD	0.39	0.34	0.453
	NSNAP	0.84	0.74	0.391
WUR (ratio)	CxRAD	2.01[a]	2.45[a]	0.340
	NSNAP	2.04	2.15	0.633
VDT (x/8)	CxRAD	7.0 (± 0.8)	6.2 (± 1.0)	**0.001**
	NSNAP	6.6 (± 1.2)	6.6 (± 1.4)	0.893
PPT (kPa)	CxRAD	492	572	**0.005**
	NSNAP	405	417	0.260

[a]n = 14

CDT: cold detection threshold; WDT: warm detection threshold; TSL: thermal sensory limen;

CPT: cold pain threshold; HPT: heat pain threshold; MDT: mechanical detection threshold;

MPT: mechanical pain threshold; MPS: mechanical pain sensitivity; WUR: wind-up ratio;

VDT: vibration detection threshold; PPT: pressure pain threshold.

SUPPLEMENTAL DIGITAL CONTENT 1 TABLE 5. Individual QST parameters of subjects with CxRAD in the maximal pain area

Subj	Pain area	Side	PD-Q	CDT (°C)	WDT (°C)	TSL (°C)	CPT (°C)	HPT (°C)	MDT (mN)	MPT (mN)	MPS (NRS_{100})	WUR (ratio)	VDT (x/8)	PPT (kPa)
1[a]	Scapula	asymp	17	0.6	3.7	4.3	28.8	40.6	5.66	17.15	2.64	1.24	4.50	154
		symp		0.6	2.5	3.6	29.6	39.5	6.50	8.57	1.22	3.08	5.83	148
2[a]	Thoracic	asymp	17	0.9	2.0	3.0	9.3	43.1	2.64	27.86	0.26	2.50	5.33	353
		symp		1.0	2.7	3.4	5.0	44.4	2.46	9.85	0.23	2.20	4.83	344
3[b]	Cervical	asymp	16	5.4	6.7	8.7	6.6	49.2	9.85	51.98	0.38	2.13	6.50	449
		symp		1.4	5.8	9.8	27.5	46.2	6.96	64.00	0.17	2.20	6.17	290
4[a]	Thoracic	asymp	19	0.8	3.0	4.1	9.0	45.	1.23	137.19	0.01		6.50	1022
		symp		1.3	2.9	3.6	7.2	44.7	2.00	194.01	0.03		6.17	1041
5[b]	Upper arm	asymp	16	0.8	4.5	6.1	19.8	47.8	2.83	103.97	0.03		6.33	538
		symp		2.7	5.2	11.5	23.8	49.8	16.00	25.99	0.02		4.67	487
6[a]	Upper arm	asymp	23	1.7	2.8	4.3	5.0	48.5	2.83	11.31	0.70	3.57	5.33	627

		symp		2.9	4.7	7.1	5.0	46.8	18.38	25.99	0.46	2.50	4.50	275
7[b]	Upper trap	asymp	15	0.7	1.4	2.2	5.0	47.4	1.32	18.38	0.01		4.50	286
		symp		0.8	1.9	2.6	7.5	46.8	0.93	29.86	0.04		4.00	162
8[b]	Cervical	asymp	25	4.3	3.3	8.7	5.0	49.5	1.41	51.98	0.93	3.40	5.33	486
		symp		4.0	5.0	9.9	5.2	45.9	3.48	477.71	0.23	2.67	4.50	338
9[a]	Upper arm	asymp	17	6.3	3.1	5.5	5.9	42.2	1.23	6.06	19.27	1.19	6.83	259
		symp		2.3	2.9	4.7	24.9	38.8	2.14	6.06	8.56	0.95	5.67	438
10[b]	Upper trap	asymp	13	2.8	3.2	7.4	7.8	48.2	2.46	238.86	0.00	2.00	5.83	839
		symp		1.5	3.9	8.5	15.5	47.6	12.13	222.86	0.07	2.74	5.17	747
11[b]	Thoracic	asymp	14	1.4	3.1	5.4	5.0	48.9	1.62	45.25	0.21	5.25	6.50	882
		symp		1.4	4.2	7.1	5.0	48.8	0.23	11.31	0.47	2.64	6.17	987
12[c]	Upper trap	asymp	7	0.8	3.5	6.8	14.3	43.8	4.00	51.98	1.33	2.64	5.83	448
		symp		2.2	5.0	7.9	22.7	45.9	8.00	84.45	1.11	4.40	5.83	610
13[a]	Thoracic	asymp	25	2.3	5.6	7.5	11.4	48.6	2.46	21.11	0.49	3.60	6.17	408
		symp		1.6	2.7	2.9	28.6	36.6	0.38	13.93	1.13	2.40	6.33	181

14[c]	Upper trap	asymp	16	1.2	2.0	3.3	19.1	44.5	0.35	12.13	0.86	4.40	7.83	248
		symp		3.4	6.9	10.8	8.1	48.7	0.47	294.07	0.12	5.00	7.83	246
15[a]	Thoracic	asymp	14	1.7	2.6	3.7	27.5	37.6	0.19	9.19	0.43	6.86	6.17	470
		symp		2.20	3.1	5.1	25.5	38.8	0.22	6.50	0.66	6.33	5.00	546
16[a]	Scapula	asymp	16	1.2	5.4	7.1	5.0	49.2	1.00	17.15	0.24	1.89	5.67	654
		symp		1.3	3.0	4.4	5.0	49.7	2.30	14.93	0.08	0.83	5.67	809
17[a]	Upper arm	asymp	8	3.9	4.2	6.1	5.0	48.6	0.50	25.99	0.00		5.83	546
		symp		4.9	2.9	6.7	5.0	49.4	1.41	8.00	0.01		5.33	558
18[b]	Thoracic	asymp	21	2.2	3.4	4.4	27.2	37.8	22.63	5.66	0.23	4.00	5.67	378
		symp		2.6	3.8	6.2	24.5	44.9	12.13	7.46	0.19	4.33	4.17	285
19[a]	Elbow	asymp	27	2.4	2.8	4.1	18.3	43.5	1.23	11.31	2.54	1.50	6.33	222
		symp		1.6	2.5	3.5	26.3	36.6	9.19	22.63	2.85	3.14	6.17	163
20[a]	Forearm	asymp	16	5.8	3.8	5.7	5.0	46.9	11.31	12.13	0.13		4.17	387
		symp		2.3	5.2	9.4	5.0	49.9	32.00	22.63	1.34	5.00	2.50	621
21[a]	Thoracic	asymp	14	3.2	12.9	19.3	5.0	50.0	6.96	9.85	0.10	6.67	6.33	564

		symp		7.7	6.8	14.3	5.0	50.0	32.00	9.85	0.11	5.00	6.33	679
22[a]	Forearm	asymp	26	1.2	2.2	5.5	8.6	50.0	4.29	64.00	0.49	1.57	7.50	573
		symp		0.9	3.4	6.2	17.6	49.3	45.25	724.08	0.00		6.00	869
23[a]	Upper arm	asymp	13	3.6	3.8	7.8	5.0	45.5	0.66	6.50	3.13	1.64	5.00	262
		symp		1.4	7.4	10.5	5.0	44.8	3.03	7.46	2.06	1.82	5.33	205

Subj: subject; PD-Q: painDETECT score; Scapula: above or below spine scapula; Thoracic: paravertebral thoracic spine; Cervical: paravertebral cervical spine; Upper trap: upper trapezius muscle; asympt: asymptomatic; sympt: symptomatic

CDT: cold detection threshold; WDT: warm detection threshold; TSL: thermal sensory limen; CPT: cold pain threshold; HPT: heat pain threshold; MDT: mechanical detection threshold; MPT: mechanical pain threshold; MPS: mechanical pain sensitivity; WUR: wind-up ratio; VDT: vibration detection threshold; PPT: pressure pain threshold.

Gain of function relative to asymptomatic side Loss of function relative to asymptomatic side

[a]Disc herniation

[b]Osteophytic stenosis

[c]Disc/osteophyte complex

SUPPLEMENTAL DIGITAL CONTENT 2 TABLE 6. Individual QST parameters of subjects with NSNAP in the maximal pain area

Subj	Pain area	PD-Q	Side	CDT (°C)	WDT (°C)	TSL (°C)	CPT (°C)	HPT (°C)	MDT (mN)	MPT (mN)	MPS (NRS_{100})	WUR (ratio)	VDT (x/8)	PPT (kPa)
1	Thoracic	14	asymp	1.5	3.6	6.9	27.9	43.1	0.44	68.59	1.94	1.63	5	428
			symp	1.1	4.0	8.5	29.0	44.6	0.54	64.00	1.10	3.15	5.67	452
2	Upper trap	16	asymp	0.7	3.2	4.2	14.1	45.4	13.93	13.93	0.62	1.26	5.50	454
			symp	1.0	4.3	5.1	13.3	44.5	4.29	14.93	1.17	1.50	6	441
3	Upper trap	18	asymp	4.4	3.6	9.8	5.8	48.5	24.25	13.00	2.88	1.67	4.67	396
			symp	2.2	3.1	5.3	11.0	42.0	42.22	137.19	1.18	1.43	3.83	330
4	Upper trap	7	asymp	0.7	0.6	2.6	16.4	41.6	1.32	17.15	2.56	2.47	4.50	226
			symp	0.8	2.3	3.0	25.3	44.1	2.00	8.00	2.12	2.63	4.67	428
5	Thoracic	21	asymp	0.8	2.2	2.5	5.0	46.5	0.81	32.00	0.07	1.50	5.33	503
			symp	1.0	3.2	3.5	5.0	47.4	1.32	51.98	0.11	6.00	5.50	572
6	Upper trap	10	asymp	0.7	1.8	2.8	6.0	44.3	0.47	27.86	0.61	3.56	5.50	195

			symp	1.2	1.5	3.7	10.0	42.9	0.20	84.45	0.37	5.00	6.83	178
7	Upper trap	5	asymp	1.2	3.2	3.9	5.0	47.6	0.38	8.57	0.96	1.86	5.50	494
			symp	1.2	2.3	3.9	5.4	46.7	0.50	6.96	0.86	2.29	4.33	466
8	Upper trap	8	asymp	1.2	2.4	2.9	26.0	45.8	1.32	14.93	0.63	15.00	5.33	385
			symp	1.3	1.7	2.7	16.7	48.3	0.47	12.13	0.21	5.08	5.00	405

Subj: subject; PD-Q: painDETECT score; Thoracic: paravertebral thoracic spine; Upper trap: upper trapezius muscle; asympt: asymptomatic; sympt: symptomatic.

CDT: cold detection threshold; WDT: warm detection threshold; TSL: thermal sensory limen; CPT: cold pain threshold; HPT: heat pain threshold; MDT: mechanical detection threshold; MPT: mechanical pain threshold; MPS: mechanical pain sensitivity; WUR: wind-up ratio; VDT: vibration detection threshold; PPT: pressure pain threshold.

Gain of function relative to asymptomatic side Loss of function relative to asymptomatic side