Agri 2022;34(4):235–244
doi: 10.14744/agri.2021.88972

ORIGINAL ARTICLE

Quantitative sensory test findings in cervical radicular pain and their relationship with the symptoms

Servikal radiküler ağrıda kantitatif duyu testi bulguları ve semptomlar ile ilişkilerinin değerlendirilmesi

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Summary

Objectives: This study aims to define and compare sensory phenotypes in cervical radiculopathy patients exhibiting neuropathic pain (NP) components with healthy volunteers using clinical examination and quantitative sensory test (QST) findings. Another aim of the study is to show whether symptomatic components of the pain detect questionnaire (PDQ) are correlated with the QST findings, which may help clinicians indicate patients with sensory abnormalities without the use of specialized tests.

Methods: Fifty-seven participants were included in the study, including patients with NP (n=20) and healthy volunteers (n=37). After obtaining the sociodemographic and clinical data of the participants, the PDQ was performed in patients with pain followed by QST analysis in all participants.

Results: Analyses between painful and non-painful extremities yielded no differences in all groups for QST (p>0.05). Sensory thresholds were found to be higher in the NP group compared to healthy volunteers, and the pain threshold test was found to be lower (p<0.05) in the intergroup analyses. The changes described were found in both painful and non-painful limbs. Pain with slight pressure was found to be correlated with the lower heat pain threshold values (R=−0.602, p=0.005).

Conclusion: Patients with NP were found to have lower thresholds for pain and higher sensory thresholds when compared to healthy volunteers. Moreover, pain with pressure component in PDQ was found to be associated with hyperalgesia in QST.

Keywords: Cervical radiculopathy; neuropathic pain; pain detect questionnaire; pain thresholds; quantitative sensory testing; sensory thresholds.

Özet

Amaç: Bu çalışma, nöropatik ağrılı servikal radikülopati hastalarında duyusal fenotipleri klinik muayene ve kantitatif duyusal testleri (QST) kullanarak tanımlamayı ve sağlıklı gönüllülerle karşılaştırmayı amaçlamaktadır. Çalışmanın bir diğer amacı, PainDetect anketinin (PDQ) semptomatik bileşenlerinin, QST bulguları ile ilişkilerini göstererek klinik pratikte duyusal anomalileri olan hastaların özellikli bir test olmaksızın tespitini sağlamada yardımcı olmaktır.

Gereç ve Yöntem: Nöropatik ağrılı hastalar (n=20) ve sağlıklı gönüllüler (n=37) olmak üzere 57 katılımcı çalışmaya dahil edildi. Katılımcıların sosyodemografik ve klinik verileri alındıktan sonra hastalara PDQ ve ardından tüm katılımcılarda QST analizi yapıldı.

Bulgular: Ağrılı ve ağrısız ekstremiteler arasındaki analizlerde QST için tüm gruplarda fark bulunmadı (p>0,05). Duyusal eşikler sağlıklı gönüllülere göre nöropatik ağrılı grupta daha yüksek, ağrı eşiği testleri daha düşük bulundu (p<0,05). Tarif edilen değişiklikler hem ağrılı hem de ağrısız ekstremitelerde saptandı. PDQ komponenti olan hafif basınçla ağrı, daha düşük ısı ağrı eşik değerleri ile korele bulundu (R=-0,602, p=0,005).

Sonuç: Nöropatik ağrılı hastaların sağlıklı gönüllülere göre daha düşük ağrı eşiklerine ve daha yüksek duyusal eşiklere sahip olduğu görüldü. Ayrıca, PDQ'da ağrı ile basınç bileşeni ve QST'de hiperaljezi arasında bir korelasyon gösterildi.

Anahtar sözcükler: Servikal radikülopati; nöropatik ağrı; PainDetect anketi; ağrı eşikleri; kantitatif duyu testi; duyusal eşikler.

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Submitted ***(Başvuru):*** **18.09.2021 Revised** ***(Revizyon):*** **21.10.2021 Accepted** ***(Kabul):*** **15.11.2021 Available online** ***(Online yayımlanma):*** **19.10.2022**

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Introduction

Neuropathic pain (NP) is a type of pain that occurs as a result of lesions or diseases in the somatosensory nervous system and may be accompanied by other sensory or motor dysfunctions.[1] Unlike other types of pain, NP is mostly more resistant to treatment and tends to become chronic.[2]

Painful cervical radiculopathy (CR) is one of many pathologies that can manifest with NP. CR refers to motor loss and accompanying sensory disorders in the upper limb after compression of the nerve roots. The NP component was found to be between 30 and 50% in disk pathologies, which suggests their radicular effects in both the cervical and lumbar region.[3,4]

Many algorithms and methods were proposed to define NP in individuals who are afflicted with it. One of the most widely accepted definitions for the diagnosis of NP involves history of a relevant neurological lesion or a disease with neuroanatomically plausible pain distribution and sensory signs in examination, and confirmation of the lesion with the diagnostic tests, including but not limited to electrophysiological studies, skin biopsy for nerves, and quantitative sensory testing (QST).[5] QST is a group of standardized tests of sensory examination, some of which are implemented through digitalized platforms, and the levels of the stimuli delivered can be measured. It contains different sensory modalities such as hot, cold, vibration, and touch.[6] In addition to the characteristics of pain and accompanying sensory changes, QST also enables the phenotyping of pain profiles showing common features with additional methods. Although there are many classifications for pain phenotyping, the main point of view is on function gain and loss. Especially the presence of hyperalgesia and hypoesthesia is the main criteria for these functional changes. It has also been shown that different treatments for each phenotype had better outcomes.[7] Another advantage of the QST is the ability to show nerve lesions belonging to the smaller fibers, which are not usually evident in electrophysiological studies such as EMG or NCS.[8]

While QST is a valuable tool to assess the integrity and the function of the sensory nerves as well as patients' perception of pain, these tests are often time consuming, subjective, and dependent on the performer. Thus, the routine use of QST in clinical settings is restricted. Clinicians often feel the need to use other tools that can help to recognize patients with distinct sensory profiles to give customized therapy for their needs. Therefore, the association of symptoms, findings, or components of pain evaluation tools with the sensory disturbances would be valuable for routine clinical settings. Moreover, a QST study involving CR-related NP in the Turkish population is also lacking.

This study aims to compare QST findings in CR patients exhibiting NP components with healthy volunteers and classify CR patients as hyperalgesic or hypoesthetic according to QST findings and show the prevalence of these components. Another aim of the study is to show whether symptomatic components of the pain detect questionnaire (PDQ) are correlated with the QST findings, which may help clinicians indicate patients with sensory abnormalities without the use of specialized tests.

Material and Methods

Participants

This study was approved by the ethics committee before the initiation of the study and was carried out in accordance with the Helsinki Declaration. Informed consent was obtained from all participants.

Fifty-seven participants who applied to Ege University Medical Faculty Hospital Physical Medicine and Rehabilitation Department between April 2019 and October 2019 were included in the study. Twenty participants had NP due to CR in C5-6 or C6-7 levels. Thirty-seven healthy controls were also included in the study.[9]

Inclusion criteria

- Presence of definitive NP according to the algorithm determined by NP Special Interest Group (NeuPSIG): Patients with the history and neuroanatomic pain distribution consistent with neurological lesions, accompanied by sensory symptoms or signs appropriate for this distribution, and demonstration of the lesion by objective tests,[10]
- Clinical diagnosis of CR by a physician and presence of a herniated disk in imaging,

- Neck pain with unilateral arm pain,
- Patients in the age range of 20–65.

Exclusion criteria

- Presence of bilateral arm pain
- Serious cognitive impairment can result in diminished cooperation
- Having an unstable medical comorbidity
- Presence of a pacemaker
- Complete or near-complete sensory loss.

Clinical evaluation of patients

After obtaining informed consent, patients were evaluated with a detailed medical history and physical examination, and their diagnoses were confirmed by a physician. Physical examination included compression test of the neck, sensory testing, evaluation of proprioception, deep tendon reflexes, and muscle testing, to look for neurological signs and radicular involvement. The presence of hypoesthesia or allodynia through physical examinations (using Von Frey filaments and a brush, respectively) was recorded. Laboratory tests and magnetic resonance imaging of the cervical vertebrae obtained in the past 6 months were also evaluated to confirm the diagnosis of a herniated disk that explains the source of the pain plausible with the anatomic distribution of the radices involved, and other pathologies that may explain the pain were excluded through history, physical examination, and imaging. After the initial evaluation, patients with pain were screened for the presence and the characteristics of NP with the pain detect scale. Eligible patients were then evaluated using QSTs.

Measurements and evaluations were performed between 10:00 AM and 1:00 PM, and patients were asked to confirm that they had enough sleep for the night, not being <6 h. Drugs such as sedatives, opioids, or stimulants, which may affect the central nervous system in patients, have been discontinued at least 12 h in advance.

Pain detect questionnaire (PDQ)

PDQ is a pain screening scale that consists of questions about the temporal properties, radiation, and characteristic features of pain. A total score between 1 and 38 is calculated from the answers. Scores 19 and above suggest the presence of NP. Scores 13–18 indicate a possible NP component. Scores 12 and below indicate that NP is unlikely.[4] Compared to clinical examinations, its sensitivity and specificity are determined to be 85% and 80%, respectively. The Turkish validity and reliability study of the PDQ questionnaire was conducted by Alkan et al.[4,11]

QST

CASE IV (WR Medical Electronics Co., Maplewood, MN 55109, USA) system was used as a QST. The CASE IV system mainly assesses heat detection threshold (HDT), vibration detection threshold (VDT), cold detection threshold (CDT), and heat sensitivity for pain components as the sensory tests.

Testing was done in a room isolated from distractions or interruptions, and the room temperature was set to 22°C using an air conditioner. The position of the patients was adjusted to a comfortable level with the testing table using an adjustable chair. All patients were given instructions about the course of the testing, and test stimuli were given to make sure they understood the process. The computed screen was turned away to make sure the patients did not see the level of the stimuli given. The vibratory testing was conducted on the third finger, and the dorsal side of the hand was chosen for the thermal tests. Both upper extremities of the patients and healthy volunteers were tested, and the results were recorded.[12]

Vibratory testing[12]

The middle finger was chosen as the site for the test and was put on a lump of putty, which was a part of the system (CASE IV, WR Medical Electronics Co., Maplewood, MN 55109, USA). The stimulator was placed on the area between the distal interphalangeal joint and the fingernail. It was made sure that the patients stood still as the tests were conducted, and all possible sources for external vibrations were eliminated with the putty and the sponges that the system provided.

Thermal testing[12]

The investigators made sure that the participants' hands were dry and drying them before the test with a towel when necessary. The thermal stimulator (3×3 cm) was placed on the dorsal side of the hand and secured firmly with velcro straps, ensuring that the hand and the stimulator were in full contact, while being comfortable enough for the participants. Skin temperatures were analyzed with the QST system and all of the stimuli were given after the measurements

and were repeated before each type of thermal test. Case IV system has many algorithms to test the sensory thresholds, and the "4-2-1" algorithm among them was used in this study.[12] In this algorithm, the investigator first tests and determines the estimated threshold. The patient is given 20 stimuli at each measurement according to this estimated threshold. The participants' responses determine the next stimulus' level, and when they fail to feel the stimulus, the next one is usually higher. Among all these stimuli, the device randomly gives null stimuli, and the accuracy of the participants' responses is tested, as the participants are expected to give a negative response to them. When positive responses to the null stimuli are obtained 3 times, the test is restarted for that component.

For the heat pain threshold (HPT) stimulus, increasing thermal stimuli were given with the non-repeating ascending null stimuli algorithm using the same thermal stimulator. During the stimulus, the participants were asked to define the level of pain according to the numerical scale (0: No pain and 10: Worst pain possible). The test was terminated when the painful stimulus reached five levels according to the numerical scale. Temperature values where the first disturbing level was determined to be numerical scale 1 (HPT 0.5) and pain level was 5 (HPT 5) compared to numerical scale were recorded. The difference between HPT 0.5 and HPT 5 was also calculated (HPT 0.5–5), to indicate how the change in pain scales with the difference in the temperatures.

In the CASE IV system, 25 standardized stimulus levels are defined for vibration and thermal tests. The difference between the levels of the stimuli is called the least noticeable difference value (just noticeable difference [JND]). The concept of JND was created according to the lowest stimulus level differences that people can distinguish to be higher or lower, and these differences were determined according to the previous physiological measurement. One relates to the lowest intensity and 25 is the highest intensity alert defined on the device. As it is not expected to discriminate the smaller differences, 1 JND is the minimum stimulus difference offered to patients.

Thermal test results obtained in the study were recorded in degree Celsius that differed from skin temperature, and the vibration amplitudes were recorded in micrometers. Besides, the stimulus levels (JND) of the device that has been used in many previous studies were found to be reliable.[13,14] As JNDs are proven to be reliable in these studies, all measurements were also recorded as JNDs, and the analyses were conducted accordingly.

Criteria for hypoesthesia and hyperalgesia

After expressing the raw QST results of the patients as Z-transformation values, the criteria for hypoesthesia and hyperalgesia were defined in the patients.
Hypoesthesia:

- 1 Standard deviation (SD) difference between the affected side and the control side for HDT, CDT, or VDT, with the affected side being higher[15]
- Values 2 SD higher than the healthy controls on the affected side[16]

Hyperalgesia:

- 1 SD difference between HPT 0.5 or HPT 5 values between affected and control sides[15]
- 2 SD difference between the affected and control sides, with the affected side being lower[16]

In addition, patients were classified whether they had unilateral or bilateral hyperalgesia according to the second criterion for hyperalgesia.

Statistical analysis

Statistical analysis was conducted using the Statistical Package for the Social Sciences (IBM Corporation, Armonk, NY), version 23 for Windows. Based on the data of the healthy group, the 95% confidence interval was defined in the data obtained with QST, and the QST parameters of all patients were expressed by the Z-transformation. The demographic and clinical characteristics of the participants were analyzed with descriptive statistics. Categorical variables were analyzed using Pearson's Chi-square test and Fisher's exact test. The normality of the data was tested using Shapiro–Wilk test. Parametric tests were used for the data with normal distribution, and non-parametric tests were used to analyze the data without normal distribution. Correlation analysis was performed using Spearman's rank-order correlation test. Statistical significance was defined as $p<0.05$.

Results

Clinical and demographical characteristics

No differences were found between the clinical and the demographical characteristics of the participants

Table 1. Demographical and clinical characteristics of the participants (mean±SD or n [%])

	NP (n=20)		Healthy controls (n=37)		p
	n	%	n	%	
Age (years)	46±10.8		43.1±13.2		0.4
Gender					
Female	8	40	17	47.2	0.66
Male	12		20		
Height (cm)	170.3±7.9		167.1±7.2		0.26
Marital status (married)	17	85	25	68	0.15
Affected side (right)	12	60	–	–	–
Pain VAS	6.4±1.1		–	–	–
Duration of pain (months)	22.3±20.1		–	–	–
Pain detect score	21±3.4		–	–	–

Pearson's Chi-square, Statistical significance was set to p<0.05. NP: Neuropathic pain; VAS: Visual analog scale.

Table 2. Comparison of the affected side and healthy side in patients with neuropathic pain in QST components

QST component	Affected side	Healthy side	p
CDT	9.72±3.1	9.32±2.9	0.68
HDT	11.3±4.5	10.1±3.75	0.37
VDT	13.9±1.78	13.3±2.3	0.33
HPT 0.5	14.7±2.6	14.3±2.3	0.62
HPT 5	21.2±2.2	21.1±2.17	0.93
HPT 0.5–5	6.43±2.78	6.75±2.47	0.69

The independent samples t-test, statistical significance was set to p<0.05. CDT: Cold detection threshold; HDT: Heat detection threshold; VDT: Vibration detection threshold; HPT: Heat pain threshold.

Table 3. Comparison of QST components in affected side for NP group and healthy controls

Component	NP (n=20)	Healthy controls (n=37)	p
CDT	9.72±3.1	6.85±2.75	**0.001**
HDT	11.3±4.5	7.1±3.3	**<0.001**
VDT	13.9±1.78	11.78±2.43	**0.001**
HPT 0.5	14.7±2.6	17.1±2.11	**0.006**
HPT 5	21.2±2.2	22±1.43	0.139
HPT 0.5–5	6.43±2.78	4.9±1.75	**0.006**

Independent samples t-test, statistical significance was set to p<0.05. NP: Neuropathic pain; CDT: Cold detection threshold; HDT: Heat detection threshold; VDT: Vibration detection threshold; HPT: Heat pain threshold.

across groups (p>0.05). The demographic and clinical characteristics of the patients are given in Table 1.

Comparison of QST values

CDT, HDT, and VDT values were found to have slightly higher thresholds on the affected side compared to the other side, but this was not statistically significant (p>0.05). The comparison of affected and healthy sides is given in Table 2.

The comparison of QST values was also performed among groups. The group with NP had higher sensory thresholds than the healthy controls in CDT, HDT, and VDT tests, both in their painful extremities and non-painful extremities (p<0.05). Moreover, HPT 0.5 and HPT 0.5-5 values in the NP group were found to be lower than the healthy controls (p<0.05). HPT 5 values were not found to be different among groups (p>0.05). The intergroup analyses are given in Tables 3 and 4.

The characteristics of the patients are given in Table 5 after the application of the criteria for hypoesthesia and hyperalgesia. NP group had a higher incidence of pathological findings when compared to healthy controls.

Correlation analyses were performed to show whether QST values correlate with the symptoms defined in the PDQ. Pain with slight pressure was found to be correlated with the lower HPT values (R=–0,602, p=0.005), while other correlation analyses gave no significant results (p<0.05) (Table 6).

Table 4. Comparison of QST components in non-painful side for NP and healthy controls

Component	NP (n=20)	Healthy controls (n=37)	p
CDT	9.32±2.9	6.85±2.75	**0.003**
HDT	10.1±3.75	7.1±3.3	**0.003**
VDT	13.3±2.3	11.78±2.43	**0.027**
HPT 0.5	14.3±2.3	17.1±2.11	**<0.001**
HPT 5	21.1±2.17	22±1.43	0.08
HPT 0.5–5	6.75±2.47	4.9±1.75	**0.003**

Mann-Whitney U-test, statistical significance was set to p<0.05. QST: Quantitative sensory test; NP: Neuropathic pain; CDT: Cold detection threshold; HDT: Heat detection threshold; VDT: Vibration detection threshold; HPT: Heat pain threshold.

Table 5. Frequencies of hypoesthesia and hyperalgesia in groups, n (%)

	NP (n=20)		Healthy controls (n=37)		p
	n	%	n	%	
Hypoesthesia	5	25	1	2.7	**0.001**
Hyperalgesia	5	25	1	2.7	
Hypoesthesia+ Hyperalgesia	6	30	0	0	
No abnormalities	4	20	35	94.6	

Fisher's exact test statistical significance was set to p<0.05. NP: Neuropathic pain.

Table 6. Correlations between the symptoms on the PDQ and the results of QST components

	CDT	HDT	VDT	HPT
Pain detect total score				
r	0.091	–0.246	0.248	–0.008
p	0.703	0.296	0.292	0.973
Burning sensation				
r	0.215	–0.220	0.300	–0.241
p	0.363	0.352	0.199	0.306
Tingling sensation				
r	0.090	0.023	0.320	–0.114
p	0.705	0.923	0.168	0.633
Pain by light touch				
r	0.115	0.050	0.403	0.021
p	0.631	0.835	0.078	0.929
Electric shock-like pain				
r	0.352	–0.070	0.073	–0.184
p	0.128	0.770	0.760	0.438
Cold/heat				
r	0.017	–0.308	–0.026	–0.130
p	0.944	0.186	0.914	0.585
Numbness				
r	0.084	–0.023	0.312	0.173
p	0.726	0.922	0.181	0.466
Slight pressure				
r	0.232	–0.216	–0.112	**–0.602**
p	0.324	0.360	0.637	**0.005**

Spearman's rank-order correlation test. Statistical significance was set to p<0.05. PDQ: Pain detect questionnaire; QST: Quantitative sensory test; CDT: Cold detection threshold; HDT: Heat detection threshold; VDT: Vibration detection threshold; HPT: Heat pain threshold.

Discussion

The results of this study imply that patients with NP exhibit differences in the QST test when compared to healthy volunteers. These changes mainly consist of increased sensory thresholds or decreased pain thresholds. Despite these differences, the comparison of affected and healthy limbs of the patients with pain showed no differences in QST.

The changes were found to be prevalent in both upper extremities, regardless of being affected, in patients with NP. There have been various studies examining the QST findings in patients with cervical radicular pain. Several patients with NP had CR in a study by Rolke et al.,[17] making the study one of the first in this patient group. Chien et al.[18] focused on patients with chronic whiplash trauma and CR and reported that pain-related thresholds were lower and sensory thresholds were higher in these patients when compared to the control group. It has been observed that these findings were not unilateral and some changes were also present in the unaffected side, and these differences were attributed to the central changes caused by chronic pain. These results are similar to the findings of our study, in which the sensory thresholds were found to be higher and pain thresholds were found to be lower. Although the study[18] reported a clinical diagnosis of CR, it did not imply any NP criteria or a radiologic diagnosis for the patients included in the study, thus hindering the diagnostic accuracy and not being able to exclude the presence of concomitant pathologies.

Similarly, Tampin et al.[19] showed that QST profiles were altered in patients with CR. The main finding

in this study was the perception thresholds of measured sensory modalities were higher in patients with radiculopathy, suggesting sensory losses. Moreover, apart from pain with pressure, no differences were reported in these groups. Similarly, the changes were also present in patients with radicular pain when compared to healthy controls. These patients also underwent these tests in their lower extremities, a place where researchers considered a safe region as a control, and most of these modalities also showed differences when compared to healthy volunteers. Similarly, in our study, it was observed that sensory thresholds were increased in both affected and unaffected limbs, while the temperature-related pain threshold decreased, which supports their findings. While choosing the lower extremities which were deemed unaffected in our patients would have been reasonable, it would not be possible to compare these values to the upper extremities since their normative values differ.[17] As we had already shown that the other side did not have pathological findings in the evaluation, the use of the contralateral side for comparisons was more preferable.

The study was conducted by Moloney et al.[20] focused on phenotyping the QST findings in patients with CR. Their results showed that patients with pain were heterogeneous for their QST phenotypes, without a distinct pattern. Abnormal phenotypes were more prevalent in the group exhibiting NP. While some of the patients only had hypoesthesia or hyperalgesia, a significant fraction of the patients had both. Interestingly, some of the patients did not have any changes in their sensory profiles. While radicular symptoms were all present in these patients, they may not have been severe enough to cause significant changes in these tests. Our findings regarding the abnormalities in the patients with NP were compatible with the findings of Moloney et al.[20] It was also found that 80% of the patients with NP showed an abnormality in the QSTs according to our criteria. Interestingly, 2 patients (5.4%) also showed sensory abnormalities even in the absence of any pathologies or clinical symptoms. As the hyperalgesia and hypoesthesia criteria were obtained through healthy controls' Z scores, some of the patients with NP could not reach QST values to be classified as hyperalgesia or hypoesthesia, even in the presence of physical and clinical findings. Likewise, some of the healthy controls were found to have marginal QST values that caused them to be classified as having abnormalities. Although QST is a sensitive and specific test for the presence of NP, there may still be false positives or negatives which emphasize the importance of clinical evaluation and combined methods for diagnosis.[21]

This is the first study to report a correlation between symptoms and sensory testing in these patients with radicular pain, especially at the cervical level, as there are no studies in the literature focusing on these patients. The results of our study imply that pain with the pressure component of the PDQ is correlated with lower HPT values in patients with NP. Although this component of PDQ mainly suggests mechanical hyperalgesia while HPT is done with thermal stimulation, both of these findings signify lower pain thresholds. While the lack of a correlation between the cold or heat pain component of the PDQ and thermal hyperalgesia may seem questionable, this is not the first study that found itself in the middle of such a situation. A study by Lang et al.[22] used self-reported NP questionnaires and QST on patients with chronic pain and reported that thermal pain thresholds were correlated with mechanical descriptors of the pain such as tenderness, and no correlations were found between thermal descriptors. Moreover, a study involving 617 patients with NP also assessed the correlation between thermal hyperalgesia and self-reported cold or hot pain and could not find one.[23] There may also be a correlation between heat and cold pain and thermal hyperalgesia, which could not be shown by the limited numbers of patients. As our patients' pain was in a chronic state (mean: 22 months), this duration can result in both peripheral and central changes for the perception of pain, resulting in central sensitization, which is characterized by an enhanced perception of pain.[24] Several studies in the literature address the correlation between QST findings and pain questionnaires, with most of them investigating the patients with other causes of NP.[25–27] These studies report correlations between QST components and pain questionnaires, namely, the items on hyperalgesia and allodynia, similar to ours. Our study shows that these changes are also present in patients with CR.

There was no correlation between other components of the PDQ and QST. The absence of correlations between higher sensory thresholds and symptoms may be due to several reasons. First of all, slight reduc-

tions in the sensory system may not have given any symptoms to patients to describe, which results in a reduction in the description of the negative sensory symptoms. In addition, PDQ seems to mainly focus on positive symptoms, since it has six different items to describe positive symptoms and only one item (numbness) that describes the presence of negative symptoms. Still, more studies are required to exclude a possible relationship between these scores and QST.

Most of the studies in this field, including ours, report that the QST findings seem to be present in both the areas relevant to the lesion or areas far away from the lesion, even if the difference not being statistically significant. Different mechanisms are suggested to explain how disc pathologies result in sensory phenomena with a distance from the lesion. Tschugg et al.[28] used wind-up ratio values to show that extraforaminal lumbar disk hernias trigger endogenous mechanisms that may deteriorate chronic pain. Lesions characterized by nerve damage, including radiculopathies, are known to cause non-lesional neural changes.[29] These changes include biochemical changes or plastic reorganizations and that take place at the cellular level, as well as in the cortical and subcortical areas of the central nervous system. Aside from these changes, chronic pain itself is known to have effects on the central nervous system plasticity as well as compromised neural functions.[30] All of these intertwined mechanisms can explain the changes occurring beyond the borders of the characteristic areas for the lesions, suggested by previous works and this study.

Using raw data obtained from QST tests are a matter of debate, as the numbers rarely show a normal distribution. Some solutions are offered to overcome this problem, such as the logarithmic transformation of the data, or the use of JND values, which exhibit similar patterns to a logarithmic transformation.[31,32] and some research groups have suggested that the healthy data obtained from the specified population should be expressed with a z-score.[17] The use of z-scores allows patients to be classified correctly in the population they belong to. Similarly, a bilateral measurement may also allow researchers to decide on the side with the lesion, although not always being accurate. In our study, these patients were classified according to the criteria created based on the criteria used by the previous studies.[20]

Strengths and limitations

This is the first study to assess the characteristics of CR and resulting NP with the QST tests in the Turkish population, although our included population should not be generalized to all Turkish patients. Moreover, these patients were compared to healthy controls. As only patients with unilateral pain were included in the study, the unaffected side of the patients was also used as a control side. Finally, the demographical characteristics of the groups did not show wide and heterogeneous distributions, since they can potentially limit the study by causing high heterogeneity in QST values.

One of the limitations of the study is the number of patients. Although the power analysis was performed before the study, it is clear that more patients could have provided healthier comparisons for QST analysis. However, most of the QST studies in the literature seem to have similar numbers for patients.[19] While a control group consisting of healthy volunteers was used in the study, our study did not include a group exhibiting other types of pain. Recruitment of such patients could show whether these changes were attributable to NP or any type of chronic pain. Another limitation of the study is the QST method. The QST method encompassing 13 different measurements suggested by the German network to study NP (DFNS) could not be used for this study. Nevertheless, the system used in our study has been used in many studies for many years and has a strong background.[12,13] For this reason, it constitutes a suitable method for showing basic sensory differences.

Finally, although the diagnoses of the patients are made with the support of imaging, examination, and history, the presence of diagnostic electrophysiological study was not the criteria for inclusion in each patient. Therefore, the presence of more than 1 pathology that may cause NP could not be ruled out in all patients. Nevertheless, pathologies that can create this picture systematically are among the exclusion criteria to cope with this potential problem.

Conclusion

Our study has shown changes in the QST tests of patients with NP compared to healthy volunteers. These changes were predominantly accompanied by an increase in sensory test thresholds and a drop in the

pain threshold. Moreover, a correlation between an item suggesting hyperalgesia in PDQ and hyperalgesia in QST is shown, which can help clinicians distinguish these patients with a particular difference. The treatment of NP is heading toward the concept of different agents for different pain phenotypes, QST remains a valuable tool to distinguish them. As CR patients with NP show prevalent changes in sensory tests, the future evidence can help clinicians customize their choice for the treatment accordingly and result in a possible improvement in the treatment response. However, more studies with a greater number of patients are needed to make a definitive statement.

Ethical Approval: The study was approved by The Ege University Faculty of Medicine Clinical Research Ethics Committee (Date: 10/01/2018, No: 18-3/37).

Conflict-of-interest issues regarding the authorship or article: None declared.

Financial Disclosure: This study has no funding or sponsor.

Peer-rewiew: Externally peer-reviewed.

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