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The added value of bedside examination and screening QST to improve neuropathic pain identification in patients with chronic pain

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Background: The assessment of a neuropathic pain component (NePC) to establish the neurological criteria required to comply with the clinical description is based on history taking, clinical examination, and quantitative sensory testing (QST) and includes bedside examination (BSE). The objective of this study was to assess the potential association between the clinically diagnosed presence or absence of an NePC, BSE, and the Nijmegen–Aalborg screening QST (NASQ) paradigm in patients with chronic (≥3 months) low back and leg pain or with neck shoulder arm pain or in patients with chronic pain due to suspected peripheral nerve damage.

Methods: A total of 291 patients participated in the study. Pain (absence or presence of neuropathic pain) was assessed independently by two physicians and compared with BSE (measurements of touch [finger, brush], heat, cold, pricking [safety pin, von Frey hair], and vibration). The NASQ paradigm (pressure algometry, electrical pain thresholds, and conditioned pain modulation) was assessed in 58 patients to generate new insights.

Results: BSE revealed a low association of differences between patients with either absent or present NePC: heat, cold, and pricking sensations with a von Frey hair were statistically significantly less common in patients with present NePC. NASQ did not reveal any differences between patients with and without an NePC.

Conclusion: Currently, a standardized BSE appears to be more useful than the NASQ paradigm when distinguishing between patients with and without an NePC.

Keywords: quantitative sensory testing, NASQ, Nijmegen–Aalborg screening QST, clinical assessment, diagnostic accuracy

Introduction

Neuropathic pain is defined by the International Association for the Study of Pain (IASP) as "pain caused by a lesion or disease of the somatosensory nervous system". It is a clinical description rather than a clinical diagnosis which would require "a demonstrable lesion or disease that satisfies the established neurological diagnostic criteria".[1] In the general population, 6%–8% suffer from neuropathic pain.[2–4] Nociceptive pain is defined as "pain that arises from actual or threatened damage to non-neural tissue and is due to activation of nociceptors". This allows us to distinguish between patients with neuropathic pain (classification based on an abnormally functioning somatosensory nervous system) and nociceptive pain (classification based on a normally functioning somatosensory nervous system). Because co-existence of both conditions (mixed-pain condition) is frequently observed in daily clinical practice, La Cesa et al suggest using the presence or absence of a neuropathic pain component (absent or present

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NePC).[5] NePC assessment is based on history taking, clinical examination, and (quantitative) sensory testing and includes bedside examination (BSE).[6–8] Clinical examination alone can never offer proof that a specific pain is of neuropathic origin, but it provides supporting evidence for alterations in the functioning of the nervous system.[6] According to the IASP neuropathic pain special interest group (NeuPSIG), abnormal sensory findings should be neuroanatomically plausible when an NePC is present, and the sensory signs should be associated with the neuroanatomically plausible distribution compatible with an underlying relevant lesion or disease of the somatosensory nervous system.[9,10] As part of a bedside clinical neurological examination, sensory testing can identify negative sensory symptoms such as hyperalgesia or hypoesthesia and/or positive sensory symptoms such as allodynia and hyperalgesia.[5] According to Haanpää et al,[6] BSE can possibly identify where the pathology causing the pain can be found in the central nervous system.

In the last decades, quantitative sensory testing (QST) has complemented traditional neurological BSE tests. QST uses psychophysical tests defined as stimuli with predetermined physical properties based on specific measurement protocols for the analysis of somatosensory aberrations.[11–13] QST measures responses to sensory stimuli and can be used to assess somatosensory system function,[11,12] the measurement of the altered peripheral and/or central pain sensitivity,[14–16] and descending pain modulation.[17,18] QST is thought to offer greater precision and reliability when assessing somatosensory system functionality than a standard BSE[19,20] because of the use of controlled automated devices. There is evidence that QST improves the diagnostic process of patients with pain, and that it may be valuable when monitoring for a specific anti-neuropathic treatment.[21,22] Moreover, an altered pain modulation can be assessed on the basis of signs and symptoms of peripheral and central sensitization[17,23–25] and by the use of conditioned pain modulation (CPM).[19,26] CPM is a physiological phenomenon that can be used to assess the quality of the endogenous pain inhibitory pathway, also known as the "pain inhibits pain" phenomena.[27] The Nijmegen–Aalborg screening QST (NASQ)[15,16,24,28] measures pain and central pain processing under standardized conditions using defined stimuli and experienced intensity ratings. There is no "gold standard" for the diagnosis of NePC, and the association between NePC and BSE/NASQ has not yet been fully evaluated. There is a need for studies to more objectively identify the presence of an NePC and to assess the diagnostic accuracy of BSE and NASQ for NePC.[5]

The objective of this study was to assess the potential association between clinically diagnosed absent or present NePC and BSE and NASQ in patients with chronic (≥3 months) low back and leg pain (LBLP) or with neck shoulder arm pain (NSAP) radiating into the leg(s) or arm(s), or in patients with chronic pain due to suspected peripheral nerve damage (sPND).

Methods

This study is based on a cross-sectional, observational research design to generate new insights into the clinical assessment of NePC. It is a sub-analysis of a study approved by the medical and ethical review board Committee on Research Involving Human Subjects, region Arnhem-Nijmegen, Nijmegen, the Netherlands, dossier number: 2008/348; NL 25343.091.08.

In the original study conducted between October 2009 and June 2013, we validated the Dutch PainDETECT[29] and the DN4.[30,31] The PainDETECT[32] and the DN4[33] were both developed to screen for the presence of neuropathic pain. The patient self-administered PainDETECT is a simple screening tool with no need for physical examination. The instrument consists of one item about the pain course pattern, one about radiating pain, and seven questions about the gradation of pain. The clinician-administered DN4 consists of a total of 10 items with yes/no answers. It is divided into two questions (symptoms) and two physical examination tests (signs). The two sign items were incorporated in the sensory examination part of the standardized assessment form.[28] The protocol was registered in the Dutch National Trial Register: NTR 3030 and published by Timmerman et al.[28] Patients provided written informed consent after screening, but before participation in the study.

Participants

We recruited patients as part of the Dutch validation studies concerning the PainDETECT and the DN4. Inclusion criteria were male and female adult patients aged over 18 years with chronic (≥3 months) LBLP or NSAP, or patients with chronic pain due to sPND. We excluded patients suspected for or diagnosed with malignancy; compression fractures; patients with diffuse pains such as fibromyalgia or ankylosing spondylitis; severe mental illness; chronic alcoholism or substance abuse; inability to fill in the questionnaire adequately; or incapable of understanding the Dutch language.

Pain classification

Classification of patients' pain was based on the NeuPSIG guidelines on neuropathic pain assessment.[6] Pain classification was performed consecutively but blinded for the outcome

on the same patient independently by two physicians working in different compositions, and then categorized into three groups: "absent NePC", "present NePC" where both physicians were in agreement, or "undetermined NePC" in cases where they did not agree. A full medical history and clinical examination including sensory BSE was taken[6,7,21,28,34] and considered as the gold standard for NePC diagnosis.

Bedside examination

Multicenter recruitment took place in the Netherlands in three academic pain centers and in four non-academic pain centers. A standardized BSE[28] was independently performed by two physicians during the validation study for the two neuropathic pain screening tools. Prior to the study, the physicians were trained in the standardized evaluation of patients with chronic pain using specific modalities such as touch, pin prick, pressure, cold, heat, vibration, and temporal summation. The location indicated by the patient as having maximum pain was compared with the mirrored location on the contralateral side. When the pain had a double-sided character, a location without pain but as close as possible to the original mirror site was tested for comparison. Patients were asked the following: 1) is a sensation present? 2) is the sensation unpleasant? or 3) is the sensation painful? (all scored as yes, no, or unclear) The outcome was noted by the physician on the standardized assessment form.[28] The following tests were performed consecutively on each patient independently by two physicians: 1) mechanical static allodynia via blunt pressure with a finger at a force that normally does not evoke pain; 2) dynamic mechanical allodynia via stroking the skin with a Soft Brush (SENSElab™, Brush-05, Somedic AB, Hörby, Sweden), 2a) one movement of 1–2 centimeter and 2b) three movements of 1–2 centimeters (wind-up response); 3) mechanical pinprick allodynia via touch of the skin with 3a) a plastic safety pin and 3b) a Von Frey hair (TOUCH TEST®, 5.07, 10.0 g, North Coast Medical Inc., Gilroy, CA, USA); 4) heat allodynia by use of TipTherm® (TipTherm, Brüggen, Germany) in a baby-bottle warmer (ISI mini Baby Bottle Warmer, Assen, the Netherlands) set at 45 degrees Celsius; 5) cold allodynia with an ice cube placed on the skin for 2 seconds; and 6) vibration with a tuning fork (128 Hz; Medipharchem, Wormerveer, the Netherlands) applied to joint, bone, or soft tissue in the region of the pain.

Nijmegen–Aalborg screening QST

Patients for the additional NASQ part of the study were recruited in one academic pain center and two non-academic pain centers. After screening in the clinical department, patients were asked to participate. The NASQ was performed in a random sub-sample of 20% of the patient population (LBLP, NSAP, and sPND) by a trained and experienced researcher (HT).[28] The NASQ paradigm[15,16,24,28] was used as screening protocol. The NASQ screens for changes in pain processing based on a systematic mechanism-oriented approach.[16] It maps pain sensitivity at multiple sites by measuring the responses (ie, painful sensations) evoked by mechanical and electrical non-invasive stimuli, and measures the patient's capacity to modulate pain using the CPM. Instructions were standardized and read to each patient from an instruction sheet.

Pressure pain threshold (PPT) test

A pressure algometer (Somedic AB) was used to measure PPTs bilaterally at each location, expressed in kilo Pascal: thenar (middle part), musculus trapezius pars median (middle part), musculus rectus femoris (15 cm above patella), and musculus abductor hallucis (middle part). In addition to the analysis with an average value over these eight measurement points, we performed additional analyses in the four central measurement points: musculus trapezius pars median (both sides) and musculus rectus femoral (both sides), and the four peripheral measurement points: thenar (both sides) and m. abductor hallucis (both sides).

Electrical pain thresholds

The QST-3 device (JNI Biomedical ApS, Klarup, Denmark) was used to measure electrical pain thresholds (EPTs) on the left and right body side. Measurement locations were the musculus trapezius pars median (middle part) and the musculus rectus femoris (20 cm above patella). Thresholds were assessed and expressed in milli-Ampère. EPTs were measured as electrical pain detection threshold (EPDT) when the current started to feel pain, and as electrical pain tolerance threshold (EPTT) when the current was as high as the patient could tolerate.

CPM response

We assessed CPM[17,27] via the PPT (CPMp) and the EPT (CPMe) on the m. rectus femoris contralateral to the dominant hand. The noxious stimulus (conditioning stimulation) was to immerse the dominant hand to the wrist in a bucket filled with water and ice cubes (ice water bucket [IWB] test).[25] The patient was instructed to "keep the hand in the water for as long as possible, until the moment that the sensation becomes unbearable and you want to stop directly". Pain was recorded every 10 seconds on the numeric rating scale. The duration

of the immersion (with a maximum of 180 seconds) was recorded and the pain intensity at the end of the immersion was also registered. The PPT and the EPT were then assessed again on the contralateral m. rectus femoris. The response was calculated by subtracting the outcome of the pre-measurement from the outcome of the post-measurement. The CPM values were calculated using the following formulas:

$$CPMp=([PPT_{post} - PPT_{pre}]/PPT_{pre}) * 100$$

$$CPMe=([EPT_{post} - EPT_{pre}]/EPT_{pre}) * 100$$

CPM was regarded as "positive" when the outcome of the calculation was equal or higher than zero and negative when it was below zero.

Data

All data were collected on paper from the patients and the physicians and stored at Radboudumc, Nijmegen, the Netherlands. Data management and monitoring were performed using MACRO (MACRO, version 4.1.1.3720, InferMed, London, UK). Data analysis and statistics were performed using Statistical Package for the Social Sciences (SPSS version 20.0, SPSS Inc., Chicago, IL, USA).

Statistical methods

Qualitative variables are presented as frequencies and percentages. Quantitative variables are presented as mean and SD or as median and interquartile range. The chi-square test was used to test for significant differences between nominal outcome data. Cramér's *V* was used as a measure of association between two nominal variables, giving a value between 0 and 1. Mann–Whitney *U*-test was used to test the differences between present and absent NePC. Kruskal–Wallis test was used to study differences between the three (absent NePC, present NePC, and undetermined) groups. We used Cohen's Kappa and the percentage of pair wise agreement to determine the agreement between the BSE between the patient's first and second assessment. A two-tailed *p*-value below 0.05 was considered statistically significant.

Results

In total, 330 patients with chronic LBLP, NSAP, or sPND were assessed for eligibility. Two patients did not provide informed consent prior to inclusion in the study. Thirty-seven patients were excluded because of not meeting the inclusion and exclusion criteria (n=13); not returning the baseline questionnaires (n=16), and missing pain classification by one physician (n=5) or both physicians (n=3).

BSE was performed in this study in 291 patients by 62 different physicians from seven hospitals. The present NePC group (n=170) consisted of 75 patients with LBLP, 23 patients with NSAP, and 72 patients with sPND. The absent NePC group (n=58) consisted of 28 patients with LBLP, 18 patients with NSAP, and 12 patients with sPND. For the undetermined group (n=63), the numbers were 29, 10, and 24, respectively (see Figure 1 and Table 1).

The NASQ was performed in a total of 69 patients. Patients were excluded after the NASQ measurements were made: not fulfilling the inclusion and exclusion criteria (n=9) or a missing assessment by a second physician (n=2). Finally, a total of 58 patients (56 Dutch natives, 1 German native, and 1 of Chinese/Indonesian origin) were included in the analysis: 25 with LBLP, 25 with NSAP, and 8 with sPND. After NePC assessment by the physicians, 16 patients were classified as absent NePC, 29 with present NePC, and 13 patients with an undetermined outcome. The absent NePC group, present NePC group, and undetermined group had 4, 14, and 7 patients with LBLP; 12, 7, and 5 patients with NSAP; and 0, 7, and 1 patient(s) with sPND, respectively (see Figure 1 and Table 1).

In Tables 2 and S1, we have shown the outcome of the BSE based on the inter-physician agreement on the existence of an NePC. In the first assessment by the physician, the answers on the question "is there a sensation (yes, no, unclear) during testing for heat, cold, touch (brush 3 times), and pricking (both safety pin and von Frey hair)" were significantly lower ($p<0.05$) for yes in the group with present NePC compared to the absent NePC group. In the second assessment, the scores for the question "is there a sensation (yes, no, unclear) of heat, cold, touch, (only brush 1 time), and pricking (von Frey hair only)" were significantly lower ($p<0.05$) for yes in the group with present NePC with a lower percentage of "yes" compared to the absent NePC. The scores for the questions "is the touch with a finger unpleasant?" and "is touch with a brush unpleasant?" were higher for the second assessment for the group with present NePC ($p=0.049$ and $p=0.006$, respectively). "Painful for touch with a finger" was more common in patients with present NePC ($p=0.026$) in the second assessment. "Wind-up" was more common in patients with present NePC compared to the patients with absent NePC (first assessment $p=0.056$; second assessment $p=0.029$). In Table S1, we have shown the outcome of the BSE based on the inter-physician agreement for the occurrence of NePC for patients with LBLP, NSAP, and sPND.

The outcomes of the NASQ measurements related to physician agreement for the existence of NePC are presented in

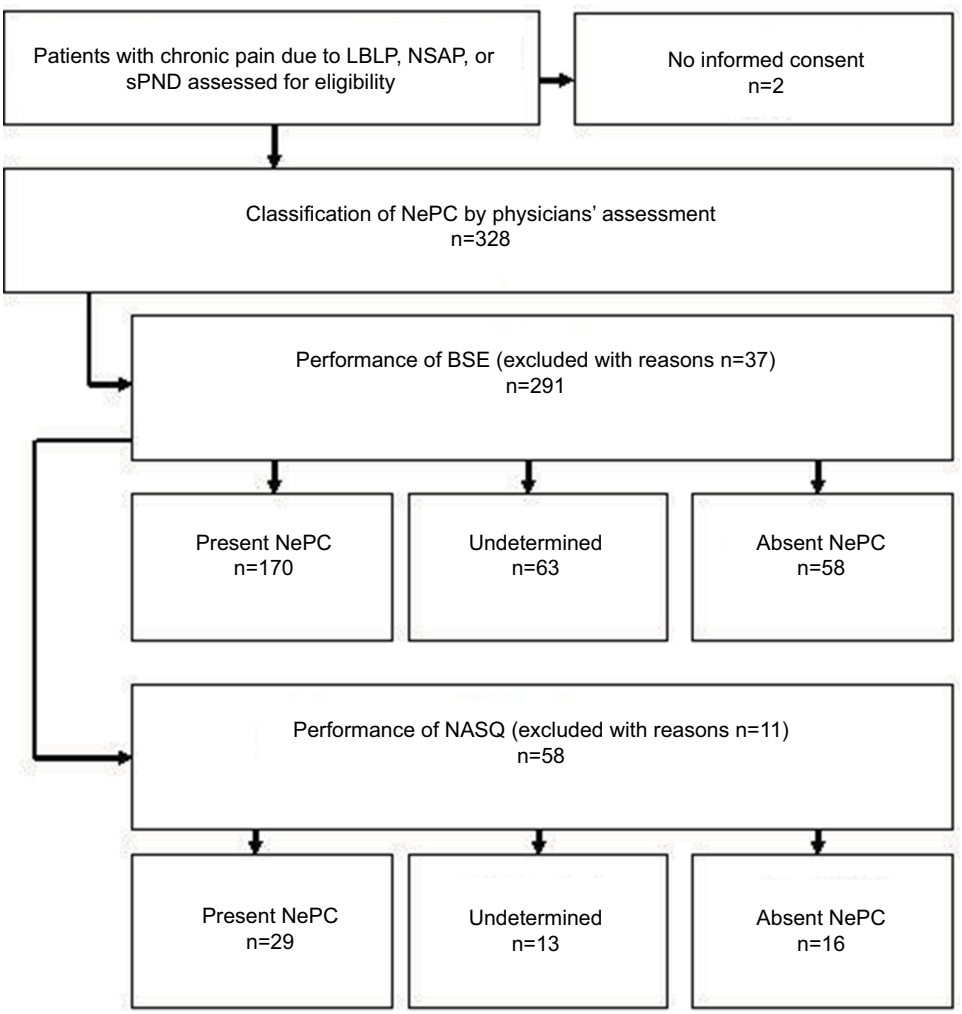

Figure 1 Flow diagram for the performance of the BSE and NASQ in patients with chronic pain with respect to the physicians' assessment.
Notes: n, number of patients in analysis; Present NePC, NePC is present; Undetermined, both physicians disagree with each other about the presence of a NePC; Absent NePC, no NePC is present.
Abbreviations: LBLP, low back and leg pain; NSAP, neck shoulder arm pain; sPND, suspected peripheral nerve damage; BSE, bedside examination; NePC, neuropathic pain component; NASQ, Nijmegen– Aalborg screening quantitative sensory testing.

Table 3. No significant difference was detected for pressure, EPDT, EPTT, and duration of submerging the hand in the IWB between the absent, present, and undetermined NePC groups. We found no congruency between the CPMp and the CPMe. When basing the CPM classification on pressure values, the significance disappeared for the outcome of the CPM test based on electricity values (response p=0.440, CPM-value p=0.374). This was also true when the CPM electricity test outcome was used to analyze the response and CPM value for pressure (p=0.728 and p=0.810, respectively). Moreover, in the IWB test, we found no significant differences regarding the duration (latency) of submerging the hand between the positive and negative CPM test for both the pressure and electricity conditions (p=0.120 and p=0.711, respectively).

Discussion

The aim of this study was to assess the potential association between a clinically diagnosed absent or present NePC, BSE, and NASQ in patients with chronic pain. BSE revealed minor differences, with a low association between patients with present NePC and patients with absent NePC following independent clinical NePC assessment by two independent physicians, while none were found with NASQ.

Bedside examination

We used BSE based on mechanical and thermal testing procedures, performed by two physicians independently and blinded for the results of the other.[28] The added value of BSE is that it gives insights into the pathology and the localization of the nerve lesion or disease causing the pain.[6,7,35,36]

Table 1 Sociodemographic characteristics for the patients included in the BSE and the NASQ examination related to the physicians' agreement for the existence of an NePC

		Total group	Absent NePC	Present NePC	*p*-value	Undetermined NePC	*p*-value
Bedside examination		**n (%) Median (IQR) (N=291)**	**n (%) Median (IQR) (N=58)**	**n (%) Median (IQR) (N=170)**	**(N=228)**	**n (%) Median (IQR) (N=63)**	**(N=291)**
Sex	Male	98 (34%)	25 (43%)	56 (33%)	0.163[a]	17 (27%)	0.164[a]
	Female	193 (66%)	33 (57%)	114 (67%)		46 (73%)	
Age (years)		57 (49;64)	57 (50;62)	57 (49;64)	0.935[b]	57 (49;67)	0.831[c]
BMI (kg/m^2)		26 (24;30)	26 (23;30)	26 (24;30)	0.943[b]	27 (24;30)	0.688[c]
Pain	Current pain	5 (3;7)	5 (3;7)	6 (3;7)	0.577[b]	4 (1;7)	0.084[c]
(NRS; 0–10)	Worst pain	8 (6;9)	8 (5;9)	8 (7;9)	0.371[b]	7 (5;8)	0.053[c]
	Average pain	6 (4;7)	6 (3.5;7)	6 (5;8)	0.233[b]	6 (3;7)	**0.018**[c]
Duration of pain (months)		36 (18;60)	48 (18;60)	31 (18;60)	0.445[b]	36 (14;60)	0.733[b]
Quantitative sensory testing		**n (%) Median (IQR) (N=58)**	**n (%) Median (IQR) (N=16)**	**n (%) Median (IQR) (N=29)**	**(N=45)**	**n (%) Median (IQR) (N=13)**	**(N=58)**
Sex	Male	31 (53%)	9 (56%)	15 (52%)	0.771[a]	7 (54%)	0.958[a]
	Female	27 (47%)	7 (44%)	14 (48%)		6 (46%)	
Age (years)		58 (52;64)	59 (52;63)	58 (52;64)	0.669[b]	56 (52;65)	0.906[c]
BMI (kg/m^2)		27 (25;31)	26 (23;30)	27 (25;31)	0.674[b]	28 (25;32)	0.908[c]
Pain	Current pain	6 (5;7)	6 (5;7)	6 (5;7)	0.887[b]	5 (2;8)	0.613[c]
(NRS; 0–10)	Worst pain	8 (7;9)	8 (8;9)	8 (7;9)	0.740[b]	8 (8;9)	0.706[c]
	Average pain	7 (6;7)	7 (6;7)	7 (6;8)	0.424[b]	7 (5;8)	0.567[c]
Duration of pain (months)		36 (18;78)	52 (30;227)	26 (18;81)	0.069[b]	24 (12;57)	0.104[c]

Notes: Classification for the existence of NePC is based on physicians' assessment of the patients. Absent NePC, no NePC is present; Present NePC, NePC is present; *p*-value, value for significant difference between groups ($p \leq 0.05$); N, total number of patients in analysis; [a]chi-square test; [b]Mann–Whitney *U*-test; [c]Kruskal–Wallis test. Bold values are statistically significant ($p \leq 0.05$).

Abbreviations: BSE, bedside examination; NASQ, Nijmegen–Aalborg screening quantitative sensory testing; NePC, neuropathic pain component; BMI, body mass index; NRS, numeric rating scale; median (IQR), median with interquartile range (25%–75%).

The BSE results showed statistical significant differences between patients with absent NePC and patients with present NePC. BSE revealed that the sensation of heat, cold, wind-up response (with a brush, three times), pricking with a safety pin, and pricking with a von Frey hair was less common in patients with a present NePC than in those with an absent NePC. In addition, wind-up response occurred more often in patients with present NePC than in those with absent NePC.

Screening QST

We used the NASQ to assess the altered pain processing, including changes in function of endogenous pain modulation as a secondary test battery.[15,28] The NASQ test protocol has standardized instructions, an important prerequisite to ensure reliability of the measurements.[20,37] We found no differences between patients with absent and present NePC regarding PPTs, electrical pain (tolerance) thresholds, and CPM outcomes (number of positive and negative CPM outcomes, the response, the CPM value, and the latency times when submerging the hand in ice water). Granovsky[38] reported that patients with chronic neuropathic pain express a less efficient (negative) CPM. In our study, we could not confirm this when comparing patients with LBLP, NSAP, or sPND with and without NePC. As suggested by Graven-Nielsen and Arendt-Nielsen,[39] lower PPTs may be indicative for central sensitization. We also could not find any differences in the pain thresholds of patients with and without NePC. Moreover, a difference in CPM may also suggest a central dysfunction. However, based on our results, we cannot state that there are signs of central sensitization or altered central pain processing as might be suspected because of lower pain thresholds for pressure pain or an impaired CPM, because we did not include age, sex, and education matched controls, which would be necessary to draw these higher level conclusions.

Limitations

We would have preferred to use the German Research Network on Neuropathic Pain (DFNS)[11,12] to BSE because of the standardization of the complete test procedure (written test instructions, application of the test stimuli, and data analyses).[12,40] However, due to time constraints in a patient care setting, it was not possible and preferable to use such a research test battery. Moreover, in simulating daily clinical practice, fulfilling the DFNS protocol is not applicable due

Table 2 Bedside examination outcome based on inter-physician (A–B) agreement on the presence of an NePC

	First assessment							Second assessment							Agreement between physicians	
	N total	Absent NePC		Present NePC		*p*-value	*V*	N total	Absent NePC		Present NePC		*p*-value	*V*	K	PA (%)
		n	%	n	%				n	%	n	%				
Touch (finger)																
Sensation	290	58	95	169	95	0.964	0.003	289	58	97	168	96	0.965	0.003	0.177	93.3
Unpleasant	288	57	35	168	45	0.181	0.089	289	58	33	168	48	0.049	0.131	0.378	69.5
Painful	286	57	28	167	37	0.215	0.083	288	57	25	168	41	**0.026**	0.149	0.315	68.8
Heat																
Sensation	283	57	91	166	68	**0.001**	0.230	287	57	91	167	66	**0.000**	0.247	0.435	77.6
Unpleasant	283	57	16	166	16	0.707	0.056	287	57	16	167	21	0.396	0.057	0.319	79.9
Painful	283	57	7	166	9	0.626	0.065	287	57	12	167	14	0.775	0.019	0.258	90.0
Cold																
Sensation	275	55	93	165	75	**0.016**	0.194	284	58	93	168	75	**0.003**	0.196	0.320	77.6
Unpleasant	274	55	2	164	12	0.052	0.164	284	58	7	168	11	0.338	0.064	0.333	87.6
Painful	273	54	0	164	5	0.178	0.126	284	58	2	168	6	0.197	0.086	0.477	95.4
Touch (brush 1 time)																
Sensation	288	58	93	167	81	0.104	0.142	286	57	93	167	79	**0.017**	0.160	0.264	79.6
Unpleasant	288	58	2	167	7	0.156	0.095	287	57	2	168	7	0.132	0.100	0.384	93.7
Painful	288	58	0	167	2	0.234	0.079	287	57	0	168	4	0.148	0.096	0.387	97.3
Touch (brush 3 times)																
Sensation	290	58	97	169	85	**0.021**	0.153	289	58	91	169	80	0.055	0.127	0.303	82.7
Unpleasant	291	58	2	170	7	0.130	0.100	290	58	0	169	12	**0.006**	0.182	0.197	89.4
Painful	291	58	0	170	2	0.308	0.067	290	58	0	169	5	0.092	0.112	0.351	96.9
Wind-up	284	56	0	167	8	0.056	0.161	276	50	0	164	12	**0.029**	0.182	0.188	87.1
Pricking (safety pin)																
Sensation	289	58	95	168	79	**0.006**	0.183	290	58	91	169	82	0.080	0.116	0.240	79.6
Unpleasant	290	58	19	169	31	0.180	0.123	290	58	24	169	31	0.298	0.069	0.357	73.4
Painful	290	58	10	169	20	0.227	0.114	290	58	16	169	21	0.388	0.057	0.286	78.3
Pricking (von Frey hair)																
Sensation	289	58	91	168	68	**0.003**	0.230	288	57	91	169	68	**0.001**	0.229	0.455	79.0
Unpleasant	289	58	7	168	14	0.228	0.114	288	58	16	167	20	0.475	0.048	0.329	81.6
Painful	289	58	3	168	7	0.473	0.081	288	58	12	167	10	0.590	0.036	0.402	90.6
Vibration																
Sensation	291	58	79	170	69	0.060	0.157	288	58	81	167	66	0.089	0.147	0.358	73.3
Unpleasant	290	57	5	170	10	0.528	0.075	290	58	5	169	11	0.275	0.107	0.225	85.4
Painful	291	58	3	170	8	0.517	0.076	290	58	0	169	7	0.114	0.138	0.435	93.0

Notes: Classification of the presence of NePC is based on physicians' assessment of the patient. n, the number of patients; %, the percentage of positive answers (yes) on the questions: Sensation: Is there a sensation?; Unpleasant: Is the sensation unpleasant?; Painful: Is the sensation painful?; *p*-value=*p*-value for statistical significant difference between groups (outcome of chi-square test, $p \leq 0.05$). Bold values are statistically significant ($p \leq 0.05$).

Abbreviation: NePC, neuropathic pain component; V, value of Cramér's V; K, Kappa value; PA, percentage of agreement.

to instrument availability and the associated costs in all participating sites. BSE as used in our study is easy to learn (one training session before execution of the study) and to carry out in daily clinical practice. Another strength of the study is that we included a range of locations and a large group of patients with chronic pain arising from different origins, which is comparable to patients in a daily clinical (pain) practice. A limitation of the BSE examination is that we only used the question "Is there a sensation?" This may have led to a lower estimation of the outcomes because the patients and/or physicians may have interpreted the question was only being related to the presence of hypoesthesia, hypoalgesia, or analgesia (answer "no": negative signs) rather than assessing the presence of hyperalgesia or allodynia positively (answer "yes"). In a following study, we will change this to a more open question that can be interpreted both ways. We did not use verbal standardized instructions, although all participating professionals were trained in a standardized way and so this is another possible limitation of our BSE method. This may have led to differences in the questioning by the physicians, thereby influencing the patients' answers and the test outcome. The order of the BSE tests was not randomized and so there may be an order effect resulting from the previously performed test. Moreover, both physicians tested the same

Table 3 Patient NASQ values related to physicians' agreement for the presence of an NePC

		Total group		Congruent outcome by the physicians		Absent NePC		Present NePC		*p*-value
		N		N		N		N		
Pressure	Summed total	39	872 (516;1117)	30	858 (506;1125)	5	846 (729;1086)	25	929 (465;1132)	0.718[b]
(kPa)	Central	56	866 (542;1068)	43	872 (545;1058)	15	892 (600;989)	28	793 (435;1068)	0.558[b]
	Peripheral	39	794 (526;1084)	30	793 (516;1095)	5	800 (701;1066)	25	787 (488;1106)	0.676[b]
CPM	Positive	23	58%	19	61%	3	60%	16	62%	0.948[a]
	Negative	17	43%	12	39%	2	40%	10	39%	
	No change									
	Response	40	131 (–13;225)	31	109 (3;221)	5	13 (–31;176)	26	155 (24;222)	0.259[b]
	CPM value	40	7.2 (–14;25)	31	7 (–18;23)	5	3 (–19;16)	26	8.0 (–16;34)	0.591[b]
EPDT (mA)	Total mean	53	11 (7;17)	42	12 (8;17)	16	11 (6;20)	26	12 (8;17)	0.969[b]
CPM	Positive	13	81%	10	40%	8	80%	2	100%	0.488[a]
	Negative	3	19%	2	8%	2	20%	0	---[c]	
	No change			13	52%					
	Response	16	0.8 (0.03;4)	12	2 (0.2;5)	10	2 (–0.05;4.0)	2	3 (0.4;---)[c]	0.747[b]
	CPM value	16	7.7 (0.3;30)	12	20 (3;34)	10	15 (–0.2;37)	2	26 (18;---)[c]	0.667[b]
EPTT (mA)	Total mean	25	10 (8;22)	19	13 (8;23)	3	13 (10;---)[c]	16	12 (8;22)	0.314[b]
CPM	Positive	17	68%	13	68%	3	100%	10	63%	0.200[a]
	Negative	8	32%	6	32%	0	---[c]	6	38%	
	No change									
	Response	25	0.5 (–0.2;2)	19	0.5(–0.2;2)	3	2 (1;---)[c]	16	0.4 (–0.3;2)	0.117[b]
	CPM value	25	7 (–2;16)	19	7 (–2;17)	3	12 (9;---)[c]	16	4.8 (–3;16)	0.219[b]
IWB test	Latency (s)	41	20 (10;170)	32	40 (10;180)	5	40 (10;170)	27	40 (10;180)	0.960[b]

Notes: Classification of presence of NePC is based on physicians' assessment of the patients. Absent, NePC is absent; Present, NePC is present; Undetermined, both physicians disagree with each other about the existence of an NePC; N, number of patients in the analysis; CPM > ±10%: patients included in the analysis with a CPM of more than 10% difference from zero. [a]Chi-square test; [b]Mann–Whitney *U*-test. $p \leq 0.05$ is considered statistically significant; [c]due to the low number of patients in the analysis, IQR is not given in the 75% range.

Abbreviations: NASQ, Nijmegen–Aalborg screening quantitative sensory testing; NePC, neuropathic pain component; CPM, Conditioned pain modulation; EPDT, electrical pain detection threshold; EPTT, electrical pain tolerance threshold; IWB, ice water bucket; IQR, interquartile range.

patient directly following each other. Although the second physician was not aware of the first results, this may have also influenced our results. Furthermore, there was no correction for multiple testing while several statistical analyses were performed. Because of this, the results must be interpreted with caution.

Another possible limitation is the fact that we only included a small group of patients with chronic pain measured via NASQ; 8 patients with sPND. This may have affected our outcome because they have a different disease origin compared to patients with LBLP or NSAP. For future NASQ research, we would suggest collecting normative data preferably matched for age, sex, and education level. With these data, the value of NASQ for clinical monitoring disease progression and the response of individual patients on treatment can be evaluated.

Conclusion

Using a standardized BSE to assess sensory dysfunction indicating the presence or absence of an NePC appears to be preferable compared to the NASQ paradigm in patients with chronic pain. However, further development of both assessments is desirable. The BSE should be adapted to detect sensory differences between absent and present NePC; the NASQ paradigm should be able to measure altered pain processing and endogenous pain modulation in patients with chronic pain due to present or absent NePC. We postulate that this will lead to a greater contribution to the assessment of neuropathic components of patients' pain.

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References

1. IASP. IASP taxonomy neuropathic pain. 2015. Available from: http://www.iasp-pain.org/Taxonomy#Neuropathicpain. Accessed May 19, 2015.
2. Dieleman JP, Kerklaan J, Huygen FJ, Bouma PA, Sturkenboom MC. Incidence rates and treatment of neuropathic pain conditions in the general population. *Pain*. 2008;137(3):681–688.
3. Freynhagen R, Bennett MI. Diagnosis and management of neuropathic pain. *BMJ*. 2009;339:b3002.
4. Bouhassira D, Lantéri-Minet M, Attal N, Laurent B, Touboul C. Prevalence of chronic pain with neuropathic characteristics in the general population. *Pain*. 2008;136(3):380–387.
5. La Cesa S, Tamburin S, Tugnoli V, et al. How to diagnose neuropathic pain? The contribution from clinical examination, pain questionnaires and diagnostic tests. *Neurol Sci*. 2015;36(12):2169–2175.
6. Haanpää M, Attal N, Backonja M, et al. NeuPSIG guidelines on neuropathic pain assessment. *Pain*. 2011;152(1):14–27.
7. Haanpää ML, Backonja MM, Bennett MI, et al. Assessment of neuropathic pain in primary care. *Am J Med*. 2009;122(10 Suppl):S13–S21.
8. Truini A, Cruccu G. How diagnostic tests help to disentangle the mechanisms underlying neuropathic pain symptoms in painful neuropathies. *Pain*. 2016;157(Suppl 1):S53–S59.
9. Treede RD, Jensen TS, Campbell JN, et al. Neuropathic pain: redefinition and a grading system for clinical and research purposes. *Neurology*. 2008;70(18):1630–1635.
10. Finnerup NB, Haroutounian S, Kamerman P, et al. Neuropathic pain: an updated grading system for research and clinical practice. *Pain*. 2016;157(8):1599–1606.
11. Rolke R, Baron R, Maier C, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values. *Pain*. 2006;123(3):231–243.
12. Rolke R, Magerl W, Campbell KA, et al. Quantitative sensory testing: a comprehensive protocol for clinical trials. *Eur J Pain*. 2006;10(1):77–88.
13. Backonja MM, Walk D, Edwards RR, et al. Quantitative sensory testing in measurement of neuropathic pain phenomena and other sensory abnormalities. *Clin J Pain*. 2009;25(7):641–647.
14. Arendt-Nielsen L, Yarnitsky D. Experimental and clinical applications of quantitative sensory testing applied to skin, muscles and viscera. *J Pain*. 2009;10(6):556–572.
15. Wilder-Smith OH. *A Paradigm-Shift in Pain Medicine: Implementing a Systematic Approach to Altered Pain Processing in Everyday Clinical Practice Based on Quantitative Sensory Testing*. Aalborg: Center for Sensory-Motor Interaction (SMI), Department of Health Science and Technology, Aalborg University; 2013.
16. Bouwense SA, de Vries M, Schreuder LT, et al. Systematic mechanism-orientated approach to chronic pancreatitis pain. *World J Gastroenterol*. 2015;21(1):47–59.
17. Yarnitsky D. Conditioned pain modulation (the diffuse noxious inhibitory control-like effect): its relevance for acute and chronic pain states. *Curr Opin Anaesthesiol*. 2010;23(5):611–615.
18. Yarnitsky D. Role of endogenous pain modulation in chronic pain mechanisms and treatment. *Pain*. 2015;156(Suppl 1):S24–S31.
19. Hansson P, Backonja M, Bouhassira D. Usefulness and limitations of quantitative sensory testing: clinical and research application in neuropathic pain states. *Pain*. 2007;129(3):256–259.
20. Geber C, Klein T, Azad S, et al. Test-retest and interobserver reliability of quantitative sensory testing according to the protocol of the German Research Network on Neuropathic Pain (DFNS): a multi-centre study. *Pain*. 2011;152(3):548–556.
21. Cruccu G, Sommer C, Anand P, et al. EFNS guidelines on neuropathic pain assessment: revised 2009. *Eur J Neurol*. 2010;17(8):1010–1018.
22. Krumova EK, Geber C, Westermann A, Maier C. Neuropathic pain: is quantitative sensory testing helpful? *Curr Diab Rep*. 2012;12(4):393–402.
23. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. *Pain*. 2011;152(3 Suppl):S2–S15.
24. Chua NHL, Timmerman H, Vissers KC, OH W-S. Multi-modal quantitative sensory testing in patients with unilateral chronic neck pain: an exploratory study. *J Musculoskelet Pain*. 2012;20(4):292–299.
25. Pud D, Granovsky Y, Yarnitsky D. The methodology of experimentally induced diffuse noxious inhibitory control (DNIC)-like effect in humans. *Pain*. 2009;144(1–2):16–19.
26. Corrêa JB, Costa LO, de Oliveira NT, Sluka KA, Liebano RE. Central sensitization and changes in conditioned pain modulation in people with chronic nonspecific low back pain: a case-control study. *Exp Brain Res*. 2015;233(8):2391–2399.
27. Yarnitsky D, Arendt-Nielsen L, Bouhassira D, et al. Recommendations on terminology and practice of psychophysical DNIC testing. *Eur J Pain*. 2010;14(4):339.
28. Timmerman H, Wilder-Smith O, van Weel C, Wolff A, Vissers K. Detecting the neuropathic pain component in the clinical setting: a study protocol for validation of screening instruments for the presence of a neuropathic pain component. *BMC Neurol*. 2014;14(1):94.
29. Timmerman H, Wolff AP, Schreyer T, et al. Cross-cultural adaptation to the Dutch language of the PainDETECT-Questionnaire. *Pain Pract*. 2013;13(3):206–214.
30. Van Seventer R, Vos C, Meerding W, et al. Linguistic validation of the DN4 for use in international studies. *Eur J Pain*. 2010;14(1):58–63.
31. Timmerman H, Steegers MAH, Huygen F, et al. Investigating the validity of the DN4 in a consecutive population of patients with chronic pain. *PLoS One*. 2017;12(11):e0187961.
32. Freynhagen R, Baron R, Gockel U, Tölle TR. PainDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin*. 2006;22(10):1911–1920.
33. Bouhassira D, Attal N, Alchaar H, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *Pain*. 2005;114(1–2):29–36.
34. Cruccu G, Anand P, Attal N, et al. EFNS guidelines on neuropathic pain assessment. *Eur J Neurol*. 2004;11(3):153–162.
35. Baron R, Binder A, Wasner G. Neuropathic pain: diagnosis, pathophysiological mechanisms, and treatment. *Lancet Neurol*. 2010;9(8):807–819.
36. Cruccu G, Truini A. Tools for assessing neuropathic pain. *PLoS Med*. 2009;6(4):e1000045.
37. Backonja MM, Attal N, Baron R, et al. Value of quantitative sensory testing in neurological and pain disorders: NeuPSIG consensus. *Pain*. 2013;154(9):1807–1819.
38. Granovsky Y. Conditioned pain modulation: a predictor for development and treatment of neuropathic pain. *Curr Pain Headache Rep*. 2013;17(9):361.
39. Graven-Nielsen T, Arendt-Nielsen L. Assessment of mechanisms in localized and widespread musculoskeletal pain. *Nat Rev Rheumatol*. 2010;6(10):599–606.
40. Pfau DB, Geber C, Birklein F, Treede RD. Quantitative sensory testing of neuropathic pain patients: potential mechanistic and therapeutic implications. *Curr Pain Headache Rep*. 2012;16(3):199–206.

Supplementary material

Table S1 Bedside examination outcome based on inter physician agreement on the presence of an NePC for the total group and for patients with LBLP, NSAP, or sPND separately

		First assessment							Second assessment						Agreement between physicians	
		N total	Absent NePC		Present NePC		*p*-value	*V*	N total	Absent NePC		Present NePC		*p*-value	*V*	
			n	%	n	%				n	%	n	%			*K*	*PA (%)*
Touch (finger)																	
Sensation	**Total**	290	58	95	169	95	0.964	0.003	289	58	97	168	96	0.965	0.003	0.177	93.3
	LBLP	131	28	100	74	99	0.536	0.061	132	28	100	75	96	0.283	0.106	–0.015	96.0
	NSAP	51	18	89	23	91	0.796	0.040	50	18	94	22	95	0.884	0.023	**0.787**	**97.5**
	sPND	108	12	92	72	92	1.000	0.000	107	12	92	71	97	0.344	0.104	–0.053	91.3
Unpleasant	**Total**	288	57	35	168	45	0.181	0.089	289	58	33	168	48	**0.049**	0.131	0.378	69.5
	LBLP	130	27	22	74	30	0.456	0.074	132	28	25	75	28	0.761	0.030	0.242	70.3
	NSAP	51	18	44	23	44	0.951	0.010	50	18	33	22	45	0.436	0.123	0.388	70.0
	sPND	107	12	50	71	62	0.433	0.086	107	12	50	71	69	0.198	0.141	0.318	68.3
Painful	**Total**	286	57	28	167	37	0.215	0.083	288	57	25	168	41	**0.026**	0.149	0.315	68.8
	LBLP	130	27	19	74	22	0.734	0.034	132	28	18	75	43	0.425	0.079	0.202	73.3
	NSAP	51	18	33	23	44	0.509	0.103	50	18	28	22	41	0.386	0.137	0.297	67.5
	sPND	105	12	42	70	51	0.532	0.069	106	11	36	71	58	0.185	0.146	0.275	63.8
Heat																	
Sensation	**Total**	283	57	91	166	68	**0.001**	0.230	287	57	91	167	66	**0.000**	0.247	**0.435**	**77.6**
	LBLP	127	27	96	71	69	**0.004**	0.288	131	27	96	75	68	**0.003**	0.290	**0.579**	**84.5**
	NSAP	48	18	89	23	74	0.230	0.188	50	18	100	22	86	0.103	0.258	0.286	82.5
	sPND	108	12	83	72	65	0.215	0.135	106	12	67	70	57	0.536	0.068	0.301	67.1
Unpleasant	**Total**	283	57	16	166	16	0.707	0.056	287	57	16	167	21	0.396	0.057	0.319	79.9
	LBLP	127	27	22	71	8	0.153	0.196	131	27	19	75	13	0.514	0.065	0.117	79.4
	NSAP	48	18	6	23	9	0.702	0.060	50	18	6	22	18	0.230	0.190	0.231	87.5
	sPND	108	12	17	72	25	0.742	0.084	106	12	25	70	30	0.725	0.039	**0.424**	**76.8**
Painful	**Total**	283	57	7	166	9	0.626	0.065	287	57	12	167	14	0.775	0.019	0.258	90.0
	LBLP	127	27	7	71	3	0.494	0.120	131	27	11	75	8	0.625	0.048	–0.057	87.6
	NSAP	48	18	6	23	9	0.702	0.060	50	18	6	22	14	0.397	0.134	0.286	90.0
	sPND	108	12	8	72	15	0.741	0.084	106	12	25	70	20	0.693	0.044	0.355	80.5
Cold																	
Sensation	**Total**	275	55	93	165	75	**0.016**	0.194	284	58	93	168	75	**0.003**	0.196	0.320	77.6
	LBLP	130	28	96	74	80	**0.038**	0.205	131	28	96	75	79	**0.031**	0.213	**0.458**	**85.3**
	NSAP	43	15	87	22	86	0.979	0.004	50	18	100	22	95	0.360	0.145	0.302	89.2
	sPND	102	12	92	69	65	0.186	0.204	103	12	75	71	65	0.489	0.076	0.148	62.5
Unpleasant	**Total**	274	55	2	164	12	0.052	0.164	284	58	7	168	11	0.338	0.064	0.333	87.6
	LBLP	129	28	4	73	10	0.489	0.119	131	28	7	75	5	0.727	0.034	0.357	91.1
	NSAP	43	15	0	22	9	0.230	0.197	50	18	0	22	18	0.057	0.302	**0.641**	**94.6**
	sPND	102	12	0	69	16	0.294	0.174	103	12	17	71	15	0.918	0.011	0.217	80.0
Painful	**Total**	273	54	0	164	5	0.178	0.126	284	58	2	168	6	0.197	0.086	**0.477**	**95.4**
	LBLP	129	28	0	73	0	0.534	0.062	131	28	4	75	1	0.464	0.072	–0.007	97.0
	NSAP	42	14	0	22	5	0.418	0.135	50	18	0	22	14	0.103	0.258	**0.478**	**94.4**
	sPND	102	12	0	69	10	0.462	0.138	103	12	0	71	8	0.296	0.115	**0.582**	**93.8**
Touch (brush 1 time)																	
Sensation	**Total**	288	58	93	167	81	0.104	0.142	286	57	93	167	79	**0.017**	0.160	0.264	79.6
	LBLP	130	28	100	73	90	0.089	0.169	132	28	100	75	88	0.055	0.189	0.187	88.1
	NSAP	51	18	89	23	96	0.409	0.129	48	17	100	22	86	0.113	0.254	0.278	89.7
	sPND	107	12	83	71	68	0.533	0.123	106	12	67	70	67	0.974	0.004	0.178	64.2
Unpleasant	**Total**	288	58	2	167	7	0.156	0.095	287	57	2	168	7	0.132	0.100	0.384	93.7
	LBLP	130	28	4	73	6	0.826	0.022	132	28	0	75	3	0.383	0.086	0.385	97.0
	NSAP	51	18	0	23	9	0.200	0.200	48	17	0	22	18	0.063	0.297	0.374	62.3
	sPND	107	12	0	71	10	0.256	0.125	106	12	8	71	8	0.989	0.001	0.375	90.2

(*Continued*)

Table S1 (*Continued*)

		First assessment							Second assessment						Agreement between physicians	
		N total	Absent NePC		Present NePC		*p*-value	*V*	N total	Absent NePC		Present NePC		*p*-value	*V*	
			n	%	n	%				n	%	n	%			*K*	*PA* (%)
Painful	**Total**	288	58	0	167	2	0.234	0.079	287	57	0	168	4	0.148	0.096	0.387	97.3
	LBLP	130	28	0	73	1	0.534	0.062	132	28	0	75	3	0.383	0.086	–0.013	97.0
	NSAP	51	18	0	23	0	---	---	48	17	0	22	5	0.373	0.143	0.000	97.4
	sPND	107	12	0	71	4	0.468	0.080	107	12	0	71	4	0.468	0.080	**0.654**	**97.6**
Touch (brush 3 times)																	
Sensation	**Total**	290	58	97	169	85	**0.021**	0.153	289	58	91	169	80	**0.055**	0.127	0.303	82.7
	LBLP	132	28	100	75	96	0.283	0.106	132	28	100	75	93	0.161	0.138	0.222	94.2
	NSAP	51	18	89	23	96	0.409	0.129	50	18	100	22	86	0.103	0.258	0.279	90.0
	sPND	107	12	100	71	70	**0.029**	0.239	107	12	58	72	65	0.642	0.051	0.190	65.1
Unpleasant	**Total**	291	58	2	170	7	0.130	0.100	290	58	0	169	12	**0.006**	0.182	0.197	89.4
	LBLP	132	28	4	75	5	0.711	0.036	132	28	0	75	8	0.123	0.152	0.136	91.3
	NSAP	51	18	0	23	87	0.200	0.200	50	18	0	22	23	**0.031**	0.342	0.304	90.0
	sPND	108	12	0	72	8	0.299	0.113	108	12	0	72	13	0.195	0.141	0.198	86.9
Painful	**Total**	291	58	0	170	2	0.308	0.067	290	58	0	169	5	0.092	0.112	0.351	96.9
	LBLP	132	28	0	75	3	0.383	0.086	132	20	0	75	4	0.283	0.106	0.386	97.1
	NSAP	51	18	0	23	0	---	---	50	18	0	22	5	0.360	0.145	0.000	97.5
	sPND	108	12	0	72	1	0.681	0.045	108	12	0	72	6	0.403	0.091	0.388	96.4
Wind-up	**Total**	284	56	0	167	8	0.056	0.161	276	50	0	164	12	**0.029**	0.182	0.188	87.1
	LBLP	131	28	0	75	7	0.304	0.152	125	26	0	71	7	0.310	0.155	0.296	91.8
	NSAP	48	16	0	22	9	0.215	0.201	44	12	0	22	5	0.290	0.270	0.145	87.1
	sPND	105	12	0	70	10	0.468	0.136	107	12	0	71	15	0.143	0.161	0.116	81.5
Pricking (safety pin)																	
Sensation	**Total**	289	58	95	168	79	**0.006**	0.183	290	58	91	169	82	0.080	0.116	0.240	79.6
	LBLP	132	28	100	75	85	**0.032**	0.211	132	28	100	75	92	0.123	0.152	0.046	85.4
	NSAP	51	18	94	23	91	0.702	0.060	50	18	100	22	95	0.360	0.145	**0.481**	**95.0**
	sPND	106	12	25	71	35	0.489	0.079	108	12	58	72	67	0.574	0.061	0.176	64.6
Unpleasant	**Total**	290	58	19	169	31	0.180	0.123	290	58	24	169	31	**0.298**	0.069	0.357	73.4
	LBLP	132	28	21	75	31	0.519	0.113	132	28	32	75	32	0.989	0.001	**0.456**	**76.7**
	NSAP	51	18	11	23	17	0.572	0.088	50	18	11	22	32	0.119	0.247	0.106	72.5
	sPND	107	12	25	71	35	0.489	0.076	108	12	25	72	31	0.697	0.043	0.308	69.9
Painful	**Total**	290	58	10	169	20	0.227	0.114	290	58	16	169	21	**0.388**	0.057	0.286	78.3
	LBLP	132	28	14	75	15	0.826	0.061	132	28	18	75	17	0.950	0.006	0.265	79.6
	NSAP	51	18	0	23	13	0.111	0.249	50	18	11	22	27	0.204	0.201	0.082	77.5
	sPND	107	12	17	71	27	0.457	0.082	108	12	17	72	22	0.664	0.047	0.364	77.1
Pricking (von Frey hair)																	
Sensation	**Total**	289	58	91	168	68	**0.003**	0.230	288	57	91	169	68	**0.001**	0.229	**0.455**	**79.0**
	LBLP	132	28	96	75	82	**0.045**	0.245	132	28	96	75	75	**0.013**	0.245	0.291	77.7
	NSAP	51	18	94	23	91	0.702	0.060	50	18	100	22	91	0.189	0.208	**0.787**	**97.5**
	sPND	106	12	75	70	54	0.180	0.148	106	11	64	72	54	0.556	0.065	**0.423**	**71.6**
Unpleasant	**Total**	289	58	7	168	14	0.228	0.114	288	58	16	167	20	0.475	0.048	0.329	81.6
	LBLP	132	28	4	75	16	0.353	0.142	131	28	18	74	14	0.580	0.055	0.171	81.4
	NSAP	51	18	0	23	13	0.111	0.249	50	18	11	22	32	0.119	0.247	**0.437**	**85.0**
	sPND	106	12	25	70	17	0.752	0.083	107	12	17	71	23	0.648	0.050	**0.410**	**80.2**
Painful	**Total**	289	58	3	168	7	0.473	0.081	288	58	12	167	10	0.590	0.036	**0.402**	**90.6**
	LBLP	132	28	4	75	4	0.823	0.062	131	28	14	74	8	0.349	0.093	0.292	90.2
	NSAP	51	18	0	23	8	0.111	0.249	50	18	6	22	14	0.397	0.134	**0.531**	**92.5**
	sPND	106	12	8	70	7	0.909	0.048	107	12	17	71	10	0.483	0.077	**0.450**	**90.1**
Vibration																	
Sensation	**Total**	291	58	79	170	69	0.060	0.157	288	58	81	167	66	0.089	0.147	0.358	73.3
	LBLP	132	28	71	75	68	0.218	0.172	131	28	71	74	58	0.217	0.122	**0.446**	**74.5**
	NSAP	51	18	89	23	78	0.369	0.140	50	18	94	22	91	0.673	0.067	0.136	82.5
	sPND	108	12	83	72	68	0.284	0.117	107	12	83	71	66	0.484	0.132	0.242	67.5

(*Continued*)

Table S1 (*Continued*)

		First assessment							Second assessment						Agreement between physicians	
		N total	Absent NePC		Present NePC		*p*-value	*V*	N total	Absent NePC		Present NePC		*p*-value	*V*	
			n	%	n	%				n	%	n	%			
Unpleasant	**Total**	290	57	5	170	10	0.528	0.075	290	58	5	169	11	0.275	0.107	0.225	85.4
	LBLP	132	28	4	75	8	0.571	0.105	132	28	0	75	7	0.304	0.152	0.362	91.3
	NSAP	50	17	6	23	9	0.738	0.053	50	18	6	22	23	0.130	0.239	0.133	87.2
	sPND	108	12	8	72	13	0.838	0.065	108	12	17	72	13	0.855	0.061	0.155	79.8
Painful	Total	291	58	3	170	8	0.517	0.076	290	58	0	169	7	0.114	0.138	**0.435**	**93.0**
	LBLP	132	28	4	75	9	0.720	0.080	132	28	0	75	3	0.562	0.106	0.380	94.2
	NSAP	51	18	0	23	13	0.111	0.249	50	18	0	22	14	0.103	0.258	**0.640**	**95.0**
	sPND	108	12	8	72	8	0.919	0.045	108	12	0	72	8	0.299	0.113	0.381	90.5

Notes: Classification for the existence of NePC is based on the physicians' assessment of the patient. n, the number of patients; %, the percentage of positive answers (yes) on the questions; Sensation, Is there a sensation?; Unpleasant, Is the sensation unpleasant?; Painful, Is the sensation painful?; *p*-value, *p* value for statistical significant difference between groups (outcome of chi-square test, $p \leq 0.05$). Bold values are statistically significant ($p \leq 0.05$).

Abbreviations: NePC, neuropathic pain component; LBLP, low back and leg pain; NSAP, neck shoulder arm pain; sPND, suspected peripheral nerve damage; V, value of Cramér's V; K, Kappa value; PA, percentage of agreement.