

# Quantitative Sensory Testing and Pain Management

Supranee Niruthisard, MD<sup>1</sup>, Nath Pasutharnchat, MD<sup>2</sup>

<sup>1</sup> Pain Management Research Unit, Department of Anesthesiology, Faculty of Medicine, Chulalongkorn University, and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand

<sup>2</sup> Division of Neurology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand

Quantitative sensory testing (QST) is a psychophysical assessment of somatosensory system that complements neurological sensory examination. The information derived from QST presents the function of unmyelinated C-fibers, small myelinated A $\delta$ -fibers, and large myelinated A $\beta$ -fibers including their central pathways to the brain. QST may be performed by simple bedside method and by standardized method developed from the German Research Network on Neuropathic Pain (Deutscher Forschungsverbund Neuropathischer Schmerz, DFNS). The standardized QST makes it possible to subgroup patients with peripheral neuropathic pain of different etiologies according to sensory profiles with emerging evidence showing predictive value of QST for treatment efficacy.

**Keywords:** Quantitative sensory testing, Neuropathic pain, Sensory profile

Received 17 Dec 2019 | Revised 14 Feb 2020 | Accepted 18 Feb 2020

**J Med Assoc Thai 2020;103(8):837-43**

**Website:** <http://www.jmatonline.com>

Traditionally, clinical neurophysiology focuses on investigation of functions of large myelinated afferent fibers i.e., A $\alpha$ -fibers (motor function) and A $\beta$ -fibers (touch, tactile detection, vibration). The standard measurements of large myelinated fibers are electromyography and nerve conduction study, which are beneficial in the diagnosis of mono- and poly-neuropathies and monitoring of somatosensory evoked potentials. However, the pathological changes causing abnormal function of small myelinated A $\delta$ -fibers and unmyelinated C-fibers may happen prior to the pathology of motor nerves and cannot be detected by nerve conduction studies.

Quantitative sensory testing (QST) is a non-invasive evaluation of the quality of function of peripheral afferent nerve fibers. It is a psychophysical

examination of the somatosensory system, which the intensity of the stimulus is objectively quantified for assessment of the perceived subjective sensation. Unlike the nerve conduction studies, the test is under voluntary control and requires co-operation of the subject tested. Results of QST reflect only the function, not the structural changes of the nervous system, which can be found in confocal corneal microscopy and assessment of intraepidermal nerve fiber density (IENFD) by skin biopsy<sup>(1,2)</sup>. The information derived from QST presents the function of unmyelinated C-fibers, small myelinated A $\delta$ -fibers, and large myelinated A $\beta$ -fibers including their central pathways to the brain. QST has been developed to complement and quantify the neurological sensory examination with more precise somatosensory investigation compared to the conventional bedside sensory examination<sup>(1-3)</sup>.

## Correspondence to:

Niruthisard S.

Department of Anesthesiology, Faculty of Medicine, Chulalongkorn University, and King Chulalongkorn Memorial Hospital, 1873 Rama IV Road, Bangkok 10330, Thailand.

**Phone:** +66-2-6494000 ext. 81514, **Fax:** +66-2-2564294

**Email:** [drsupsanee@hotmail.com](mailto:drsupsanee@hotmail.com)

## How to cite this article:

Niruthisard S, Pasutharnchat N. Quantitative Sensory Testing and Pain Management. J Med Assoc Thai 2020;103:837-43.

[doi.org/10.35755/jmedassocthai.2020.08.10941](https://doi.org/10.35755/jmedassocthai.2020.08.10941)

## History

1835, Weber initially introduced a two-point discrimination to test the ability in spatial separation of two tactile stimuli. This test has become one of the clinical examinations of the somatosensory system<sup>(4)</sup>.

1895, Von Frey proposed a correlation between the recently described histological structures in the skin as receptors and specific cutaneous sensibility. In the following year, he used horse or boar hair of different stiffness and length to determine the tactile

sensation in human<sup>(5)</sup>. The materials used as von Frey filaments for QST nowadays are made from plastic or optical glass fibers.

1911, Head and Holmes used the algometer to measure pressure pain. They quantified deficits of sensation in patients suffered from cortical lesions with an algometer and other devices<sup>(6,7)</sup>.

1978, Dyck et al introduced an automated method for the quantification of pressure, temperature perception, vibration, and touch<sup>(8)</sup>. After that, the increasing interest to quantify the sensation on thermal and mechanical detection and pain thresholds led to the development of additional devices like the thermotester and the pressure algometer.

2002, the German Research Network on Neuropathic Pain (Deutscher Forschungsverbund Neuropathischer Schmerz, DFNS) developed standardized QST battery of sensory tests<sup>(9)</sup>. Since then, the standardized QST according to DFNS has been employed in Germany and in many countries worldwide.

### Methods for QST

QST includes thermal and mechanical evaluation. Based on the endpoint measures, QST may be categorized into two groups, static and dynamic. Measurement of static QST includes threshold determination and rating of stimulus intensity or pain magnitude. The limited endpoint of static QST measures identifies one point on a scale of sensation within a complex pain processing system, while dynamic QST quantitatively assesses central integration (e.g., temporal and spatial summation) and function of the descending pain control (e.g., inhibitory conditioned pain modulation)<sup>(10)</sup>.

### Bedside method

QST is a complement method that can be partly integrated into the routine neurological examination, especially for comprehensive assessment of neuropathic pain. The bedside method determines subjective experience of loss or gain of sensation in response to a range of particular stimuli, i.e., thermal, mechanical, vibration, or pressure stimuli<sup>(11)</sup>. To get the most useful of bedside QST, the patient should complete a pain diagram with pain descriptors first. Then, the examiner identifies the area of abnormal sensation by mapping out this area with a toothpick or a cotton swab starting in a normal area and progressing toward the abnormal area. The examination is repeated in a radial pattern until the area of abnormal sensation has been identified. Drawing the abnormal

area on the skin helps identify the pattern of sensory loss as mononeuropathy, polyneuropathy, or non-dermatomal distribution.

During examination, the other side of the similar area with normal sensation is used as a control site. The initial test starts at the normal side and compares the same stimulation to the abnormal area. Evaluation of punctate or pinprick sensation and summation testing with a more standardized device such as a NeuroPEN will allow production of a consistent stimuli. The feasible modalities tested are shown in Table 1.

### Standardized QST method

The increasing interest to explore somatosensory modalities leads to many different approaches for sensory assessment with diversity of operational procedures. To get relevant findings, standardized QST using the DFNS protocol has been developed based on rigorous standardization of instructions for the investigator and the patient, stimuli applied in a standardized way by trained investigators, and technical standards<sup>(9)</sup>. The standard instruction for the patients has been translated from German to many languages. The QST battery consists of 13 parameters for assessing the function of afferent nerve fibers (Table 2)<sup>(1,9,12)</sup>.

Based on the empirical and theoretical concept of sensory threshold, two different methods have been utilized in threshold measurement, the method of limits and the method of levels. The method of limits is an empirically developed method. It is influenced by reaction time, which is particularly relying on motor function and attention of the patients. In this method, the stimulus intensity is gradually increased or decreased until the subject feels pain and terminate the stimulus. The threshold values of a series of stimuli are finally calculated as mean values. The method of levels is a signal detection-based method. In this method, a series of preset stimuli are delivered to the skin. The patient then reports whether it is felt, or it produces pain as “yes” or “no”. The intensity of the next stimulus is then systematically changed, based on the previous response. For example, if the patient reports “no”, then the intensity of next stimulus will be increased. Although this method is time consuming, it may provide more stable responses. By selection of different sensory inputs, the standardized QST becomes a comprehensive tool to assess the sensory function of both large and small afferent nerve fibers (Table 2).

Results of the standardized QST data are usually

**Table 1.** Suggested bedside method for quantitative sensory testing

Test	Clinical testing instrument	Procedure
Light touch	A cotton wisp, cotton wool tip, Q-tip, or soft brush	Start on the normal skin and move toward the area of sensory change.
Vibration	Tuning fork (64 or 128 Hz)	Test over the bony prominences. Moving from distal to proximal.
Punctate/pinprick	Wooden cocktail sticks, NeuroPEN	Test in the area with abnormal positive or negative sensations.
Cold	• Tuning fork held under cool water (20°C)	• Compare to the control side.
Noxious cold	• Tuning fork under iced water	• Apply to the affected area. (Feels cool? or Feels paradoxical heat?)
Warm	• Heating the round end of tuning fork in warm or hot water (40°C)	• Compare to the control side.
Noxious heat (burning)	• None	• Apply to the affected area. Most useful to confirm the involvement of small fibers, especially if light touch and vibration are normal.
Wind-up	NeuroPEN	Apply single stimulus and then apply 10 stimuli to a single location at the rate of 1 per second. If the sensation is both painful and increased with each stimulus, and the answer is Yes=summation <ul style="list-style-type: none"> <li>• Normal if the numerical pain score increases for 10 to 30/100.</li> <li>• Referring to central sensitization if the numerical pain score is much higher.</li> <li>• Hyperpathia if answer of the first stimulus is absent or decreased but the following stimuli cause pain.</li> </ul> No=nonpainful summation
Grading the tests		
Reduced sensation		Express the degree of loss on 1 to 100 scale compared to the normal skin.
Increased sensation		Express the degree of gain on 1 to 100 scale compared to the normal skin. And record any appropriate term (dysesthesia <sup>a</sup> , hyperalgesia <sup>b</sup> , allodynia <sup>c</sup> , hyperpathia <sup>d</sup> )

<sup>a</sup> Increased sensation but not painful after nonpainful stimuli; <sup>b</sup> Increasing pain after painful stimuli; <sup>c</sup> Pain after nonpainful stimuli; <sup>d</sup> Pain after stimuli that had been reported of stimuli intensity less than the normal site.

Adapted from Irving and Squire<sup>(11)</sup>

presented as *z*-scores with adjustment to mean and SD and compared to an appropriate reference population. Report of the reference data from healthy volunteers revealed factors that may influence the results of QST such as the ability to understand and response to the tests, age (increasing thermal and mechanical thresholds with age), and gender (e.g., more sensitivity to heat pain threshold in female)<sup>(9)</sup>.

### Limitations and caveats

Since QST is a psychophysical method, active participation of the subject tested is mandatory to get the most reliable results<sup>(13,14)</sup>. The test depends on the cooperation and the effort of the subject. Thus, reporting errors may happen related to the subject's attention and reaction time. The investigator is advised to record any relevant observation to comply with the investigation. Although the standardized QST according to DFNS protocol reveals more relevant information than bedside method, it is time-consuming as assessment of one body site requires

about 30 minutes and usually additional area for side to side comparison need to be done. It is not feasible to perform QST in several areas at a time. In addition, no assessment of conditioned pain modulation is included in the standardized QST protocol. All of these might be a disadvantage in some clinical settings.

There is limited sensitivity of QST to detect the loss of IENFD. Normal detection threshold can be found even when there is significant loss of IENFD<sup>(15)</sup>. Interpretation of the whole sensory profile can help to increase the sensitivity. Patients with non-neuropathic pain syndrome with hypoesthesia usually have results of QST within the normal range of healthy subjects of which increase sensitivity can be done by group comparison. Another drawback of standardized QST is that it usually examines only one area, which may not be able to reveal the distribution of sensory loss or gain.

Although allodynia to cold and heat, soft touch and temporal summation are usually found in patients with neuropathic pain, it is not a pathognomonic

**Table 2.** Sensory mechanism assessed by quantitative sensory testing according to the German Research Network on Neuropathic Pain

Sensory channel or function	Sensory tests	Sensor	Axon type	Method of assessment
Cold	Cold detection threshold (CDT)	Cold receptors	Aδ-fiber	Cooling ramp at 1°C/second
Warmth	Warmth detection threshold (WDT)	C-fiber warmth fibers	C-fiber	Warming ramp at 1°C/second
Cold and warmth <sup>1</sup>	Thermal sensory limen (TSL)	Warmth and cold fibers	C- and Aδ-fiber	Alternating warming and cooling ramps at 1°C
Cold pain	Cold pain threshold (CPT)	Cold sensitive nociceptors	C-fiber	Cooling ramp at 1°C/second
Heat pain	Heat pain threshold (HPT)	Heat-sensitive C-nociceptors	C-fiber	Warming ramp at 1°C/second
Pressure pain	Pressure pain threshold (PPT)	Pressure-sensitive C-nociceptors	C-fiber	Pressure algometer (pressure ramp at 50 kPa/second)
Pricking pain (sharp)	<ul style="list-style-type: none"> <li>Mechanical pain threshold (MPT)</li> <li>Pain rating to pricking stimuli (mechanical pain sensation, MPS)</li> </ul>	High-threshold mechanoreceptors <sup>2</sup> (with some contribution from Aδ type I and II, and C-fiber mechanosensitive nociceptors)	• Aδ-fiber	Calibrated pinprick stimuli threshold (up and down rule)
			• Aδ-fiber	Pain rating (0 to 100 NRS)
Pain summation	Wind-up ratio of pain sensation (WUR)		Aδ-fiber	Ratio of train of 10 vs. single
Tactile detection (blunt)	Mechanical detection threshold (MDT)	Slowly adapting mechanoreceptor (SA-I)	Aβ-fiber	Calibrated von Frey hairs
Touch/vibration	Vibration detection threshold (VDT)	Rapidly adapting mechanoreceptor (RA and PC)	Aβ-fiber	8/8 Rydel-Seiffer tuning fork
Mechanical dysesthesia <sup>5</sup>	Dynamic mechanical allodynia (DMA)- pain to light touch	Rapidly adapting mechanoreceptor (RA) <sup>3</sup>	Aβ-fiber	Gentle tactile stroking ('dynamic')
Thermal dysesthesia <sup>5</sup>	Paradoxical heat sensation (PHS) <sup>4</sup>	Afferent mechanisms hitherto unresolved		Alternating warmth and cold

<sup>1</sup> Alternating warmth and cold stimuli (cold following warmth); a cold stimulus following preceding warmth can be perceived as warm, hot, or burning pain

<sup>2</sup> Aδ high-threshold mechanoreceptors (Aδ-HTM); a very-fast conducting heat-sensitive Aδ-nociceptor subgroup (sometimes also termed Aβ nociceptor): the signaling pathway for punctate hyperalgesia (the most frequent subtype of central sensitization-type hyperalgesia)

<sup>3</sup> Rapidly adapting low-threshold mechanoreceptors cross-talking into spinal nociceptive pathways (a distinct subtype of central sensitization-type hyperalgesia)

<sup>4</sup> A gentle cold stimulus following preceding warmth is mistaken as warm, hot, or burning pain

<sup>5</sup> Somatosensory dysesthesia

Adapted from Ploner, et al<sup>(12)</sup>

sign<sup>(16)</sup>. Nonneuropathic pain such as myofascial pain may be found to have loss of sensation to touch and pinprick<sup>(17)</sup>.

### Application of QST data

QST should always be used with a clinical sensory examination to get a pain mapping diagram of sensory deficit or gain, ongoing pain, and pain descriptors. QST has a distinct advantage over electrophysiological tests in being able to detect sensory impairment and quantify both positive and negative sensory phenomena from a wide variety of peripheral and central neural pathologies, which make QST useful for clinicians and researchers<sup>(18,19)</sup>. Clinically, sensory assessment using QST not only gives information of the associated nerve function but also provides diagnosis of the problem. For example, cold hyperalgesia is found in all patients with sympathetically maintained pain. Therefore, it

is a highly sensitive although not specific, indicator for sympathetically maintained pain.

The reference data of healthy volunteers under the standardized QST according to DFNS protocol have been reported, based on different body areas (face, hand, foot, trunk) and different age groups<sup>(9,20,21)</sup>. The information provides the use of correction factors for gender, age, and site of the tested area, which can be performed manually or by the computer software (eQUISTA) resulting in more precise quantification of sensory assessment than those from bedside method.

The continuous and intensive investigation of QST according to DFNS protocol in human surrogate models and patients have given valuable information in the prediction of risk of chronic pain, efficacy of pharmacological treatment of neuropathic pain according to sensory phenotypes, and the underlying neural mechanisms<sup>(22)</sup>. Studies of genotype-phenotype association in neuropathic pain patients have shown

**Table 3.** Predictive efficacy of treatment response and rational pharmaceutical treatment according to sensory profiles

Predictive efficacy	Cluster 1: sensory loss	Cluster 2: thermal hyperalgesia	Cluster 3: mechanical hyperalgesia
NSAIDs	-	+	-
Botox		+	
Topical capsaicin		+	
NMDA-antagonist			+
Antidepressant	++	+	+
Gabapentinoid	+	+	++
Na-channel blocker	+	++	++
Opioid	++	+	+

NMDA=N-methyl-D-aspartate; NSAIDs=nonsteroidal anti-inflammatory drugs

Predicted efficacy in clusters 1 to 3, based on studies identifying predictors of treatment response in subgroups. “++” very efficient, “+” moderate efficient, “-” not efficient

Adapted from Forstenpointner, et al<sup>(30)</sup>

that a frequent loss-of-function variant of transient receptor potential vanilloid 1 (TRPV1) and Sigma-1 receptors rendered homozygous allele carriers<sup>(23,24)</sup>. These people have less hyperalgesia and may have less risk for chronic pain. In contrast, patients with deficit in conditioned pain modulation may be more vulnerable to have chronic widespread pain<sup>(25)</sup>.

QST can detect both loss and gain of sensory function, thus it discloses valuable information to predict underlying mechanisms of neuropathic pain syndrome<sup>(26)</sup>. Recent report showed evidence that standardized QST, using the DFNS protocol, may help to subgroup peripheral neuropathic pain syndrome of different etiologies into three subtypes (sensory loss, thermal hyperalgesia, and mechanical hyperalgesia)<sup>(27)</sup>. The neuronal mechanisms of deafferentation, peripheral sensitization and central sensitization have been found as prototypical QST profiles in patients and human surrogate models with thermal and mechanical sensory loss, thermal hyperalgesia and no sensory loss, and mechanical hyperalgesia with some thermal sensory loss, respectively<sup>(28,29)</sup>. Stratification of patients with neuropathic pain into sensory profiles, which is supported by mechanism-based, may be useful to guide more rational treatment algorithms (Table 3), and to develop and evaluate pharmacological trials as personalized management for neuropathic pain<sup>(30)</sup>. Although the long-term reliability and agreement of results of standardized QST have been reported in healthy volunteers<sup>(31,32)</sup>, future developments are needed to confirm the reliability of QST as an outcome in clinical research and follow-up of disease progression for interventional trials of neuropathic pain.

## Conclusion

QST is an assessment technique of somatosensory system that complement the neurological sensory examination. It is sensitive to lesions or diseases of peripheral nerves and the central pathway to the brain. The standardized QST according to the DFNS protocol makes it possible to subgroup patients with peripheral neuropathic pain of different etiologies into distinct clusters of sensory profiles. Emerging evidence provided that such sensory profiles with their relations to pathophysiological mechanisms had predictive validity and reliability for treatment response. Therefore, QST may be helpful to improve treatment efficacy of neuropathic pain in the future.

## What is already known in this topic?

QST is a psychophysical method that complements neurological sensory examination.

## What this study adds?

This review shows future trend of using standardized QST as a tool for an individual patient with any combination of sensory profiles of neuropathic pain to predict the efficacy of pharmacological treatment.

## Acknowledgement

The authors thank Professor Andrew Rice for his valuable advice on the manuscript.

## Conflicts of interest

The authors declare no conflicts of interest.

## References

1. Backonja MM, Attal N, Baron R, Bouhassira D,

- Drangholt M, Dyck PJ, et al. Value of quantitative sensory testing in neurological and pain disorders: NeuPSIG consensus. *Pain* 2013;154:1807-19.
2. Cruccu G, Truini A. Tools for assessing neuropathic pain. *PLoS Med* 2009;6:e1000045.
  3. Krumova EK, Westermann A, Maier C. Quantitative sensory testing: a diagnostic tool for painful neuropathy. *Future Neurol* 2010;5:721-33.
  4. Weber EH. E. H. Weber on the tactile senses. 2nd ed. New York: Routledge; 2017.
  5. Von Frey M. Über die Beziehungen zwischen Kitzel-, Berührungs- und Druckempfindung. *Skand Arch Physiol* 1923;43:93-100.
  6. Head H, Holmes G. Sensory disturbances from cerebral lesions. *Brain* 1911;34:102-254.
  7. Yarnitsky D, Pud D. Quantitative sensory testing. In: Binnie CD, Cooper R, Manguiere F, Osselton JW, Prior PF, Tedman BM, editors. *Clinical neurophysiology: EMG, nerve conduction and evoked potentials*. Volume 1. Amsterdam: Elsevier; 2004. p. 305-32.
  8. Dyck PJ, Zimmerman IR, O'Brien PC, Ness A, Caskey PE, Karnes J, et al. Introduction of automated systems to evaluate touch-pressure, vibration, and thermal cutaneous sensation in man. *Ann Neurol* 1978;4:502-10.
  9. Rolke R, Baron R, Maier C, Tolle TR, Treede RD, Beyer A, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values. *Pain* 2006;123:231-43. Erratum in: *Pain*. 2006 Nov;125:197.
  10. Arendt-Nielsen L, Graven-Nielsen T. Translational aspects of musculoskeletal pain: From animals to patients. In: Graven-Nielsen T, Arendt-Nielsen L, Mense S, editors. *Fundamentals of musculoskeletal pain*. Seattle: IASP Press; 2008. p. 347-66.
  11. Irving G, Squire P. Evaluation of the chronic pain patient. In: Ballantyne JC, Fishman SM, Rathmell JP, editors. *Bonica's management of pain*. 5th ed. Philadelphia: Wolters Kluwer Health; 2019. p. 225-42.
  12. Ploner M, Magerl W, Schmelz M, Albrecht PJ, Rice FL. Emerging techniques in the diagnosis of neuropathic pain. In: Gold MS, Pogatzki-Zahn EM, Wallace MS, editors. *Pain 2018: Refresher courses 17th world congress on pain*. Washington, D.C.: IASP Press; 2018. p. 169-86.
  13. Hansson P, Backonja M, Bouhassira D. Usefulness and limitations of quantitative sensory testing: clinical and research application in neuropathic pain states. *Pain* 2007;129:256-9.
  14. Walk D, Sehgal N, Moeller-Bertram T, Edwards RR, Wasan A, Wallace M, et al. Quantitative sensory testing and mapping: a review of nonautomated quantitative methods for examination of the patient with neuropathic pain. *Clin J Pain* 2009;25:632-40.
  15. Devigili G, Rinaldo S, Lombardi R, Cazzato D, Marchi M, Salvi E, et al. Diagnostic criteria for small fibre neuropathy in clinical practice and research. *Brain* 2019;142:3728-36.
  16. Treede RD, Handwerker HO, Baumgärtner U, Meyer RA, Magerl W. Hyperalgesia and allodynia: taxonomy, assessment, and mechanisms. In: Brune K, Handwerker HO, eds. *Hyperalgesia: molecular mechanisms and clinical implications*. Progress in pain research and management, vol 30. Seattle, WA: IASP Press; 2004. p. 3-15.
  17. Rasmussen PV, Sindrup SH, Jensen TS, Bach FW. Symptoms and signs in patients with suspected neuropathic pain. *Pain* 2004;110:461-9.
  18. Zaslansky R, Yarnitsky D. Clinical applications of quantitative sensory testing (QST). *J Neuronal Sci* 1998;153:215-38.
  19. Baron R, Förster M, Binder A. Subgrouping of patients with neuropathic pain according to pain-related sensory abnormalities: a first step to a stratified treatment approach. *Lancet Neurol* 2012;11:999-1005.
  20. Magerl W, Krumova EK, Baron R, Tölle T, Treede RD, Maier C. Reference data for quantitative sensory testing (QST): refined stratification for age and a novel method for statistical comparison of group data. *Pain* 2010;151:598-605.
  21. Pfau DB, Krumova EK, Treede RD, Baron R, Tölle T, Birklein F, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): reference data for the trunk and application in patients with chronic postherpetic neuralgia. *Pain* 2014;155:1002-15.
  22. Treede RD. The role of quantitative sensory testing in the prediction of chronic pain. *Pain* 2019;160 Suppl 1:S66-9.
  23. Binder A, May D, Baron R, Maier C, Tölle TR, Treede RD, et al. Transient receptor potential channel polymorphisms are associated with the somatosensory function in neuropathic pain patients. *PLoS ONE* 2011;6:e17387.
  24. Sachau J, Bruckmueller H, Girthmuhlen J, Magerl W, Kaehler M, Haenisch S, et al. SIGMA-1 receptor gene variants, affect the somatosensory phenotype in neuropathic pain patients. *J Pain* 2019;20:201-14.
  25. Gerhardt A, Eich W, Treede RD, Tesarz J. Conditioned pain modulation in patients with nonspecific chronic back pain with chronic local pain, chronic widespread pain, and fibromyalgia. *Pain* 2017;158:430-9.
  26. Maier C, Baron R, Tölle TR, Binder A, Birbaumer N, Birklein F, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): somatosensory abnormalities in 1236 patients with different neuropathic pain syndromes. *Pain* 2010;150:439-50.
  27. Baron R, Maier C, Attal N, Binder A, Bouhassira D, Cruccu G, et al. Peripheral neuropathic pain: a mechanism-related organizing principle based on sensory profiles. *Pain* 2017;158:261-72.
  28. Vollert J, Maier C, Attal N, Bennett DLH, Bouhassira D, Enax-Krumova EK, et al. Stratifying patients with peripheral neuropathic pain based on sensory profiles:

- algorithm and sample size recommendations. *Pain* 2017;158:1446-55.
29. Vollert J, Magerl W, Baron R, Binder A, Enax-Krumova EK, Geisslinger G, et al. Pathophysiological mechanisms of neuropathic pain: comparison of sensory phenotypes in patients and human surrogate pain model. *Pain* 2018;159:1090-102.
  30. Forstenpointner J, Otto J, Baron R. Individualized neuropathic pain therapy based on phenotyping: are we there yet? *Pain* 2018;159:569-75.
  31. Marcuzzi A, Wrigley PJ, Dean CM, Adams R, Hush JM. The long-term reliability of static and dynamic quantitative sensory testing in healthy individuals. *Pain* 2017;158:1217-23.
  32. Nothnagel H, Puta C, Lehmann T, Baumbach P, Menard MB, Gabriel B, et al. How stable are quantitative sensory testing measurements over time? Report on 10-week reliability and agreement of results in healthy volunteers. *J Pain Res* 2017;10:2067-78.