Investigator’s Brochure

A standardized battery of Quantitative Sensory Testing according to the protocol of the
German Research Network on Neuropathic Pain (DFNS)

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1. INTRODUCTION

This protocol for Quantitative Sensory Testing (QST) has been developed as a comprehensive battery of sensory tests to quantify functions of the human somatosensory nervous system and to test the characteristics of different nociceptive and non-nociceptive submodalities which are subserved by different groups of afferent nerve fibres and central pathways.

The intention of the protocol is to test two symmetrical body sites in a standardized manner. Before commencing the actual test-battery, each test procedure should be demonstrated within an independent skin area in order to familiarize participants with the different tests (see standard operating procedures). In patients with a skin area affected by the disease, the control site should always be tested before the affected site. Precisely which areas will actually be tested should always be specified by a clinical examination and/or a “pain sketch” prior to the QST-examination (cf. appendix I, Territories to determine the vibration detection threshold/pressure pain threshold). The testing procedure of the entire protocol for two areas takes about an hour.

The central part of the protocol consists of more detailed and standardized descriptions of the test procedures for each test section and of instructions for the investigator on how to perform them in practice. Some of the variables are combined in one sub-test, meaning that two or more aspects of sensory processing are tested simultaneously if appropriate.

Training at a DFNS-training center is recommended (cf. appendix III). Since 2008, a certification of QST-laboratories is possible (Geber et al., 2009).

At the end of this document, a short reference list for further reading is followed by an appendix with a list of the recommended examination territories, a list of the devices recommended to perform the tests, the addresses of the device manufacturers as well as those of the DFNS Training Centers and the Center for Certification, the QST-Documentation Form, and lastly the verbal instructions for patients and healthy participants respectively.

The following shortlist describes the content and the chronological order of the tests (cf. appendix IV, QST-Documentation Form).

a.) Thermal detection and pain thresholds.

The tests for thermal sensation should always be performed at the beginning of the test procedure, prior to any of the mechanical tests. At first, cool (CDT) and warm detection thresholds (WDT) are measured, followed by thermal sensory limen (TSL, the difference threshold for alternating cool and warm stimuli), to detect paradoxical heat sensations (PHS). The thermal testing battery is concluded by measuring cold and heat pain thresholds (CPT; HPT). For each threshold test, 3 repetitions are performed at each site. The actual threshold is determined by the arithmetic mean of the three results using the difference between the measured threshold temperature and the baseline temperature (32 °C) for WDT and CDT, and using the absolute temperature values (in °C) for CPT and HPT. The thermal sensory limen is calculated by subtracting the arithmetic mean of the cold detection threshold from the arithmetic mean of the warm detection threshold as measured by the TSL test (three measurements for both qualities).

b.) Tactile detection threshold (MDT).

Using von Frey hairs the tactile detection threshold is determined by performing a modified method of limits. Five threshold determinations are made, each with a series of ascending and descending stimulus intensities. The final threshold is the geometric mean of these five series of supra- and subthreshold stimuli intensities.
c.) **Mechanical pain threshold (MPT).**

This test is performed with weighted pinprick stimuli. Five threshold determinations are made, each with a series of ascending and descending stimulus intensities. The final threshold is the geometric mean of the five supra- and subthreshold readings (modified method of limits).

d.) **S/R-(Stimulus/Response) functions: Mechanical pain sensitivity (MPS) and dynamic mechanical allodynia (DMA).**

To test for mechanical pain sensitivity weighted pinprick stimuli of different stimulus intensities are used, so that a stimulus-response function is obtained for pinprick-evoked pain (numerical rating scale; range 0-100). Seven stimuli intensities are applied 5 times each at both test sites in a randomized order, during which the subject is asked to give a numerical pain rating immediately after each stimulus. Dynamic mechanical allodynia is tested by using the same test pattern as described for the S/R-function. Dynamic innocuous stimuli (Q-tip, cotton wisp, and soft brush) are applied in between the pinprick stimuli in a randomized order. Each of the three innocuous stimuli is tested five times on each test site. Including innocuous stimuli and pinpricks, a total of 50 stimuli is delivered at both sites, each followed by a numerical pain rating. The degree of pain sensitivity is calculated by the geometrical mean of the pain ratings given for pinprick stimuli (MPS) and innocuous stimuli (DMA) separately.

e.) **Wind-up ratio (WUR).**

In this test, the numerical pain rating (NRS; range 0-100) given for an applied series of repetitive pinprick stimuli of the same intensity (10 stimuli with a repetition rate of 1/s, 256 mN; face 128 mN) is compared to the numerical pain rating of a single stimulus again of the same intensity. This procedure is repeated 5 times. A "wind-up" ratio is calculated by the arithmetic mean of the pain intensity rating for the series of stimuli divided by the arithmetic mean of the pain intensity rating for the single stimulus.

f.) **Vibration detection threshold (VDT).**

This test is performed with a standardized tuning fork (64 Hz; also available as a 128 Hz tuning fork with attachable mutes that are able to reduce the frequency to 64 Hz) that is placed over a bony prominence of the extremities, the head or the trunk (cf. appendix I). The vibration detection threshold is determined by three series of descending stimulus intensities determined from the “wandering” tip of a triangle moved by means of the vibration and indicated on the tuning fork (Goldberg & Lindblom, 1979; Fagius & Wahren, 1981) using the arithmetic mean of the values when the participant just stopped perceiving vibration (in x/8).

g.) **Pressure pain threshold (PPT).**

Using a pressure algometer (contact area 1 cm²) the threshold for pressure induced pain is measured above a muscle (cf. appendix I) in 3 series of slowly increasing stimulus intensities (0.5 kg/s, corresponding to ca. 50 kPa/s). The threshold is then determined as the arithmetic mean of the 3 series (in kPa).
2. **Standard Operating Procedures for Quantitative Sensory Testing**

**General instruction for the patient/subject**

Please adhere strictly to the test instructions and the exact wording of the instructions given to the patients and volunteers. Note that this is part of the standardization; and changed wording could jeopardize the comparability of the test results!

Please read aloud each of the italicized text passages to the patients or volunteers:

Introductory sentences:

> "In the following tests, we will explore, using various procedures, how you perceive temperature changes as well as touch and vibration stimuli. In addition, we will examine, from what point on different test stimuli are felt as being painful. The results of these tests are compared to normative data gained from healthy volunteers. To make this possible, these tests are always performed in the same manner. To ensure this, among others, the test instructions will be read to you aloud.

> *If you have not understood the test instructions, please always feel free to immediately ask for clarification."

**General practical hints for the investigator**

If the skin area to be tested is very hairy interfering with the measurement, these hairs may be carefully shortened using a pair of scissors. **By no means should the skin area to be tested be shaved directly before the measurement!**
a.) Thermal detection thresholds and thermal pain thresholds

**Equipment**: A thermal sensory testing device. The standard paradigm listed below can be performed with either the Thermal Sensory Analyzer (TSA, Medoc, Israel) or the Modular Sensory Analyzer (MSA, Somedic, Sweden) (see device list for both devices).

**Methods and background**: Using either of these instruments cold threshold, warm threshold, and thermal sensory limen will be determined (Fruhstorfer et al., 1976; Yarnitsky et al., 1995). Remember, the testing of the thermal sensory limen (TSL, the difference threshold for alternating cool and warm stimuli) is applied in order to register paradoxical heat sensations (PHS), meaning that patients and volunteers may report a warm, hot or painfully hot sensation in response to the cold stimulation. This is followed by the determination of cold pain (CPT) and heat pain thresholds (HPT) using the same device.

Generally, pain thresholds are defined as the range of stimulus intensities in which certain somatosensory qualities such as burning or stinging, which are associated with an activation of the nociceptive system, are just being perceived in addition to non-nociceptive perceptions such as cold, warm or touch. These sensations may differ according to stimulus modality. The following values being termed “pain thresholds”, more accurately describe the range of stimulus intensities in which the nociceptive system is activated (“nociceptive threshold”). Note that the perceived sensation at the “nociceptive threshold” has not necessarily to be interpreted as “pain” in the classical sense.

All thresholds will be obtained with ramped continuously increasing or decreasing thermal stimuli (1 °C/s) that are terminated when the patient or volunteer presses a button. Cut-off temperatures are 0 °C (TSA), resp. 5 °C (MSA) and 50 °C. The baseline temperature is 32 °C and the contact area of the thermode about 9 cm². The average threshold temperature of 3 measurements will be entered into the database.

**How to perform the procedure – Instructions for the investigator**

Please set the control software of the thermal testing device to a baseline temperature of 32 °C and a ramp slope of 1 °C/s for warming and cooling (a verification of the temperature is possible by measuring the temperature of the surface of the thermode via a infrared-thermometer). Between the 3 rounds of the individual tests, an interstimulus interval of 4 to 6 seconds should be set for CDT and WDT, and an interval of 10 seconds for CPT and HPT.

**Familiarization – Demonstration of the test procedure**

Place the thermode on the skin of the patient/volunteer at a “practice” area that is not identical to either the control or test site later being used.

After a short period of contact of the thermode with the skin (10 - 30 seconds) please instruct the patient/volunteer using the following phrase:

“The device placed on your skin is able to either warm or cool the skin. In addition you are given a stop button that enables you to immediately stop the ongoing test stimulus at any time. For every test I will explain to you when to use the stop button.

Please tell me, whether the device on your skin feels warm, cool or neutral.”

This is done to adequately judge the adaptation of the skin to the thermode. Should the patient/volunteer state that the thermode is felt as being warm or cool, one should wait another 1 to 2 minutes. If adaptation of temperature sensitivity is still not reached at this point, meaning that the thermode still feels either warm or cold, please replace the term “cold” by “cooler” or the term “warm” by “warmer” in the following instructions accordingly.

Please make sure that the subject is not able to see the computer screen at any time during the procedures.
Should this not be possible give them the following instruction:

“Please do not look at the computer screen during the test procedures."

Please continue with the following instructions:

“First we will test your ability to perceive cold sensations. Please press the stop button immediately once you perceive a change in temperature to cool/cooler for the first time. Subsequently, the thermode will warm up again, until it reaches the baseline temperature. This procedure will start in a few seconds.”

Discontinue testing for the following instructions:

“Now we will test your ability to perceive warm sensations. Please press the stop button immediately once you perceive a change in temperature to warm/warmer for the first time. Subsequently, the thermode will cool down again, until it reaches the baseline temperature. This procedure will start in a few seconds.”

Discontinue the test for the following instructions:

“Now we will test how well you are able to discern between successive temperature changes. Please press the stop button immediately once you feel a temperature change towards “warm” or “cold” sensations, and tell us explicitly whether you felt the temperature change as “warm” or “cold”. It may well be that some of the temperature changes are felt as “hot” or “painfully hot.”

During cooling of the skin, some of the volunteers/patients will report of “warm”, “hot” or even “painfully hot” sensations. These sensations, and the number of occurrences (0 to 3), should be documented as paradoxical heat sensations.

The volunteer/patient should indicate an actual sensation of “warmth” or “coldness”, not when he/she doesn’t perceive warmth as “warm” or coldness as “cold” anymore (indifference range). Please make this clear should you be asked.

Discontinue the test for the following instructions:

“Now we will test as to when you perceive the cooling of the thermode as painful. Your skin will be slowly cooled. At some point in time you will feel a second sensation on top of the “cold” sensation. The impression of “cold” will change its quality towards an additional impression of a “burning”, “stinging”, “drilling” or “aching” sensation. Please press the stop button immediately once you perceive such a change. Please DO NOT wait to press the stop button until the sensation has become unbearably painful. Subsequently, the thermode will warm up again, until it reaches the baseline temperature. This procedure will start in a few seconds.”

Discontinue the test for the following instructions:

“Now we will test as to when you perceive the warming of the thermode as painful. Your skin will be slowly warmed. At some point in time you will feel a second sensation on top of the “warm” or “hot” sensation. The impression of “warmth” or “heat” will change its quality towards an additional impression of a “burning”, “stinging”, “drilling” or “aching” sensation. Please press the stop button immediately once you perceive such a change. Please DO NOT wait to press the stop button until the sensation has become unbearably painful. Subsequently, the thermode will cool down again, until it reaches the baseline temperature. This procedure will start in a few seconds.”
Testing within the control and test site

The thermode will now be placed and strapped on the skin of the control and test site respectively. Similar to the demonstration round, after a short period of contact of the thermode with the skin (10 to 30 seconds), please ask the volunteer/subject:

“Please tell me, whether the device on your skin feels warm, cool or neutral.”

Should the patient/volunteer state that the thermode is felt as being warm or cool, one should wait another 1 to 2 minutes. Has adaptation of temperature sensitivity still not been reached, meaning that the thermode still feels either warm or cold, please replace the term “cold” by “cooler” or the term “warm” by “warmer” in the following instructions, accordingly.

If you are sure that the patient/volunteer has carried out the instructions correctly during the demonstration of the procedure, the individual tests may be announced in a shortened form.

Please use the following instructions:

Testing of cold detection threshold (CDT)

“Just as we have done in the practice round, you will first perceive a cooling of the skin. Please press the stop-button immediately as soon as you first feel a change of temperature to “cool or cooler”. This procedure will be performed a total of 3 times.”

Testing of warm detection threshold (WDT)

“Please press the stop-button immediately as soon as you first perceive a warming of the skin. Again this procedure will be performed a total of 3 times.”

Testing of thermal sensory limen (TSL)

“Please press the stop-button immediately as soon as you first perceive any kind of temperature change. Please state, whether the sensation was “cold”, “warm”, “hot” or “painfully hot”. This procedure will be performed a total of 6 times.”

Testing of cold pain threshold (CPT)

“Please press the stop-button immediately as soon as the “cold” sensation changes its quality to an additional sensation of “burning”, “stinging”, “drilling” or “aching”. This procedure will be performed a total of 3 times.”

Testing of heat pain threshold (HPT)

“Please press the stop-button immediately as soon as the “warm” or “hot” sensation changes its quality to an additional sensation of “burning”, “stinging”, “drilling” or “aching”. This procedure will be performed a total of 3 times.”

If you have the impression that the pauses between the single tests are not long enough to give the instructions, please interrupt the respective test after each of its 3 rounds.
b.) Tactile detection thresholds (MDT)

Equipment: one set of standardized von Frey hairs (0.25, 0.5, 1, 2, 4, 8, 16, 32, 64, 128, 256, and 512 mN). The contact area of the von Frey hairs should be of uniform size (approx. 1 mm²) and shape (blunted contact area to avoid sharp edges that may facilitate nociceptor activation).

Methods and background: Using standardized von Frey hairs (Weinstein 1968, Fruhstorfer et al. 2001) the geometrical mean of the tactile detection threshold is determined using a modified method of limits with five series each of ascending and descending stimulus intensities (Baumgärtner et al. 2002).

How to perform the procedure – Instructions for the investigator

The procedure starts using a von Frey hair with a force of 16 mN. Subsequently, von Frey hairs of the corresponding next lower intensity (8 mN) are applied until the volunteer/patient does NOT feel any touch sensation anymore. The equivalent force applied represents the first subthreshold stimulus intensity that is to be entered into the documentation form (see appendix). Now follows the reversed procedure with increasing stimulus intensities (suprathreshold value). Both procedures are repeated until a total of five sub- and five suprathreshold values have been obtained that represent the turning points for the threshold detection.

If the subject/patient is not able to feel the von Frey hair with an intensity of 16 mN, the hair with the corresponding next higher stimulus intensity is applied until a touch sensation is felt. Nevertheless, this value is NOT entered into the documentation form. Now again follows a reversal of the stimulus application order with the corresponding next lower intensity until again the patient/volunteer DOES NOT feel any touch sensation anymore while applying a von Frey hair. This last intensity is entered into the documentation form as the first suprathreshold value. Now proceed as described above.

(Note with regard to the documentation: Please always document the applied force in mN that is indicated on the von Frey hair (e.g. 0.5, 1, 2 mN etc.) and NOT the numbering of the hair! If the patient/volunteer is able to perceive the weakest von Frey hair with an intensity of 0.25 mN, half of this value (0.125 mN) is entered in the documentation form as “not perceived”. The next stimulus applied is again the same stimulus intensity as before (0.25 mN). Should this stimulus be perceived again, 0.25 mN are recorded in the documentation form as “stimulus noticed” etc. If, vice versa, the von Frey hair with the strongest applicable force (512 mN) is not perceived, a value of 1024 mN is documented in the form as “stimulus noticed”.

Avoid any contact with the volunteer’s/ patient’s hairs during application of the von Frey hairs, since this may bias the results!

Familiarization – Demonstration of the test procedure

Please demonstrate this procedure in the same “practice” area you have specified during thermal testing.

“This is a test of your ability to detect light touch. Please do not look at the skin area we are testing at any time during the test procedures. I will now touch your skin with these thin hairs. Please say “yes” as soon as you perceive a touch sensation.”

Testing within the control and test site

“Please say “yes” as soon as you perceive a touch sensation.”
c.) Mechanical pain threshold (MPT)

**Equipment:** A set of 7 pinprick stimulators with standardized stimulus intensities (8, 16, 32, 64, 128, 256, and 512 mN) and contact areas (tip diameter 0.25 mm).

**Method and background:** Using standardized pinprick stimulators and employing a modified method of limits, five series each of ascending and descending stimulus intensities are conducted to determine the geometric mean of the mechanical pain threshold (Chan et al. 1992, Greenspan und McGillis 1994, Hampf et al. 1990, Ziegler et al. 1999).

**How to perform the procedure – Instructions for the investigator**

The examiner uses different pinprick stimulators to determine the mechanical pain threshold of the skin. The skin of the volunteer that is **perpendicularly** (90° angle towards the skin and the floor) stimulated with the pinprick stimulators, should only come in contact with the needle tip itself and not with any other parts of the stimulator. Touching the skin and removing the pinprick needle should take place in a “flowing” movement with a contact time of 1 second.

Starting with a stimulation intensity of 8 mN, in each case the next higher pinprick stimulator is carefully placed on the skin until the perception of “touch” changes its quality towards an additional “sharp”, “pricking” or “stinging” impression. The corresponding intensity then represents the first suprathreshold value. As soon as the first painful stimulus is perceived, the direction of the testing is changed towards lower stimulus intensities until the first stimulus when applied to the skin, is now perceived as “blunt” and no longer as being “sharp”, “pricking” or “stinging” (subthreshold value). Now again a directional change towards higher intensities occurs, etc. until in all 5 supra- and 5 subthreshold values are found that represent the inflection point to determine the mechanical pain threshold.

**Familiarization – Demonstration of the test procedure**

Please demonstrate this procedure in a “practice” area:

“This is a test of your ability to perceive “sharp”, “pricking” or “stinging” stimuli. Various fine metal rods that are able to exert different pressure intensities will be carefully placed onto your skin.

Please say “sharp” as soon as you no longer perceive only a touching sensation on your skin, but experience an additional “sharp”, “pricking” or “stinging” sensation.

Please say “blunt” when you only perceive a touching sensation.

Under no circumstances, you should look at the skin area we are testing during the test procedure!”

**Testing within the control and test site**

Please repeat the instructions given above before you test the control and test site:

Please say “sharp” as soon as you not only perceive a touching sensation on your skin, but an additional “sharp”, “pricking” or “stinging” sensation.

Please say “blunt” when you only perceive a touching sensation.
d.) S/R- (Stimulus/Response) functions: Mechanical pain sensitivity (MPS) and dynamic mechanical allodynia (DMA)

Equipment: A set of 7 pinprick stimulators with standardized stimulus intensities (8, 16, 32, 64, 128, 256, and 512 mN) and contact areas (tip diameter 0.25 mm). A set of three stimulators for slight tactile stimuli: a cotton wisp that exerts a force of 3 mN, a Q-tip fixed to an elastic strip exerting a force of 100 mN, and a soft brush that is able to exert a force between 200 and 400 mN (Ziegler et al. 1999).

Method and background: These needle and tactile stimuli are applied in a balanced order and the painfulness of each stimulus is then psychometrically recorded by means of a numerical rating scale. Contrary to the determination of thresholds, this stimulus/response function allows the conclusion whether hyper- or hypoalgesia exists in the supra-threshold range. Moreover, one may objectify whether dynamic mechanical allodynia is apparent (LaMotte et al. 1991, Ziegler et al. 1999).

How to perform the procedure – Instructions for the investigator

Analogical to the determination of the mechanical pain threshold, the skin of the subjects / patients should strictly be touched perpendicularly (90° angle towards the skin and the floor) only by the needle and not by any other part of the guide tube of the stimulator. The applying and removing of the needle should be in a “flowing” motion with a contact time of one second. The stimulators for light touch will be conducted in a single sweeping motion (1-2 cm length) on the skin. A uniform application is of crucial importance, since the length of the stimulated area is directly correlated with the level of pain perception (Samuelsson et al. 2005).

The volunteers/patients are asked to judge the stimulus intensity by means of a numerical rating scale (0-100) “0” in this case means “no pain”. Analogue to the determination of the pain thresholds each “pricking”, “stinging” or “burning” sensation is defined as a painful sensation, which should always be evaluated by giving a value greater than “0”. A stimulus that is not perceived should be marked as “Ø”. “100” corresponds to the individual maximum pain imaginable. Ratings with a decimal should be accepted.

Familiarization – Demonstration of the test procedure

To demonstrate the test procedure, apply about 10 stimuli (e.g., the first box on the documentation form) in the demonstration area and let the subjects/patients estimate the painfulness (these pain ratings in the demonstration area need not be documented) after you have given the following instructions:

“As in the test before, blunt fine metal rods will be carefully pressed against your skin with varying pressure. In between these punctual stimuli your skin will occasionally be touched by a cotton wisp, a Q-tip, and a brush. Some of these stimuli may be accompanied by a “sharp”, “pricking”, “stinging” or “burning” sensation. Other stimuli may only be perceived as a touching sensation, others may not be perceived at all.

Please rate the painfulness of each stimulus by giving a number between “0” and “100”. Any “sharp”, “pricking”, “stinging” or “burning” sensation should be defined as being painful and given a rating value above “0”. You may also use decimals.
“0” meaning: No pain, no “sharp”, “pricking”, “stinging” or “burning” sensation.
“100” meaning: Most intense pain sensation imaginable.

Under no circumstances, you should look at the skin area we are testing during the test procedure!”

Should the subject/patient give a rating of “100”, please ask:

“Are you sure that this was the most intense pain sensation imaginable for you?”

This is to ensure that the subject/patient has understood the instructions, and allows the identification of uncertainties. Repeat the above instructions if necessary.

**Testing within the control and test site**

“Again, please rate the painfulness of each stimulus by giving a number between “0” and “100”.

“0” meaning: No pain, no “sharp”, “pricking”, “stinging” or “burning” sensation.
“100” meaning: Most intense pain sensation imaginable.”

For the ratings, decimals will be accepted.

Should the subject/patient give a rating of “100”, again please ask:

“Are you sure that this was the most intense pain sensation imaginable for you?”

If applicable: “Then we will no longer use this or any other of the more severe stimuli.”

If this is correct, this stimulus will not be re-applied in the affected area in the course of further testing. For all stimuli equaling or being above the maximally painful stimulus a rating of “100” is documented in the documentation sheet (see Appendix).
e.) Wind-up ratio (WUR)

Equipment: 1 pinprick stimulator with standardized stimulus intensity (256 mN, face: 128 mN) and contact areas (tip diameter 0.25 mm).

Method and background: In this test, a single stimulus is applied with a pinprick stimulator (256 mN and face: 128 mN). 10 seconds after the single stimulus a series of ten stimuli using the same needle stimulator is applied with a frequency of 1 s⁻¹ within the same skin area of about 1 cm². Immediately after the single stimulus, and again after the subsequent stimulus series a combined assessment of the pain intensity is given by means of a numerical scale. A ratio is then calculated by dividing the combined pain rating of the stimulus series by the pain rating of the single stimulus. “Wind-up” is then calculated as the geometrical mean of all five ratios of the estimated pain ratings of the single stimuli and the following stimulation series (Price et al. 1977, Magerl et al. 1998).

How to perform the procedure – Instructions for the investigator

After a 10 second interval following the single stimulation with the pinprick stimulator (256 mN and face: 128 mN) a series of 10 stimuli are applied to the skin. Every stimulus of the series should take place every second (synchronized by a metronome) within a stimulus area of about 1 cm² in close proximity to the single stimulus. Directly after the first stimulus and then again after the series of 10 stimuli a pain rating is given for the stimulus and the combined stimuli. This procedure is repeated 5 times. The stimulation areas should be located only a few centimeters apart.

Annotation: The first stimulus should be above threshold, meaning that the rating should be greater than “0” NRS. Should a rating of “0” occur three times for the single stimulus, an assessment of WUR is not possible. Should a rating of “0” occur twice, these ratings should be replaced by the mean value of the other ratings.

If the pinprick stimulation with stimulation intensities of 256 mN (128 mN on the skin of the face) not be tolerated a stimulus with a weaker intensity may be used. It is required to document any of these changes on the documentation form and should be annotated during data entry. It may then be necessary to repeat the testing within the control site with the lower intensity to assure consistent measurements.

Familiarization – Demonstration of the test procedure

Please demonstrate the procedure within a “practice” area:

“Like in the former test I will now press a single fine metal rod against your skin. Please rate the painfulness of this single stimulus by giving a number between “0” and “100”. Any “sharp”, “pricking”, “stinging” or “burning” sensation should be defined as being painful and given a rating value above “0”. You may also use decimals.

“0” meaning: No pain, no “sharp”, “pricking”, “stinging” or “burning” sensation.

“100” meaning: Most intense pain sensation imaginable.”

Please apply the single stimulus.

“Now I will apply a series of 10 stimulations with the same metal rod at 1 second intervals on your skin. Once the entire series is over, please rate its average painfulness by giving a number between “0” and “100”.

“0” again meaning: No pain, no “sharp”, “pricking”, “stinging” or “burning” sensation.

“100” meaning: Most intense pain sensation imaginable.”

Please apply the stimulation series.
**Testing within the control and test site**

“The whole procedure of applying one single stimulus followed by the stimulus series will be carried out within this area and will be performed 5 times. Please rate again how painful this single stimulus was on a scale of 0 to 100.

“0” meaning: *No pain, no “sharp”, “pricking”, “stinging” or “burning” sensation.*

“100” meaning: *Most intense pain sensation imaginable.*

Please apply the single stimulus.

*Please rate again how painful the stimulus series was on a scale of 0 to 100.*

Please apply the stimulation series.
f.) **Vibration detection threshold (VDT):**

**Equipment:** A tuning fork (64 Hz, available as a 128 Hz tuning fork with mountable dampers that are able to reduce the frequency to 64 Hz, 8/8 scale).

**Method and background:** The tuning fork is placed on a bony prominence within the control and test site. The vibration detection threshold is determined with a series of three descending stimulus intensities as the last noticeable vibration (Goldberg and Lindblom 1979, Fagius and Wahren 1981).

**How to perform the procedure – Instructions for the investigator**

To determine the vibration detection threshold, please place the tuning fork on a bony prominence of the body area tested (see the recommendations for the selection of the examination territories for testing of vibration in the appendix).

**Familiarization – Demonstration of the test procedure**

Please make sure that the volunteer/patient is able to feel the vibration after the tuning fork has been placed on the bony prominence and demonstrate the procedure within a “practice” area.

> “This procedure tests your ability to perceive ‘vibrations’. I will now place this vibrating tuning fork on your skin. Please tell me if you are able to feel the vibrations?

**Please immediately** say “NOW” as soon as you are no longer able to feel any further vibrations!

> You may hear the vibrations of the tuning fork as a sound. Please try to pay attention only to the vibration, and not to the sound.”

**Testing within the control and test site**

> “A series of 3 consecutive tests will now be carried out within the control and the test site. I will now place this vibrating tuning fork on your skin. Please tell me if you are able to feel the vibrations?

**Please immediately** say “NOW” as soon as you are no longer able to feel any further vibrations!”
g.) Pressure pain threshold (PPT)

**Equipment**: 1 blunt mechanical stimulator (contact area 1 cm², applicable force 10 kg/1000 kPa/100 N or 20 kg/2000 kPa/200 N, respectively) with a built-in pressure display (pressure algometer).

**Method and background**: The pressure algometer is placed on the skin above pre-defined muscles within the control and test site. To characterize deep muscular pain, the pressure pain threshold is determined by 3 continuous ramps of increasing intensity (about 0.5 kg/s corresponding to 50 kPa/s).

**How to perform the procedure – Instructions for the investigator**

Place the pressure algometer on the skin above the muscle that will be examined (see the recommendations for the selection of the examination territories for testing of pressure pain in the appendix). If you are using a pressure algometer with an analogue scale please make sure that the volunteer/patient is not able to look at the readings during the measurement.

**Familiarization – Demonstration of the test procedure**

“This procedure tests your ability to feel pressure pain above muscles.

*I will press this pressure measuring device against one of your muscles. Please immediately say “NOW” as soon as the usual sensation of pressure changes towards an additional sensation of “burning”, “stinging”, “drilling” or “aching”."

**Testing within the control and test site**

“Again, I will press this pressure measuring device against one of your muscles. Please immediately say “NOW” as soon as the usual sensation of pressure changes towards an additional sensation of “burning”, “stinging”, “drilling” or “aching”. This procedure will be carried out a total of 3 times.”
3. Recommended Literature


Appendix I

Examination territories to determine the vibration detection threshold

1) In diseases with **generalized pain syndromes** or in pain syndromes of the **distal limb segments** (typical example: PNP) the tuning fork is placed on bony prominences from which standard values are already available:

   a) Upper extremity: .......................................................... ulnar styloid process
   b) Lower extremity: .......................................................... medial malleolus
   c) Face: .......................................................... zygomatic process

2) In patients with **facial pain**, the tuning fork is placed on the bony prominence for which standard values are already available: ........................................... zygomatic process

3) In patients with pain due to **peripheral nerve lesions** or **radicular lesions** the tuning fork is placed preferably on the bony prominence for which standard values are already available:

   d) Upper extremity: .......................................................... ulnar styloid process
   e) Lower extremity: .......................................................... medial malleolus
   f) Face: .......................................................... zygomatic process

The selection of the test area generally depends on neuroanatomical criteria. For the most common lesions the following guidelines are effective:

Lesion of the median nerve: .......................................................... proximal end of metacarpal bone I
Lesion of the radial nerve: .......................................................... radial styloid process
Lesion of C7: .......................................................... distal end of the metacarpal bone III
Lesion of S1: .......................................................... lateral malleolus
Lesion of the femoral nerve/Lesion of L4: ........................................ patella

4) In patients with **shoulder-/neck-pain**: ........................................... acromion

5) In patients with pain after **lesions of the thoracic nerves**:
   Tuning fork is placed on the costal arch when pain is located...
   …primarily ventral: .......................................................... anterior axillary line
   …primarily dorsal: .......................................................... mid-scapular line

6) In patients with **abdominal** pain, in which no natural bony prominences are available
   .......................................................... alternatively anterior superior iliac spine
Examination territories to determine the pressure pain threshold

1) In diseases with **generalized pain syndromes** or in pain syndromes of the **distal limb segments** (typical example: PNP) the pressure algometer is placed on the muscle group from which standard values are already available:

   a) Upper extremity: thenar eminence
   b) Lower extremity: abductor hallucis muscle
   c) Face: masseter muscle

2) In patient with **facial pain**, the tuning fork is placed on the bony prominence for which standard values are already available: masseter muscle

3) In patients with pain due to **peripheral nerve lesions** or **radicular lesions** the pressure algometer is placed preferably on the muscle group for which standard values are already available:

   d) Upper extremity: thenar eminence
   e) Lower extremity: abductor hallucis muscle
   f) Face: masseter muscle

The selection of the test area generally depends on neuroanatomical criteria. For the most common lesions the following guidelines are effective:

Lesion of the axillary nerve, C5, upper plexus: deltid muscle
Lesion of the ulnar nerve, C8, lower plexus: hypothenar eminence
Lesion of the radial nerve: depends on the location of pain: triceps muscle or extensor muscle of the forearm
Lesion of the femoral nerve: vastus medialis muscle
Lesion of L5: a.o. anterior tibial muscle, extensor hallucis longus muscle, gluteus medius muscle

4) In patients with **shoulder-/neck-pain**: trapezius muscle

5) In patients with pain after lesions of the thoracic nerves: paravertebral muscles (according to the dermatome, 5 – 8 cm lateral of the spinous process

6) In patients with **abdominal** pain: alternatively in a corresponding muscle paravertebral to the lumbar spine
Appendix II

Manufacturers of equipment used for Quantitative Sensory Testing according to the rules of the German Research Network on Neuropathic Pain (DFNS)

**Thermal testing**

TSA 2001-II by Medoc (Israel)
Medoc Ltd.
1 Ha’dekel St., Ramat Yishai 30095, PO Box 423
ISRAEL
Tel.: +972-4-9038800
Fax: +972-4-9038808
E-mail: info@medoc-web.com
www.medoc-web.com

MSA by Somedic (Sweden)
Bo Johansson, Somedic Sales AB
PO Box 194, S-242 22 Hörby, Sweden
Tel.: +46-415-165-50 / Fax: +46-415-165-60
E-mail: bo.johansson@somedic.com
www.somedic.com

**Mechanical testing**

**Tactile detection**

von Frey hairs Ophair2-Set (ca. 225,- € + VAT)
MARSTOCKnervtest
Dr. H. Fruthstorfer
Weinbergweg 24
69198 Schriesheim, Germany
Tel.: +49-6203-108594
Fax: +49-6203-925192
E-mail: info@marstock.de
www.marstock.de

Pinprick pain threshold

"The Pin-Prick“ and equipment for testing alldynia
Dr. Marcus Goetz
MRC Systems GmbH
Hans-Bunte-Strasse 10
69123 Heidelberg, Germany
Tel.: +49-6221-13803-00 / Fax: +49-6221-13803-01
E-mail: info@mrc-systems.de
www.mrc-systems.de

Equipment includes devices to test dynamic mechanical alldynia and a metronome (KorgMa 30) to clock the application of the wind-up ratio.

**Vibration**

Tuning fork:
Conventional 64 Hz-tuning fork with an 8/8-scale.

**Pressure pain threshold**

Pressure algometer FDN200 + Rubber tip (1 cm²)
(Testing of the test site face requires a pressure algometer with a more precise graduation: FDN 100)
(each ca. 230,- € incl. customs, postage, packaging)
For pressure algometry 1-10 kg and 2-20 kg
(Please do not forget to order the rubber tips)
Wagner Instruments, PO Box 1217
Greenwich, CT (USA) 06836-1217
Tel.: +1-203-698-9681 or: +1-800-345-4188
Fax: +1-800-443-4149
E-mail: sales@wagnerinstruments.com
www.wagnerinstruments.com

Electronic pressure algometer
Somedic Products
Frestavägen 6
PO Box 519, S-192 05 Sollentuna, Sweden
Tel.: +46-8-35-68-27, Fax: +46-8-35-68-74
E-mail: info@somedicprod.se
www.somedicprod.se or
SOMEDIC Sales AB
PO Box 194, S-242 22 HÖRBY, Sweden
Tel.: +46-415-165-50 / Fax: +46-415-165-60
E-mail: info@somedic.com / www.somedic.com
Appendix III

Addresses of the DFNS, the DFNS Training Center, and the Center for Certification

German Research Network on Neuropathic Pain (DFNS)

Speakers: Prof. Dr. R. Baron  
Prof. Dr. Dr. Thomas R. Tölle

Office:  
Ms. Vedrana Romanovic  
Deutscher Forschungsverbund Neuropathischer Schmerz (DFNS)  
(German Research Network on Neuropathic Pain (DFNS))  
Neurologische Klinik und Poliklinik  
Klinikum rechts der Isar der Technischen Universität München  
Ismaninger Str. 22  
D-81675 München, Germany  
Tel.: +49-89-4140-4635  
E-mail: romanovic@lrz.tum.de

DFNS Training Centers

Prof. Dr. R.-D. Treede  
Lehrstuhl für Neurophysiologie  
Contact person: Dr. Doreen Pfau  
Zentrum für Biomedizin und Medizintechnik  
Mannheim  
Medizinische Fakultät Mannheim  
der Universität Heidelberg  
Ludolf-Krehl-Str. 13-17  
D-81675 Mannheim, Germany  
Tel.: +49-621-383-9929  
Fax: +49-621-383-9921  
E-mail: doreen.pfau@medma.uni-heidelberg.de

Prof. Dr. C. Maier  
Abteilung für Schmerztherapie  
Contact person: Dr. Andrea Westermann  
Klinik für Anästhesiologie, Intensiv-, Palliativ- und Schmerzmedizin  
Berufsgenossenschaftliches Universitätsklinikum Bergmannsheil GmbH  
Bürkle-de-la-Camp-Platz 1  
D-44789 Bochum, Germany  
Tel.: +49-234-302-3497  
Fax: +49-234-302-6367  
E-mail: andrea.westermann@rub.de

Center for Certification of QST-Laboratories

Gesellschaft für Qualifizierte Schmerztherapie  
(Society for Qualified Pain Therapy)  
Certkom e.V.  
Kortumstr. 121  
D-44787 Bochum, Germany  
Tel.: +49-234-325-3095  
Fax: +49-234-325-3096  
E-mail: info@certkom.com
### Appendix IV, QST-Documentation form

<table>
<thead>
<tr>
<th>Name:</th>
<th>Control site:</th>
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<tbody>
<tr>
<td>Date of birth:</td>
<td>Test site:</td>
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<tr>
<td>Localization of pain:</td>
<td>Pain intensity prior to QST: (0-100)</td>
</tr>
<tr>
<td>Room temperature: °C</td>
<td>Skin temperature Control site: °C Test site: °C</td>
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</tbody>
</table>

**QST - Documentation Form**

**Control site**

<table>
<thead>
<tr>
<th>CDT</th>
<th>WDT</th>
<th>TSL</th>
<th>CPT</th>
<th>HPT</th>
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</thead>
<tbody>
<tr>
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**Test site**

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<tr>
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<th>TSL</th>
<th>CPT</th>
<th>HPT</th>
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</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

**MDT: Mechanical detection threshold (sensory testing)**

<table>
<thead>
<tr>
<th>Control site</th>
<th>Test site</th>
</tr>
</thead>
<tbody>
<tr>
<td>128 CW 256</td>
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</tr>
<tr>
<td>32 128 8</td>
<td>32 16</td>
</tr>
<tr>
<td>256 8 16</td>
<td>16 128</td>
</tr>
<tr>
<td>16 16 8</td>
<td>16 8</td>
</tr>
</tbody>
</table>

**MPT: Mechanical pain threshold (pressure)**

<table>
<thead>
<tr>
<th>Control site</th>
<th>Test site</th>
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</thead>
<tbody>
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</tr>
<tr>
<td>32 128 8</td>
<td>32 16</td>
</tr>
<tr>
<td>256 8 16</td>
<td>16 128</td>
</tr>
<tr>
<td>16 16 8</td>
<td>16 8</td>
</tr>
</tbody>
</table>

**WUR: von Frey hair (degree of single stimulus)**

<table>
<thead>
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<th>Test site</th>
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</thead>
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<td>16 8 128</td>
</tr>
<tr>
<td>64 8 256 128</td>
<td>16 8 128</td>
</tr>
</tbody>
</table>

**VDT: vibration detection threshold**

<table>
<thead>
<tr>
<th>Control site</th>
<th>Test site</th>
</tr>
</thead>
<tbody>
<tr>
<td>128 CW 256</td>
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<td>32 128 8</td>
<td>32 16</td>
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<td>256 8 16</td>
<td>16 128</td>
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<tr>
<td>16 16 8</td>
<td>16 8</td>
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</tbody>
</table>

**PPT: Pressure pain threshold**

<table>
<thead>
<tr>
<th>Control site</th>
<th>Test site</th>
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<tbody>
<tr>
<td>128 CW 256</td>
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<td>16 128</td>
</tr>
<tr>
<td>16 16 8</td>
<td>16 8</td>
</tr>
</tbody>
</table>

The patient has understood the instructions and completed with them.

---

QST instructions according to the protocol of the German Research Network on Neuropathic Pain (DFNS)  
Version 2.1 - 08.07.2010  
© Chair of Neurophysiology, University Medicine Mannheim; Heidelberg University
Appendix V

General instructions for the volunteers/patients

“In the following tests, we will explore, using various procedures, how you perceive temperature changes as well as touch and vibration stimuli. In addition, we will examine, from what point on different test stimuli are felt as being painful. The results of these tests are compared to normative data gained from healthy volunteers. To make this possible, these tests are always performed in the same manner. To ensure this, among others, the test instructions will be read to you aloud.

If you have not understood the test instructions, please always feel free to immediately ask for clarification.”

a.) Thermal detection thresholds and thermal pain thresholds

Demonstration of the test procedure

“The device placed on your skin is able to either warm or cool the skin. In addition you are given a stop button that enables you to immediately stop the ongoing test stimulus at any time. For every test I will explain to you when to use the stop button.

Please tell me, whether the device on your skin feels warm, cool or neutral.

Please do not look at the computer screen during the test procedures.”

CDT “First we will test your ability to perceive cold sensations. Please press the stop button immediately once you perceive a change in temperature to cool/colder for the first time. Subsequently, the thermode will warm up again, until it reaches the baseline temperature. This procedure will start in a few seconds.”

WDT “Now we will test your ability to perceive warm sensations. Please press the stop button immediately once you perceive a change in temperature to warm/warmer for the first time. Subsequently, the thermode will cool down again, until it reaches the baseline temperature. This procedure will start in a few seconds.”

TSL “Now we will test how well you are able to discern between successive temperature changes. Please press the stop button immediately once you feel a temperature change towards “warm” or “cold” sensations, and tell us explicitly whether you felt the temperature change as “warm” or “cold”. It may well be that some of the temperature changes are felt as “hot” or “painfully hot”.

CPT “Now we will test as to when you perceive the cooling of the thermode as painful. Your skin will be slowly cooled. At some point in time you will feel a second sensation on top of the usual “cold” sensation. The impression of “cold” will change its quality towards an additional impression of a “burning”, “stinging”, “drilling” or “aching” sensation. Please press the stop button immediately once you perceive such a change. Please DO NOT wait to press the stop button until the sensation has become unbearably painful. Subsequently, the thermode will warm up again, until it reaches the baseline temperature. This procedure will start in a few seconds.”

HPT “Now we will test as to when you perceive the warming of the thermode as painful. Your skin will be slowly warmed. At some point in time you will feel a second sensation on top of the usual “warm” or “hot” sensation. The impression of “warmth” or “heat” will change its quality towards an additional impression of a “burning”, “stinging”, “drilling” or “aching” sensation. Please press the stop button immediately once you perceive such a change. Please DO NOT wait to press the stop button until the sensation has become unbearably painful. Subsequently, the thermode will cool down again, until it reaches the baseline temperature. This procedure will start in a few seconds.”
Testing within the control and test site

Please tell me, whether the device on your skin feels warm, cool or neutral."

CDT “Just as we have done in the practice round, you will first perceive a cooling of the skin. Please press the stop-button immediately as soon as you first feel a change of temperature to “cool or cooler”. This procedure will be performed a total of 3 times.”

WDT “Please press the stop-button immediately as soon as you first perceive a warming of the skin. Again this procedure will be performed a total of 3 times.”

TSL “Please press the stop-button immediately as soon as you first perceive any kind of temperature change. Please state, whether the sensation was “cold”, “warm”, “hot” or “painfully hot”. This procedure will be performed a total of 6 times.”

CPT “Please press the stop-button immediately as soon as the “cold” sensation changes its quality to an additional sensation of “burning”, “stinging”, “drilling” or “aching”. This procedure will be performed a total of 3 times.”

HPT “Please press the stop-button immediately as soon as the “warm” or “hot” sensation changes its quality to an additional sensation of “burning”, “stinging”, “drilling” or “aching”. This procedure will be performed a total of 3 times.”

b.) Tactile detection thresholds

Demonstration of the test procedure

MDT “This is a test of your ability to detect light touch. Please do not look at the skin area we are testing at any time during the test procedures. I will now touch your skin with these thin hairs. Please say “yes” as soon as you perceive a touch sensation”

Testing within the control or test site

MDT “Please say “yes” as soon as you perceive a touch sensation.”
c.) Mechanical pain threshold

Familiarization – Demonstration of the test procedure

MPT “This is a test of your ability to perceive “sharp”, “pricking” or “stinging” stimuli. Various fine metal rods that are able to exert different pressure intensities will be carefully placed onto your skin.

Please say “sharp” as soon as you no longer perceive only a touching sensation on your skin, but experience an additional “sharp”, “pricking” or “stinging” sensation.

Please say “blunt” when you only feel a touching sensation.

Under no circumstances, you should look at the skin area we are testing during the test procedure!”

Testing within the control or test site

MPT Please say “sharp” as soon as you not only perceive a touching sensation on your skin, but an additional “sharp”, “pricking” or “stinging” sensation.

Please say “blunt” when you only perceive a touching sensation.

d.) S/R-(Stimulus/Response) functions: Mechanical pain sensitivity (MPS) and dynamic mechanical allodynia (DMA)

Familiarization – Demonstration of the test procedure

MPS “As in the test before, blunt fine metal rods will be carefully pressed against your skin with varying pressure.

DMA In between these punctual stimuli your skin will occasionally be touched by a cotton wisp, a Q-tip, and a brush. Some of these stimuli may be accompanied by a “sharp”, “pricking”, “stinging” or “burning” sensation. Other stimuli may only be perceived as a touching sensation, others may not be perceived at all.

Please rate the painfulness of each stimulus by giving a number between “0” and “100”. Any “sharp”, “pricking”, “stinging” or “burning” sensation should be defined as being painful and given a rating value above “0”. You may also use decimals.

“0” meaning: No pain, no “sharp”, “pricking”, “stinging” or “burning” sensation.

“100” meaning: Most intense pain sensation imaginable.

Under no circumstances, you should look at the skin area we are testing during the test procedure!

(Should the subject/patient give a rating of “100”, please ask:

Are you sure that this was the most intense pain sensation imaginable for you? ”)

Testing within the control or test site

MPS “Again, please rate the painfulness of each stimulus by giving a number between “0” and “100”.

DMA “0” meaning: No pain, no “sharp”, “pricking”, “stinging” or “burning” sensation.

“100” meaning: Most intense pain sensation imaginable.

(Should the subject/patient give a rating of “100”, again please ask:

“Are you sure that this was the most intense pain sensation imaginable for you?”

If applicable: “Then we will no longer use this or any other of the more severe stimuli.”)
e.) Wind-up ratio

**Familiarization – Demonstration of the test procedure**

**WUR**

“Like in the former test I will now press a single fine metal rod against your skin. Please rate the painfulness of this single stimulus by giving a number between “0” and “100”. Any “sharp”, “pricking”, “stinging” or “burning” sensation should be defined as being painful and given a rating value above “0”. You may also use decimals.

“0” meaning: No pain, no “sharp”, “pricking”, “stinging” or “burning” sensation.
“100” meaning: Most intense pain sensation imaginable.

Now I will apply a series of 10 stimulations with the same metal rod at 1 second intervals on your skin. Once the entire series is over, please rate its average painfulness by giving a number between “0” and “100”.

“0” again meaning: No pain, no “sharp”, “pricking”, “stinging” or “burning” sensation.
“100” meaning: Most intense pain sensation imaginable.”

**Testing within the control or test site**

**WUR**

“The whole procedure of applying one single stimulus followed by the stimulus series will be carried out within this area and will be repeated 5 times. Please rate again how painful this single stimulus was on a scale of 0 to 100.

“0” meaning: No pain, no “sharp”, “pricking”, “stinging” or “burning” sensation.
“100” meaning: Most intense pain sensation imaginable.

Please rate again how painful the stimulus series was on a scale of 0 to 100.”

f.) Vibration detection threshold

**Familiarization – Demonstration of the test procedure**

**VDT**

“This procedure tests your ability to perceive “vibrations”. I will now place this vibrating tuning fork on your skin. Please tell me if you are able to feel the vibrations?

Please immediately say “NOW” as soon as you are no longer able to feel any further vibrations!

You may hear the vibrations of the tuning fork as a sound. Please try to pay attention only to the vibration, and not to the sound.”

**Testing within the control and test site**

**VDT**

“A series of 3 consecutive tests will now be carried out within the control and the test site. I will now place this vibrating tuning fork on your skin. Please tell me if you are able to feel the vibrations?

Please immediately say “NOW” as soon as you are no longer able to feel any further vibrations!”
g.) Pressure pain threshold

Familiarization – Demonstration of the test procedure

PPT “This procedure tests your ability to feel pressure pain above muscles. I will press this pressure measuring device against one of your muscles. Please immediately say “NOW” as soon as the usual sensation of pressure changes towards an additional sensation of “burning”, “stinging”, “drilling” or “aching”.”

Testing within the control and test sites

PPT “Again, I will press this pressure measuring device against one of your muscles. Please immediately say “NOW” as soon as the usual sensation of pressure changes towards an additional sensation of “burning”, “stinging”, “drilling” or “aching”.”

This procedure will be carried out a total of 3 times.”