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Quantitative sensory tests (perceptual thresholds) in patients with spinal cord injury

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Abstract—This article was presented at the Premeeting Workshop on Outcome Measures at the American Spinal Injury Association (ASIA) Annual Scientific Meeting in Dallas, Texas, in May 2005. The article summarizes preliminary findings of three quantitative sensory tests that were evaluated as part of the International Spinal Research Trust Clinical Initiative study: perceptual thresholds to electrical, vibration, and thermal stimulation. The results gathered so far suggest that the three tests are simple, reproducible, and applicable in a clinical setting. The tests seem to add resolution and sensitivity to the standard clinical testing and could be useful adjuncts in longitudinal monitoring of spinal cord injury for research purposes.

Key words: clinical trials, electric current, electrodiagnosis, quantitative sensory tests, rehabilitation, sensory outcome measures, sensory perceptual threshold, spinal cord injury, thermal sensation, vibration sensation.

INTRODUCTION

This report summarizes preliminary findings of three quantitative sensory tests (QSTs) that were evaluated as part of the International Spinal Research Trust (ISRT) Clinical Initiative study. ISRT commissioned this work in preparation for future clinical trials of new spinal cord injury (SCI) interventions. The wider Clinical Initiative study assesses numerous clinical and neurophysiological tests of motor, sensory, and autonomic function that could be used for monitoring the efficacy of new therapeutic interventions.

The ISRT Clinical Initiative has a few specific requirements. Firstly, to minimize functional loss to the patient in case of any neurological deterioration, ISRT anticipates that the first clinical trials of spinal cord repair sponsored by them will be conducted in patients with thoracic lesions. Therefore, the newly developed tests must be applicable in the thoracic region, for which SCI diagnosis currently relies mainly on clinical sensory testing. Secondly, the first interventions are expected to produce only minor improvements and possibly over a few spinal segments only; therefore, the newly developed tests must be able to detect these small changes. The tests presented here were developed with these requirements in mind, although they can be used in patients with any level and type of injury.

Abbreviations: ASIA = American Spinal Injury Association, C = cervical, ISRT = International Spinal Research Trust, L = lumbar, PT = perceptual threshold, QST = quantitative sensory test, S = sacral, SCI = spinal cord injury, SD = standard deviation, T = thoracic.

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An overall progress review of the ISRT Clinical Initiative study was presented in the ISRT lecture at the International Spinal Cord Society's Annual Scientific Meeting in Beijing, China (October 2003) and was published in 2004 by Ellaway et al. [1].

The present article includes three of the sensory tests discussed in Ellaway et al. [1] and provides additional data acquired since that publication. However, at the time this article was prepared, the ISRT Clinical Initiative study was still ongoing and final results were unavailable. Hence, all the results reported here should be treated as preliminary. Once complete, final results will be submitted for publication as separate articles in peer-reviewed journals.

The three tests discussed in this article are QSTs that assess the perceptual thresholds (PTs) (lowest stimulus intensity that a subject can perceive) for three types of stimulation: electrical, vibration, and thermal. All three stimulation types had been used previously for assessing sensory function, mainly in peripheral neuropathies [2–6], radiculopathies [7–8], and brachial plexus lesions [9]. Some QSTs have been used in patients with incomplete SCI [10–12]. For this study, the techniques were adapted to suit patients with SCI of any level, including thoracic, and of any impairment grade. Between them, the three QSTs were expected to include both of the sensory modalities tested in clinical examination (i.e., pinprick and light touch); thermal thresholds would predominantly test spinothalamic function, vibration threshold would test posterior column function, and electrical threshold would test both sensory functions.

METHODS AND PRELIMINARY RESULTS

The ISRT Clinical Initiative study was approved by the Aylesbury Vale Local Research Ethics Committee. Control subjects and patients with SCI were given a written information sheet and a verbal explanation of all the procedures. Written consent was obtained from all subjects.

For each of the three tests (electrical, vibration, and thermal PTs), normative values and reproducibility of the technique were established in control subjects before performing the test in the patients with SCI. Wherever possible, stimuli were applied over American Spinal Injury Association (ASIA) sensory key points or, at least, within ASIA dermatomes (**Figure 1**). All patients also had a clinical neurological examination and classification performed according to ASIA standards [13–14] so that the QST results could be correlated with clinical sensory examination results. Consistent with ASIA standards, clinical sensory level was determined separately for the right and left sides of the body and defined as the most caudal spinal segment with normal sensory function for both sensory modalities (i.e., pinprick and light touch).

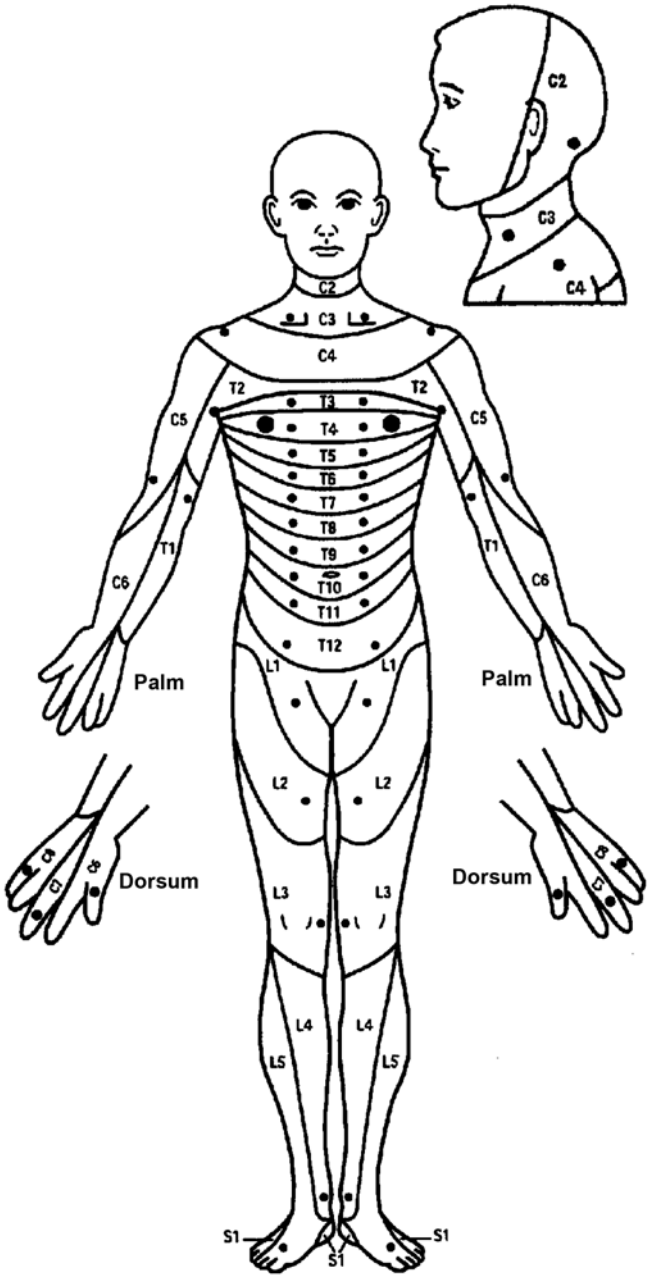

Figure 1.
American Spinal Injury Association (ASIA) sensory key points. Reprinted by permission from ASIA. ASIA. International Standards for Neurological Classification of Spinal Cord Injury, revised 2002. Chicago (IL): ASIA; 2002. C = cervical, L = lumbar, S = sacral, T = thoracic.

Perceptual Threshold to Cutaneous Electrical Stimulation

The technique used was originally described by Davey et al. in 2001 [15]. A Digitimer D4030 and a DS7 electrical stimulator (Digitimer Ltd, Welwyn Garden City, Hertfordshire, England) produced square electrical pulses of 0.5 ms duration and 3 Hz frequency (**Figure 2**). Stimuli were delivered to the skin via self-adhesive electrodes over ASIA sensory key points for each dermatome between third cervical (C3) and second sacral (S2) bilaterally. PT was recorded as the lowest ascending stimulus intensity out of three trials (in milliamperes) at which the subject reported sensation.

Electrical PTs have been measured in 18 control subjects and 30 patients so far. In the control group, electrical PTs were measured bilaterally for each dermatome between C3 and S2 and expressed as mean ± 2 standard deviation (SD). The measurements were repeated within 3 months in half of the control sample. Mean electrical PT values in the control group varied depending on the dermatome tested and were lowest for the first thoracic (T1) (1.1 ± 0.3 mA) and highest for the fourth lumbar (L4) (4.1 ± 2.0 mA). Results for the corresponding right and left dermatomes were strongly correlated, as were repeated assessments. Control group results were used for construction of a normative PT template (**Figure 3**), with which the results of the patients could be compared later.

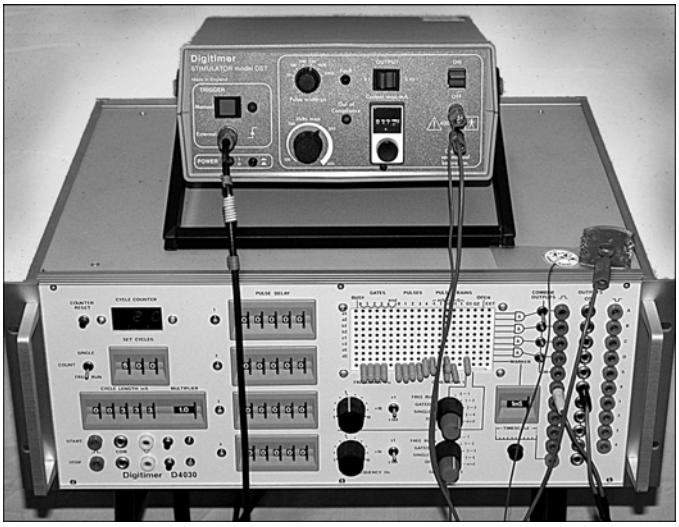

Figure 2.
Digitimer D4030 and DS7 electrical stimulator with surface electrodes (Digitimer Ltd, Welwyn Garden City, Hertfordshire, England) used for testing perceptual threshold to electrical stimulation.

After the control study confirmed the simplicity and reproducibility of the electrical PT test, testing was performed in 30 patients with SCI of different levels and impairment grades. Electrical PTs were measured in several dermatomes above the clinically determined level of injury, in dermatomes below the level of incomplete SCI, and in the zone of partial preservation in complete SCI. Each patient's electrical PT results were then compared with the normative PT values for every dermatome tested.

The level of SCI according to electrical PT results was established for the right and left sides of each patient and defined as the last segment in which the patients' PT was within the control group PT range (mean ± 2 SD). Electrical PT level was then compared with the clinical sensory level derived by ASIA standards. The electrical

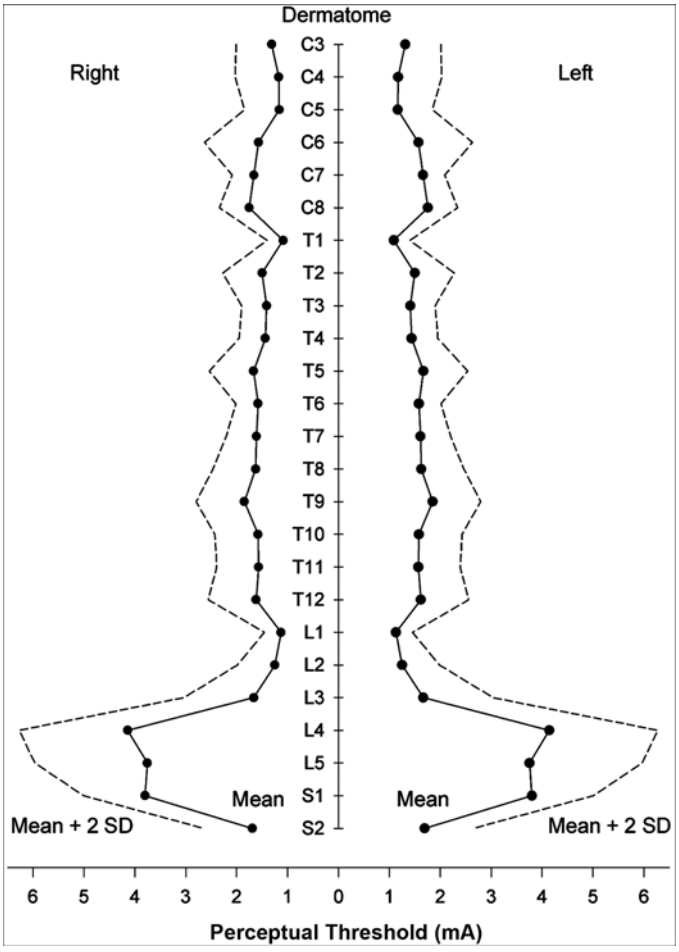

Figure 3.
Normative template for perceptual threshold to electrical stimulation (mean + 2 standard deviation [SD]) by American Spinal Injury Association dermatomes (third cervical [C] to second sacral [S]). L = lumbar, T = thoracic.

PT and clinical levels of injury were the same in one-third of the patients. In the remaining two-thirds, the levels differed and the PT level was usually higher than the clinical level (in just over one-half of all patients), usually by one to two segments. This finding indicates that the electrical PT test could be sensitive to small sensory impairments not detectable by standard clinical testing.

In conclusion, electrical PT seems to be a simple and reproducible QST. It can assess both the level and the degree of impairment of SCI and may be more sensitive than clinical testing in detecting minor sensory impairments.

Vibration Perceptual Threshold

Vibration PTs were similarly measured in 12 control subjects and 18 patients. A Bio-Thesiometer (Biomedical Instrument Co, Newbury, Ohio) was used in this test (**Figure 4**). A 100 Hz frequency vibration was applied via a handheld probe to bony prominences within ASIA dermatomes C3 to S1 bilaterally and over spinous processes C7 to L5 (**Table**). Vibration PT was recorded as the lowest ascending stimulus intensity out of three trials (in volts) at which the subject reported vibration sensation.

Figure 4.
Bio-Thesiometer (Biomedical Instrument Co, Newbury, Ohio) used for testing vibration perceptual thresholds.

In the control group, the mean vibration PT varied depending on the dermatome tested and was lowest for the C8 dermatome (mean = 5.5 V, range = 4–7 V) on the little finger and highest over the iliac spines (mean = 20.5 V, range = 16–25 V). Results for corresponding dermatomes on the two sides of the body correlated well and strong correlation was found between repeated measurements.

Preliminary results for 18 patients were analyzed as described for electrical PTs: each patient's vibration PT results were compared with the control vibration PT values for every dermatome tested. The level of SCI according to vibration PT results was established for the right and left sides of each patient and defined as the last segment in which the patients' vibration PT was within the control vibration PT range. Levels of injury according to vibration PT were then compared with the clinical sensory levels derived by ASIA standards. Results were similar to those of electrical PT: the vibration PT and clinical levels of injury were the same in one-third of the subjects. In the

Table.
Stimulation sites for vibration perceptual threshold testing within American Spinal Injury Association dermatomes.

Vibration Stimulation Site	Dermatome
Clavicle	C3
Acromion	C4
Lateral Epicondyle	C5
Styloid Process Radius	C6
Thumb (proximal phalanx)	C6
Middle Finger (proximal phalanx)	C7
Little Finger (proximal phalanx)	C8
Styloid Process Ulna	C8
Medial Epicondyle	T1
Rib 2	T2
Rib 3	T3
Rib 4	T4
Rib 5	T5
Rib 6	T6
Rib 7	T7
Rib 8	T8
Anterior Superior Iliac Spine	T12
Patella	L3
Medial Malleolus	L4
Lateral Malleolus	L5
Hallux (proximal phalanx)	L5
Little Toe (proximal phalanx)	S1

C = cervical, L = lumbar, S = sacral, T = thoracic.

remaining two-thirds in whom levels differed, the vibration PT levels were usually higher than the clinical levels (just under one-half of the patients) but the difference in levels was often by two or more segments.

Interestingly, in those patients who underwent both QSTs (i.e., electrical and vibration PTs), if the level of injury was higher according to electrical PT than clinical testing, the level was usually higher according to vibration PT, as well. This finding supports the indication that the two QSTs may detect minor sensory impairments undetectable by clinical sensory examination.

In conclusion, vibration PT is a simple and reproducible QST. It seems to be more sensitive than clinical testing in detecting minor sensory impairments and may be particularly useful in assessing the degree of impairment below the level of injury in incomplete lesions and in the zone of partial preservation in complete spinal cord lesions.

Thermal Perceptual Thresholds

Since presentation of this research at the 2005 ASIA meeting (Dallas, Texas), the study of thermal PTs was published by Nicotra and Ellaway [16]. The readers are referred to their article for details. The aim of the study was investigation of the extent to which QSTs could reveal subclinical deficits at the neurological level of injury in subjects with chronic SCI.

Four thermal thresholds were measured with the Medoc Thermal Sensory Analyzer (TSA-2001, Medoc Advanced Medical Systems Ltd, Ramat Yishai, Israel): cool and warm PTs and cold and heat pain thresholds. Tests were carried out in 10 control subjects and 28 patients. Cool and warm stimuli were applied in random order via a handheld probe (thermode) to the skin over ASIA sensory key points at, directly above, and below the clinically determined level of SCI. The patients were asked to indicate the first perception of warmth or coolness (PTs) and, in a separate test, the moment when the feeling of heat and cold became painful (pain thresholds).

When analyzing patients' results, an abnormal value was defined as any value more than 2 SD from the control mean value. Above the clinically determined level of injury, cool and warm PTs were raised in one and sometimes two segments above the clinical sensory level. Cold and heat pain thresholds were not significantly different from controls above the level of injury. In the zone of partial preservation, the thermal thresholds for both cool and warm perception were raised. In addition, some patients reported a misinterpretation of sensation (cold for warm or vice versa) or an undefined rather than thermal sensation. Thermal allodynia, a painful sensation to hot and/or cold stimuli well below the control group's pain threshold, was also observed in 12 patients (8 with complete and 4 with incomplete SCI). Repeated thermal PTs in 10 patients showed that the tested modalities did not significantly change above or below the level of injury between the subjects' first and second visits (average 27-week separation).

In conclusion, thermal perceptual and pain thresholds seem to be uncomplicated, reproducible, capable of assessing both level and density of SCI, as well as thermal allodynia, and possibly more sensitive to minor sensory impairments than clinical sensory examination. The time required for thermal testing can be lengthy and judicious assessment should be made of the number of dermatomes to be tested.

In all three described QSTs, a total sensory loss existed below the zone of partial preservation as judged by the limits of the tests.

CONCLUSIONS

Even though some of the QST findings presented here are still preliminary, the three tests seem to have definite advantages. They are simple, applicable in a clinical setting, and reproducible. They minimize the examiner's subjectivity when assessing sensory function and add resolution to clinical sensory testing, results of which are expressed on an ordinal scale (0 = absent, 1 = impaired, and 2 = normal). By giving a continuous numeric threshold value, QSTs can quantify the sensory impairment within the ASIA sensory grade "1 = impaired." This quantification could be very useful in monitoring any changes in the degree of impairment and would make statistical analysis of the results much easier and more robust. The three tests also seem to add sensitivity to clinical testing by detecting subclinical sensory impairments in the segments directly above the level of SCI that are clinically described as "normal."

Although simple to use, all three tests require specialized portable equipment, trained staff, and additional time, which may make them unsuitable for everyday clinical practice.

Based on our preliminary results, we believe that the three QSTs could be useful as adjuncts to standard clinical testing in longitudinal monitoring of SCI for research purposes, both during natural recovery and therapeutic clinical trials.

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The authors have declared that no competing interests exist.

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