

## Neurodiagnostic Evaluation of the Pain Patient

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### Abstract

Subjective sensory abnormalities, such as radiating pain, dysesthesia and allodynia, are a common feature of patients presenting to a pain clinic. Objectively quantifying those abnormalities using subjective tests (eg tuning fork, safety pin) may be difficult. There are a number of non-invasive neurodiagnostic technologies available to supplement the history and physical exam including MRI, thermal perception threshold and vibratory perception threshold test. The sensory Nerve Conduction Threshold (sNCT) electrodiagnostic evaluation generates Current Perception Threshold (CPT) and Pain Tolerance Threshold (PTT) measures provide objective measures of sensory nerve functional integrity from the periphery to the central nervous system. Neuroselective sinusoidal electrical stimuli permits the sNCT evaluation to quickly, painlessly and objectively quantify the conduction and functional integrity of the large and small myelinated and unmyelinated sensory nerve fibers. Areas of abnormal function are localized to aid in diagnosis, determine clinical severity and evaluate the therapeutic outcome.

### Introduction

Subjective sensory abnormalities are a common feature of patients presenting to a pain clinic. Reliable documentation of the degree and distribution of a patient's sensory abnormalities is essential to arriving at a diagnosis. Accurate timely diagnosis of pathology at the earliest stages is preferable, improving the prognosis and reducing the cost of treating advanced stages of pathology. A thorough history can be very effective at elucidating a description of the symptoms, however, objectively quantifying these abnormalities can be difficult.

The Visual Analogue Scale (VAS) is the most frequent diagnostic pain measure used. The VAS represents the patients' subjective rating of their pain intensity. Other commonly used measures include clinical examinations with safety pins, tuning forks or pinwheels. These measures are subjective, highly variable and prone to examiner bias making their use for serial assessment difficult. There are a number of non-invasive neurodiagnostic technologies available to supplement the history and physical exam. Imaging studies provide a structural view, however, a bulging disc on Magnetic Resonance Imaging (MRI) does not necessarily indicate pathology[1]. Sensory Nerve Conduction Velocity (sNCV) studies provide a physiological measure that is limited to the sub-population of large myelinated nerve fibers confined within a segment of a peripheral nerve, however, a nerve conduction block does not necessarily indicate a complete loss of nerve function[2]. Lesions occurring proximal to the dorsal root ganglion, such as a radiculitis secondary to nerve root inflammation are generally not detectable by either sNCV or MRI studies. Sensory electrodiagnostic procedures supply an objective measure that can be compared to established normative data providing a gauge of the severity of the neuropathology.

The electrodiagnostic sensory Nerve Conduction Threshold evaluation generates

neuroselective Current Perception Threshold (CPT) and Pain Tolerance Threshold (PTT) measure which provide an objective measure of sensory nerve functional integrity from the periphery to the central nervous system. The quantitative vibratory detection threshold test provides a measure of mechanoreceptive sensory end-organ transduction to the large diameter sensory fibers. Variations in skin thickness, temperature and bone conduction are confounding variables of this measure. Quantitative thermal discrimination tests evaluate thermal receptor transduction to the smaller diameter sensory fibers. This test is also affected by variations in skin thickness and temperature. The sNCT quantitative evaluation uses a neuroselective electrical stimulus to directly excite both the large and small diameter sensory nerve fibers in a manner not affected by skin thickness or temperature.

#### Definition of CPT and PTT

The CPT measure represents the minimal amount of a painless, neuroselective, transcutaneous electrical stimulus required to reproducibly evoke a sensation. This test provides an objective, quantitative gauge of sensory nerve integrity and is obtainable from any cutaneous site[3]. The CPT evaluation achieves neuroselectivity by using different frequencies of an electrical sine wave stimulus. The 2000 Hz stimulus measure reflect large myelinated fiber function, the 250 Hz stimulus measure reflect small myelinated fiber function and the 5 Hz stimulus measure reflects small unmyelinated fiber function[4]. Electrodes can be applied to any cutaneous site and an automated double blind forced choice testing procedure determines CPT measures to within  $\pm 20$  microAmperes ( $p<0.006$ ). CPT measures are compared to established normative values to determine if the patient's values are normal or not. Abnormally low CPT measures indicate hyper-sensitive nerve function (commonly associated with inflammation or irritation) reflecting a hyperesthetic condition. Abnormally elevated CPT measures indicate a loss of nerve function reflecting a hypoesthetic condition. Pain Tolerance Threshold (PTT) is the maximum amount of electrical stimulus which evokes pain that can be tolerated. The PTT test uses the same neuroselective stimulus (double blind automated methodology) to evoke pain from the large myelinated fibers (when present), small myelinated and unmyelinated fibers. The PTT evaluation is atraumatic in that it does not cause tissue damage. The PTT measure permits the evaluation of allodynia. The sNCT evaluation CPT and PTT measures are obtained using Neurometer(R) CPT/C neuroselective sNCT devices (Neurotron, Inc, Baltimore, MD USA). These diagnostic devices are constant current simulators which are microprocessor controlled.

#### Peripheral Cutaneous Sensory Nerve Anatomy

The large myelinated (A beta ) fibers which conduct up to 60 m/s, convey touch sensation and comprise only 5-10% of the total number of fibers comprising the typical sensory nerve. The small myelinated (A delta) fibers which convey sharp pain are also relatively few in number (<10%). Approximately 80% of the sensory fibers in the sensory nerve are the small unmyelinated (C) fibers which convey sensations such as temperature and dull pain[5].

The pain management specialist does not have to limit patient evaluation to tests solely of large fiber function (sNCV) or smaller fiber function (thermal perception threshold). The sNCT evaluation is multimodal and can assess both large and small sensory fiber function in a single procedure. Both of those classes of fibers may mediate pain and should be evaluated. All modes of sensation may be effected in a patient with neuropathy, however, there may be

selective impairment of large or small fiber functions[6]. The fiber neuroselectivity of the sNCT evaluation enhances its sensitivity for detecting sensory dysfunction by testing the three major sub-populations of nerve fibers within any cutaneous test site. This additional information permits more appropriate selection of therapeutic intervention.

#### Clinical Research Establishing Neuroselectivity

There have been over 200 publications clinical and basic science studies utilizing, referencing and validating the sNCT evaluation. These studies include:

1. Comparison studies of the sNCT evaluation CPT measures with other neurodiagnostic techniques performed at the Manchester Royal Infirmary (UK), Tokoku Kosei-Nenkin Hospital in Sendai (Japan) and other institutions have demonstrated that sensory abnormalities detected with the 2000 Hz CPT measures correlate best with the sNCV test which evaluates large myelinated fiber function. The 250 Hz CPT measures correlate best with quantitative vibratory tests which evaluate primarily smaller myelinated fiber function. The 5 Hz CPT measures were reported to correlate best with the thermal quantitative sensory tests which evaluate primarily small unmyelinated fiber function[7,8].
2. Histological studies of sural nerve biopsies from diabetics and healthy controls using electron microscopy reported that low frequency 5 Hz CPT measures correlated with small fiber density and the 2000 Hz CPTs correlated with large fiber diameter. This same study failed to find any correlation between unmyelinated fiber pathology and myelinated fiber density with sNCV, vibratory and thermal perception threshold tests[9].
3. Pharmacologic studies have demonstrated that the 5 Hz measures are most sensitive to the effects of lidocaine[10,11,12]. This is consistent with evidence suggesting that small unmyelinated fibers are most sensitive to the effects of local anesthetics[13,14].
4. Regeneration studies show recovery of small fiber function first, correlating with 5 Hz and 250 Hz CPTs whereas recovery of large fiber function, correlating with 2000 Hz CPTs, occurs approximately 9 months later[15].
5. Imaging studies from Harvard University and the Massachusetts General Hospital using functional MRI have demonstrated that the 5 Hz pain stimulus elicits metabolic activity in the same cortical regions as heat pain stimuli. Interestingly, there was no habituation to the electrical stimuli, however, there was habituation to the heat pain stimulus. This is presumably because heat sensation is nerve end-organ mediated, whereas the electrical stimulus directly excites the nerve fibers. The 250 Hz and 2000 Hz activated different regions of the brain[16].
6. Human, as well as, animal studies have demonstrated neuroselective and reproducible pain thresholds[3,17].

#### Clinical and Research Applications of the CPT Evaluation

The sNCT evaluation CPT and PTT measures are capable of objectively quantifying sensory abnormalities consistent with polyneuropathy[18,19] compressive neuropathy/peripheral nerve injuries (eg carpal tunnel syndrome)[20], radiculopathy[21], Complex Regional Pain Syndrome (CRPS)[22]. Areas of abnormal

function are localized to aid in diagnosis, determine clinical severity and evaluate the therapeutic outcome. The painless nature of the test ensures high patient compliance with the follow up examinations.

#### Conclusion

The ability to objectively quantify neuroselective pain and non-pain sensations is a powerful new tool for the pain clinician. More clinical and basic research utilizing the sNCT evaluation CPT and PTT measurements in characterizing sensory abnormalities and pain tolerance thresholds in various chronic pain conditions and assessing the efficacy of various interventional strategies is needed. The effects of spinal cord stimulation, using implantable technologies and commonly used oral agents (eg Neurontin) are just a few of the areas needing further research. The sNCT evaluation will continue to provide a valuable measures in the objective evaluation of the patient with pain.

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