NEUROMETER® CPT

Selected abstracts from publications referencing Neurometer® CPT electrodiagnostic neuroselective sensory nerve evaluations are enclosed. A bibliography of selected publications grouped by topic and specialty is also included along with answers to frequently asked questions.
Neurotron, Incorporated, Medical Electronics

Neurometer® CPT® and NervScan Neuroselective Electrodiagnostic Sensory Nerve Testing Equipment

Neuroselective Sensory Nerve Conduction Threshold (sNCT®), Current Perception Threshold (CPT®) and Pain Tolerance Threshold (PTT) Publications and FAQ

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Selected Bibliographies of Neurometer® CPT Related Papers and Publications Grouped by Topic and Specialty ................................. 49-64.
Neurotron Incorporated was founded in Baltimore, MD USA in 1981. FDA permission to market the Neurometer® electrodiagnostic technology was granted in 1986. Initial clinical studies, approved by the Johns Hopkins Medical School Investigational Review Board, were conducted at various affiliated Hopkins health facilities as well as at the University of Maryland in Baltimore. Initially the Neurometer® device was used only by Neurologists. This easy to perform procedure soon came to be used by orthopedic surgeons, endocrinologists, pain clinicians and many other specialties including toxicology, urology, dermatology and laboratory animal research. Presently there are more than 500 peer-reviewed scientific publications demonstrating the utility of Neurometer® technology. This Abstract Booklet includes selected abstracts grouped according to 8 major topics as well as 13 bibliographies of selected publications also grouped by topic.

Today Neurometer® devices are in routine clinical use around the world. Additionally, there are non-clinical applications including field-testing for environmental and industrial applications, pharmaceutical, cosmetic, epidemiological and laboratory animal applications. Neurotron, Inc. is constantly upgrading and expanding the applications of its technology. We invite you to visit our website www.neurotron.com for updates and take advantage of our “Documents & Download” extensive reference library.

Frequently Asked Questions (FAQs)

What are Neurometer® electrodiagnostic devices?

Neurometer® devices measure sensory nerve thresholds for detecting an electrical stimulus. The electrical stimulus is neuro-selective and it is applied to measure the selective sensory detection threshold for each of the three major sub-populations of sensory nerve fibers innervating the test site. Just as the hearing test determines the auditory detection threshold for different sub-populations of auditory nerve fibers with different frequencies of painless auditory stimuli. The Current Perception Threshold (CPT) test determines the sensory detection threshold for different sub-populations of sensory nerve fibers with different frequencies of painless electrical stimulus. CPTs are determined using an automated double-blind testing methodology. The Neurometer® device stimulus is microprocessor controlled. The neuroselective electrical stimuli quickly and painlessly quantify the conduction and functional integrity of the large and small myelinated and small unmyelinated sensory nerve fibers at any cutaneous site, mucosal or tooth test site. CPT measures have the unique capability to map the distribution of impairments ranging from neuritis (hyperesthesia) to neuropathy (hypoesthesia). Additionally, the Neurometer® device may provide atraumatic Pain Tolerance Threshold’s (PTT’s) and laboratory Animal Response Threshold (ART) measures.

What are the characteristics of the Neurometer® electrical stimulus?

Neurometer® devices generate three different constant alternating current sinusoid waveform stimuli at 2000 Hz, 250 Hz and 5 Hz. Stimulus output intensities range from 0.001 to 9.99 mAmperes (mA). A constant current output maintained by impedance feedback circuitry. This assures highly
reproducible measures which are unaffected by variables such as trophic skin changes, thickness or temperature variations or edema. The device’s microprocessor is capable of performing both single-blind and fully automated double-blind examinations as well as permitting external computer control. Other device functions include an automated system integrity check and a continuous monitoring of stimulus output parameters and battery charge levels with appropriate warning alarms and messages. The external computer control enhances its utility for clinical, laboratory, fMRI imaging and other applications. Both the printer and the Neurometer® unit are powered by the device’s internal rechargeable battery.

Neurometer® devices are currently being employed for routine clinical purposes at thousands of locations around the world, as well as in research and industrial settings. Use of the neuroselective sNCT evaluation has been taught in AMA accredited and international continuing medical education courses starting with the American Academy of Neurology in 1985. To date, more than 1 million Neurometer® CPT examinations have been performed.

What types of procedures can Neurometer® CPT devices perform?

The Neurometer® CPT/C device has two automated double blind painless Current Perception Threshold determination modes of operation: automated forced choice CPT (p<0.006), ranged R-CPT(p<0.05) as well as a single-blind manual CPT determination mode. The Pain Tolerance Threshold (PTT) mode allows a reproducible, non-invasive and atraumatic method for measuring Pain Tolerance Threshold (PTT) levels in small and large fibers (if present) for evaluation of analgesic interventions or the patient with pain. The Windows® based CPT/C Computer Control Package allows the output of the CPT/C unit to be controlled through a PC. It allows the setting of repetitive stimuli at specific durations and intensity profiles. The Computer Control Package is also ideal for fMRI testing and laboratory animal investigations.

How is the CPT procedure conducted?

Neurometer® electrodiagnostic examinations use a standardized, automated procedure to generate objective, quantitative measures of the conduction and functional integrity of sensory nerve fibers. The unit emits non-aversive transcutaneous electrical stimuli through a pair of gold plated electrodes to evoke sensation for CPT determination. The procedure includes testing the patient at one or more body sites with three different sinusoidal frequencies of electrical stimulus. Each frequency, 2000 Hz, 250 Hz, and 5 Hz, evokes a response from a different subpopulation of sensory nerve fibers: large myelinated, small myelinated and small unmyelinated fibers, respectively. Normative CPT values have been established and published for multiple body sites and they are used to analyze patient measures. Windows® based software included with each device can be used to analyze the data and print a report summarizing the results. The following is a brief description of the standard CPT examination.

The technician turns the unit on and conducts a Pre-Exam Cable Test by following directions displayed on the unit’s Liquid Crystal Display (LCD) screen. Successful completion of this test confirms the proper functioning of the CPT unit, electrodes and cables.

The patient is placed in a comfortable position - sitting or reclining - and
preferably in a location with minimal distractions. The examination procedure is explained to the patient. The prescribed skin sites to be evaluated are examined to confirm that the skin is intact. The skin may be cleaned and prepared for testing using a skin prep paste. A pair of 1 cm. diameter disposable gold electrodes are coated with a thin layer of conductive gel and then taped to the test site. Specialized electrodes and catheter electrodes are available for animal, mucosal and other evaluations.

The patient performs an automated Intensity Alignment procedure which quickly narrows down the threshold level to a range of +/- 50µAmperes out of a total range of 0 to 9.99 mAmpere. Next, the patient begins the Auto Test Mode which is a fully automatic, double-blind, forced choice procedure to determine the actual Current Perception Threshold measures (p<0.006). The patient is presented with randomly generated pairs of real and placebo stimuli which they are then asked to identify verbally or by pressing a button on a remote unit. Based upon the patient’s response, the CPT device adjusts the output level of the stimulus and randomly generates a new testing order for the next pair of tests in the series. The automated design of the CPT testing procedure assures that neither the patient nor the operator can influence the test outcome based upon subjective impressions. When a sufficient number of tests have been performed, the device determines and displays the CPT value for the test series and optionally prints out the results. The Auto Test Mode follows a testing paradigm similar to that used in standard auditory tests and determines the patient’s CPT measures to within +/- 20 µAmperes. Compliance Guard® technology monitors patient responses for consistency and accuracy. This testing sequence is repeated for each of the three frequencies of stimulus before moving on to the next body site.

How long does it take to perform the CPT evaluation?

The CPT evaluation of the 3 sub-populations of nerve fibers measure requires approximately 8 minutes whereas the “Ranged-CPT” or “R-CPT” evaluation requires approximately 2 minutes at each test site. A typical clinical evaluation may involve testing 2 to 6 sites (1 to 3 sites bilaterally).

What specific information does the CPT evaluation provide?

CPT measures provide objective, quantitative determinations of sensory nerve conduction and functional integrity from any cutaneous/mucosal site. Each CPT measure represents the minimum amount of a painless, neuroselective, transcutaneous electrical stimulus required to reproducibly evoke a sensation approximately 50% of the times it’s presented. Three independent CPT measures are obtained from each test site by using three different sinusoidal frequencies of electrical stimuli: 2000 Hz, 250 Hz and 5 Hz. These measures selectively quantify the functioning of the three major sub-populations of sensory nerve fibers providing innervation to the test site: the large myelinated, small myelinated and small unmyelinated fibers. Abnormally low CPT measures indicate a hyper-sensitive nerve function (commonly associated with inflammation or neuritis) reflecting a hyperesthetic condition. Abnormally elevated CPT measures indicate a loss of nerve function reflecting a hypoesthetic condition or neuropathy.

CPTs are measured in units equivalent to 0.01 mAmpere (mA) of output intensity. At output intensities below 0.10 mA, CPT measures are resolved
in increments of 0.1 CPT units (1 µAmpere). For example, a CPT measure of 100 indicates a stimulus output intensity of 1.0 mA; a CPT of 9.5 indicates an output intensity of 0.095 mA. The stimulus output range of the CPT device is 0.001 mA (CPT=0.1) to 9.99 mA (CPT=999).

Ranged R·CPTs are from 1 through 25. They are determined using previously established site and stimulus frequency specific normative values indicating hyperesthetic (1-5), normal (6-13) and hypoesthetic (14-25). R·CPT of 25 = 9.99 mA.

**How does the CPT evaluation assist in clinical evaluations?**

**Differential Diagnosis:** The CPT evaluation is used to objectively quantify sensory nerve function when the history (sensory symptoms) and physical examination (abnormalities detected with tuning fork, pinwheel, radiating pain reproduced with provocative orthopedic maneuvers etc.) merit further investigation of sensory function. The CPT evaluation is not indicated for routine use with every patient.

The differential diagnosis of sensory neuropathy can include: radiculopathy (disc injury), compressive lesion (e.g., carpal or tarsal tunnel syndrome), as well as axonal versus demyelinating vs distal axonal polyneuropathy (e.g. Guillain‐Barré Syndrome, diabetic, uremic, alcoholic, toxic), spinal impairment or other types of central nervous system dysfunction (e.g. syringomyelia). Different sensory nerve pathologies typically exhibit distinctly different distributions of sensory impairment and may selectively effect the functioning of specific sub-populations of nerve fiber function (e.g. demyelinating neuropathies or large versus small fiber dysfunction). For instance, the impairment resulting from radiculopathy will be confined to a dermatomal distribution whereas the impairment from polyneuropathy secondary to axonopathy is most often confined to a distal distribution, involving primarily the toes, fingers and multiple nerves/dermatomes. CPTs can be mapped from any cutaneous location in order to assist in identification and diagnosis. Patients may also have a combination of sensory neuropathies such as an alcoholic with “Saturday Night Palsy”, a diabetic with radiculopathy or a uremic with carpal tunnel syndrome superimposed on polyneuropathy.

The objective nature of the CPT exam can also help in determining if a patient has sensory neuropathy consistent with their reported symptoms or if instead they might be suffering possible non-neurological impairments or seeking secondary gain. Conditions such as vascular or soft tissue lesions or arthritis, a ligamentous sprain or muscular sprain which can include symptoms of radiating pain, may mimic neuropathic conditions. For these reasons, it is sometimes necessary to conduct the automated CPT evaluation in patients with complaints of pain to confirm the differential diagnosis in order to prescribe appropriate treatment.

**Determining Clinical Severity:** The neuro-selective CPT evaluation objectively documents the clinical severity of neurogenic abnormalities. The evaluation measures whether the impairment is in the sub-clinical or early clinical stages (hyperesthesia) versus late stage neuropathy, hypoesthesia (loss of function) or anesthesia (complete loss of sensation). Serial mapping of the distribution of impairment permits the assessment of the progression of disease. This information guides the clinician's decision for the most
appropriate treatment and/or medical/surgical referral. Generally, the earlier the therapeutic intervention the better the prognosis.

The Neurometer® CPT evaluation enables physicians to evaluate those sensory fibers which mediate both pain and non-pain sensation. Both types of fibers should be evaluated because disease conditions may selectively impair large fiber function (position and vibratory sense) and/or smaller fiber function (pain and temperature). The evaluation of small fiber function is also critical for assessing protective sensation and can provides an indirect index of autonomic function.

Monitoring Therapeutic Intervention: The CPT evaluation is also used to monitor the efficacy and gauge the outcome of therapeutic intervention by providing objective serial measurements of the neuropathy, disability and neuro-regenerative processes. The painless nature of the test ensures high patient compliance for follow-up examinations.

How does the CPT exam compare to other neurodiagnostic exam procedures (sNCV, SSEP, EMG, MRI)?

There are numerous publications comparing CPT studies to traditional nerve conduction velocity studies, and they generally demonstrate a strong correlation between both their findings and levels of reliability. Several studies comparing CPT to MRI and intraoperative neurophysiological evaluations have demonstrated similar levels of correlation. While the CPT evaluation does have much in common with other neurodiagnostic procedures, many publications have also pointed out specific areas in which its capabilities surpass those of the other procedures. It is a painless measurement and patient compliance with serial testing is extremely high. It is also relatively insensitive to changes in skin temperature, thickness, scar tissue or edema which can distort or block the measures from other types of exams. The test is neuroselective for large myelinated, small myelinated and unmyelinated sensory fibers. It is a functional evaluation that can be performed at early stage neuritis or late stage neuropathy, and healthy control CPT values are available for measures of the shortest afferents on the face to the longest afferents on the toe. The Neurometer® CPT device is extremely safe, battery powered, and easy to use. (Comparison chart available at: http://www.neurotron.com/compare.html)

The sNCV and SSEP tests evaluate the large diameter myelinated sensory nerve fibers, which typically comprise less than 10% of a peripheral nerve. Conditions which selectively effect the smaller nerve fibers are undetectable by these tests. The CPT evaluation measures the conduction and functional integrity of all three major sub-populations of sensory nerves fibers, including the large myelinated, small myelinated and unmyelinated fibers. Together, these make up more than 90% of the sensory fibers in a typical nerve. Many conditions, particularly in the early stages, selectively effect a specific sub-population of fibers while leaving the other fibers untouched. The sNCT/CPT test is indicated for neuropathologies effecting large and/or small sensory fiber pathology.

The sNCV and SSEP tests are limited to measuring reductions in amplitude or conduction velocity resulting from a significant loss of nerve function. The sNCT/CPT evaluation is not limited to evaluating only those conditions which result in a significant loss of nerve function since it detects and quantifies hyperesthesia as well as hypoesthesia. Hyperesthetic conditions
reflect inflamed or irritated sensory nerve fibers with elevated resting membrane potentials and resultant lower electrical thresholds that have not yet lost their functioning (i.e. become hypoesthetic). Hyperesthesia commonly precedes hypoesthesia or anesthesia in progressive peripheral nerve damage. Detection of hyperesthesia allows for earlier therapeutic intervention in a disease condition with the potential of limiting more severe damage. The ability to quantify the functioning of the smallest unmyelinated afferents also makes CPT exam capable of detecting patients at risk for autonomic dysfunction as well as a loss of protective sensation.

The needle EMG test and motor nerve conduction velocity (mNCV) tests only provide information about muscle function and motor nerve innervation. These tests provide no information about sensory nerve function. The automated CPT evaluation only provides information about the sensory nerves. Sensory nerves are usually affected at an earlier stage than motor nerves in most common types of progressive neuropathology.

The Neurometer® CPT evaluation is also capable of monitoring recovery of sensory nerve functional integrity following carpal tunnel release, nerve repair or treatments such as plasmapheresis or immunoglobulin therapy. All of these therapeutic interventions result in scar formation which causes an artifact that impairs physiological measures such as the sNCV or the SSEP.

The CPT evaluation is indicated in the early stages of suspected radiculopathy, instead of a needle EMG, to perform an objective evaluation of the patient’s condition and ascertain the efficacy of therapeutic intervention. In the case of a compressive radiculopathy from, for example from a bulging disc, Wallerian degeneration is required before a needle EMG will show any abnormal findings. This degeneration typically requires three to six weeks to occur before the needle EMG can document this impairment which can result in a delay in the application of effective therapeutic intervention. The CPT evaluation has been shown to be capable of documenting immediate changes in spinal nerve function. Various publications have demonstrated the effects of spinal lidocaine and narcotics on CPT and/or PTT measures concurrent with loss and recovery of sensory function.

The sensory nerve conduction velocity (sNCV) evaluation tests only a small segment of a peripheral nerve, typically less than 50 cm on an arm or a leg. With most radiculopathies, sensory nerve function is impaired by an injury of the spinal nerve roots but these lesions and are not detectable by peripheral sNCV measures (e.g. from the arms and legs). The automated sNCT CPT or PTT evaluation is sensitive to an impairment of sensory nerve function occurring anywhere between the nerve test site and the cortex. Studies have documented the ability of the sNCT CPT and/or PTT measures to evaluate the sensory abnormalities resulting from a radiculopathy as well as the loss of sensory nerve function resulting from spinal pathology, spinal anesthesia and analgesia.

The CPT evaluation may also be a test to be considered instead of the MRI for certain patients, not only because of the financial savings, but primarily to help improve the quality of patient care. According to the 1994 publication by Jensen, et al from the New England Journal of Medicine, (331:69-73) titled "Magnetic resonance imaging of the lumbar spine in people without back pain" and in more recent publications, the MRI evaluation has a high number of false positive findings yielding erroneous diagnostic
interpretations (disc herniations without symptoms). The MRI is a structural and not a functional test - and as such is insensitive to inflammatory conditions such as disc irritation or nerve root irritation which may result in sensory dysfunction within a dermatomal distribution but not effect MRI imaging findings (i.e. an unremarkable or normal MRI). CPT measures have also been identified as superior to intraoperative neurophysiological measures of spinal cord sensory function.

What are the indications for conducting the CPT examination?

The CPT test is indicated in any patient with a presumptive diagnosis of sensory nerve dysfunction. Peripheral sensory nerve impairments have four major categories: poly-neuropathy, radiculopathy, compressive neuropathy and focal nerve lesions. The CPT test is used to identify and localize areas of abnormal function, to determine the severity of the abnormality and to aid in diagnosis, prognosis, guiding and evaluating treatment. The following is a partial list of those conditions associated with neuropathology that may be evaluated by the CPT evaluation:

Metabolic: Uremic, hepatic, thyroid, diabetic and other endocrine disorders.
Compressive or Traumatic: Carpal and tarsal tunnel syndrome, thoracic outlet syndrome, brachial plexopathy, radiculopathy, vibration neuropathy and focal nerve lesions.
Toxic: Ethanol, heavy metals (such as lead), arsenic, acrylamide, organophosphate (pesticides), PCBs, trichloroethane, organic solvents and antineoplastic chemotherapeutic agents.
Acquired: HIV, Lyme disease, Hansen’s disease (leprosy), post herpetic neuralgia.
Hereditary and Others: Charcot Marie Tooth, Laurence Moon Bidal, Freidricks Ataxia, Multiple Sclerosis, Vitamin B12 deficiency, reflex sympathetic dystrophy (RSD) or Complex Regional Pain Syndrome (CRPS), neurona, regeneration, ruling-out psychogenic (hysterical sensory loss), neuropathy of cancer, COPD associated neuropathy, high altitude neuropathy, syringomyelia, cerebral vascular accident related sensory loss, and immune mediated sensory dysfunction (e.g. neuropathy associated with Anti-Myelin-Associated Glycoprotein Antibodies).

How much training is required to be able to properly perform the procedure?

Technicians can be trained in a few hours by a qualified sales representative for both clinical and laboratory animal applications. Manufacturer’s technical certification courses are also available. A manual detailing the examination procedure is included with each device.

What type of training is required to interpret the procedure?

Any licensed physician can interpret the results of the sNCT/CPT test procedure by using the data generated by the NEUVAL® CPT data analysis software in conjunction with other clinical data and impressions of the patient. The location and distribution of the sNCT/CPT or PTT abnormalities on the patient (if present) can help the physician corroborate a diagnosis made based on history and physical examination findings. A manufacturer’s clinical certification course is offered to physicians and provides training by a certified physician on the clinical use of the sNCT/CPT test and the
interpretation of the results of the test.

How are the examination results interpreted?

The NEUVAL® CPT evaluation and database software, included with each CPT device, evaluates and stores a patient's CPT values and generates a report detailing the condition of the nerves tested. These evaluations are based upon comparisons with standardized ranges of healthy CPT values and ratios included in the software. Both the CPT values and their ratios are considered when determining the degree of sensory nerve impairment and both contribute to the overall neurological diagnosis. The data analysis may include a determination of hyperesthetic and/or hypoesthetic conditions. Normative data is provided for more than thirty different test sites. All normative CPT values employed are either published in peer reviewed journals or available for review. They are not confidential.

Most importantly, as with any neuro-diagnostic test, a clinician's interpretation including a clinical correlation is essential and necessary for diagnostic purposes.

Is the CPT test an objective or subjective procedure?

The Neurometer® CPT examination is an objective test for quantifying the functional integrity of sensory nerve fibers. The automated double-blinded CPT procedure is based on the same objective paradigm used for evaluating hearing and vision. These methodologies are widely used, well characterized, and legally recognized.

Where is additional information?

Extensive information and reference material is available from www.neurotron.com the following is a partial list: Utilization Guidelines, Comprehensive Bibliography, Governmental, Insurance and Legal Citations, Evaluation of sNCT Measures, Differential Diagnosis and Mapping of Sensory Neuropathy, Neurometer® sNCT/CPT Electrodiagnostic Evaluation Neuroselectivity and Hyperesthesia, Unmyelinated C-fiber Polyneuropathy in Endocrinology, Animal Research Using Neurometer® Neurodiagnostic Neuroselective Sensory Nerve Evaluation as well as generic Investigational Review Board applications.
Neurometer® CPT® Multi Modal Evaluation of the Peripheral Nerve

Neurometer® CPT® electrodiagnostic sensory nerve tests selectively evaluate the functioning of all major subpopulations of sensory nerve fibers comprising more than 90% of the typical peripheral sensory nerve. Traditional electrodiagnostic tests (sNCV, SSEP) evaluate less than 10% of the fibers i.e. Aδ only.

Fiber Diameter Spectra Cutaneous Nerve

![Fiber Diameter Spectra Cutaneous Nerve](image)

CPT/sNCT Sensitivity Comparison to Traditional (sNCV) Procedure

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<td><strong>Small Fiber Neuropathy</strong>&lt;sup&gt;(326, 392)&lt;/sup&gt;</td>
<td>16</td>
<td>sNCV 0% CPT 50%</td>
<td>&lt;0.001</td>
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<td><strong>Nerve Regeneration</strong>&lt;sup&gt;(42)&lt;/sup&gt;</td>
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<td>sNCV 0% CPT 100%</td>
<td>&lt;0.001</td>
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<td><strong>Metabolic Polyneuropathy</strong>&lt;sup&gt;(150)&lt;/sup&gt;</td>
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<td>sNCV 79% CPT 92%</td>
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<td>Stage 3</td>
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<td>sNCV 0% CPT 77%</td>
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<th>Diabetic Neuropathy&lt;sup&gt;(319)&lt;/sup&gt; *</th>
<th>71</th>
<th>Correlation Significance</th>
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<td>“Abnormal” vs. “Very Abnormal”</td>
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<td>sNCV ns</td>
<td>p&lt;0.01</td>
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</table>

* Discrimination of severity based on Symptom & Physical Scores examinations
Comparative Analgesic and Mental Effects of Increasing Plasma Concentrations of Dexmedetomidine and Alfentanil in Humans

Angst, S. M, Ramaswamy, B., Davies, M.F.
Stanford University Medical Center, Stanford, CA, USA

“BACKGROUND
In animals, systemic and intrathecal administration of the α2-adrenergic receptor agonist dexmedetomidine results in robust antinociceptive effects in models of heat pain. In humans, systemically administered dexmedetomidine is approved for sedating patients in the intensive care unit. However, whether systemic administration of dexmedetomidine in humans produces significant analgesia at doses causing sedation but not unconsciousness remains controversial.

METHODS
This study in human volunteers used a placebo controlled, double-blind, and randomized design to examine whether dexmedetomidine at doses causing mild to severe sedation produces analgesia in experimental models of heat and electrical pain. Results were compared to the effects of the μ-opioid receptor agonist alfentanil. A computer-controlled infusion provided four median step-up plasma concentrations of dexmedetomidine (0.09, 0.24, 0.54, and 1.23 ng/ml) and alfentanil (13.4, 33.8, 67.8, and 126.1 ng/ml).

RESULTS
Sedative and cognitive effects of dexmedetomidine were dose-dependent, resulting in a median sedation score of 95 of 100 and slowing of cognitive speed (reaction time, trailmaking test) by a factor of about two at the highest plasma concentration. Dexmedetomidine did not attenuate heat or electrical pain. Alfentanil caused severe sedation (median sedation score 88 of 100) and slowed cognitive speed by a factor of approximately 1.4 at the highest plasma concentration. Alfentanil attenuated heat and electrical pain dose dependently.

CONCLUSION
This study documents that systemic dexmedetomidine lacks analgesic efficacy for heat and electrical pain at doses causing mild to severe sedation. These results provide further evidence suggesting that systemic administration of dexmedetomidine lacks broad analgesic activity in models of acute pain at doses not rendering humans unconscious.”
Influence of Topical Capsaicin on Facial Sensitivity in Response to Experimental Pain

Lee, Y-S., Kho, H-S., Kim, Y-K., Chung, S-C.
Department of Oral Medicine and Oral Diagnosis
College of Dentistry and Dental Research Institute
Seoul National University, Seoul Korea

ABSTRACT

“Capsaicin, the pungent component of the red pepper, has been used as an analgesic in a variety of pain conditions, but sensory impairment after long-term treatment has been concerned. This study investigated the influence of topical capsaicin on various types of sensations including pain in the facial areas innervated by the mental nerve, and also evaluated whether the measurement of cutaneous current perception threshold (CPT) is reliable for the quantification of sensory change following capsaicin application. Twenty healthy subjects were given topical capsaicin cream (0.075%), which was applied to the mental area unilaterally, four times daily for 2 weeks. Burning sensation after capsaicin application gradually decreased with repeated applications. Repeated topical capsaicin resulted in reduced sensation to mechanical, heat and cold pain without changing non-painful tactile sensation. It also resulted in increased CPTs at 5 Hz and 250 Hz stimuli but no change in the CPTs at 2000 Hz from the first evaluation after capsaicin treatment and throughout the treatment period. This study demonstrated that topical capsaicin treatment for the management of chronic localized pain can be safely applied to the face without affecting non-painful normal sensations, and that CPT testing is a clinically useful tool for the quantification of sensory changes following capsaicin application.”
Neuroselective Sensory Electrodiagnostic Evaluation of 4% Liposomal Topical Lidocaine

Julia C. Finkel, M.D. *, Charles I. Yang, M.D. **, Jessica L. Yarvitz, B.S.N. *
Kantilal M. Patel, Ph.D. **
Departments of Anesthesiology * and Department of Pediatrics **
Children’s National Medical Center. and George Washington University, Washington, D.C.

Abstract

“We used a neuroselective transcutaneous electrical stimulus to determine the onset time of cutaneous anesthesia with 4% Liposomal Lidocaine under occluded and non occluded conditions. The pain tolerance threshold (PTT) was used to atraumatically evaluate nociception. Twenty adult volunteers had liposomal lidocaine applied to the volar surface of each forearm for durations ranging from 0 through 30 min(at 5 min intervals) under occluded and nonoccluded conditions. The PTT was determined using three different frequencies (2000Hz, 250Hz, 5Hz) stimulating the A beta, A delta, and C fibers respectively. The time to reach the Maximum PTT achieved defined the anesthetic onset time for each frequency. A differential onset of cutaneous anesthesia among the three frequencies was clearly demonstrated, however there was no significant difference in onset time between occluded and non occluded conditions. Blockade of C fiber transmission occurred significantly earlier than that of A delta (P=0.029), which occurred earlier than that of A beta (P = 0.001 as determined using the Wilcoxon’s signed rank test. We conclude that a mean onset time of approximately 4 ± 2min for blockade of C fiber transmission and 6 ± 4 min for A delta transmissions suggests the painful stimuli such as venipuncture may be attenuated as early as 7 min.”
The Pharmacodynamics of Orally Administered Sustained Release Hydromorphone in Humans

Angst, M.S., Drover, D.R., Lötsch, J., Ramaswamy, B., Naidu, S., Wada, D.R., Stanski, D.R.
Stanford University Medical Center, Stanford, CA, U.S.A.

Background

"The disposition kinetics of hydromorphone generally mandates 4-hourly oral administration of the conventional immediate release tablet to provide sustained pain relief. However, multiple daily dosing may result in decreased compliance and more pronounced pain. This trial examined time course and magnitude of analgesia to experimental pain after administration of sustained release hydromorphone as compared with that following immediate release hydromorphone or placebo."

Methods

"Using a 4x4 Latin square double-blind design 12 subjects were randomized to receive a single dose of 8, 16, and 32 mg sustained release hydromorphone and placebo. The same subjects had received 8 mg immediate release hydromorphone prior to this study. Using an electrical experimental pain paradigm analgesic effects were assessed for up to 30 hours after administration and venous hydromorphone plasma concentrations were measured at corresponding times."

Results

"The hydromorphone plasma concentration peaked significantly later (12.0 h [12.0-18.0] versus 0.8 h [0.8-1.0]; median and inter-quartile range) but was maintained significantly longer at greater than 50% of peak concentration (22.7 ± 8.2 h versus 1.1 ± 0.7 h: mean ± SD) after sustained than after immediate release hydromorphone. Similarly, sustained release hydromorphone produced analgesic effects that peaked significantly later (9.0 h [9.0-12.0] versus 1.5 h [1.0-2.0]) but were maintained significantly longer at greater than 50% of peak analgesic effect (13.3 ± 6.3 h vs 3.6 ± 1.7 h). A significant relationship between the hydromorphone plasma concentration and the analgesic effect on supra-threshold nociceptive stimuli existed."

Conclusion

"A single oral dose of a new sustained release formulation of hydromorphone provided analgesia to experimental pain beyond 24 hours of its administration."

* Electrodiagnostic sensory test device: Neurometer® CPT/C
Introduction

“The purpose of this study is to evaluate both painless and painful sensory transmission in patients with Complex Regional Pain Syndrome (CRPS) using the automated electrodiagnostic sensory Nerve Conduction Threshold (sNCT) test. This test generates reliable, painless Current Perception Threshold (CPT) and atraumatic Pain Tolerance Threshold (PTT) measures.”

Methods

“Standardized CPT and PTT measures using constant alternating current sinusoid waveform stimulus at three different frequencies 5 Hz, 250 Hz and 2 kHz (Neurometer® CPT/C Neurotron, Inc. Baltimore, MD) were obtained from CRPS subjects at a distal phalange of the affected extremity and at an ipsilateral asymptomatic control site. Matched sites were tested on healthy subjects. Detection sensitivities for an abnormal PTT and CPT test was calculated based on specificity of 90% as determined from data obtained from healthy controls. A Spearman rank correlation was used to test for a significant association between presence of allodynia and an abnormal PTT or CPT at any frequency tested.”

Results

“Thirty-six CRPS subjects and fifty-seven healthy controls were tested. The highest detection sensitivity of the PTT test from symptomatic test sites was 63% for the finger and 71% for the toe. PTT abnormalities were also detected, to a lesser degree, at the asymptomatic control site (41% finger control site, 16% toe control site). The highest CPT detection sensitivity at the symptomatic site was 37% for the finger site and 53% for the toe site. CPT abnormalities were also detected at the asymptomatic control site (29% finger control site, 37% toe control site). Eighty-six percent of the CRPS subjects had either a PTT or CPT abnormality at any frequency at the symptomatic site. There was a significant correlation between presence of allodynia and presence of an abnormal CPT and PTT, respectively (p<0.01). The correlation coefficient was lower for CPT than for PTT, i.e. 0.34 versus 0.6 for the finger and 0.48 versus 0.67 for the toe, respectively.”

Discussion

“CRPS patients displayed a greater number of abnormal PTT measures than abnormal CPT measures. Assessing PTT may become a useful electrodiagnostic quantitative sensory test for diagnosing and following the course of neuropathic pain conditions.”
Comparison of different quantitative sensory testing methods during remifentanil infusion in volunteers

B. Gustorff¹*, K. H. Hoerauf¹, P. Lierz² and H. G. Kress¹

¹Department of Anaesthesia and General Intensive Care Medicine (B), University of Vienna, Währinger-Gürtel 18-20, A-1090 Vienna, Austria.
²Department of Anaesthesia and Intensive Care, Marienkrankenhaus, Soest, Germany

Background

“The aim of this study was to compare thermal and current sensory testing stimuli with respect to opioid responsiveness.”

Methods

“Eighteen healthy volunteers were randomized in a placebo-controlled, double-blind crossover study to receive an infusion of remifentanil 0.08 µg kg⁻¹ min⁻¹ or saline for 40 min. Test procedures included determination of pain perception thresholds (PPT) and pain tolerance thresholds (PPT) to heat, cold, and current at 5, 250 and 2000 Hz, at baseline and at the end of the infusion.”

Results

“Both current at 5 Hz (PPT 3.69 (SD 2.48) mA vs 2.01 (1.52) mA; PTT 6.42 (2.79) mA vs 3.63 (2.31) mA: P<0.001) and 250 Hz (PPT 4.31 (2.42) mA vs 2.89 (1.57) mA; PTT 7.08 (2.68) mA vs 4.81 (2.42) mA: P<0.001) and heat (PPT 47.4 (2.7)°C vs 45.2 (3)°C; PTT 51.1 (1.8)°C vs 49.7 (1.8)°C; P<0.05) detected a significant analgesic effect of remifentanil compared with placebo. No analgesic effect was shown on cold or current at 2000 Hz. The magnitude of responsiveness of current stimuli at 5 Hz and 250 Hz was superior to heat stimuli.”

Conclusion

“Both current (5 and 250 Hz) and heat sensory testing detected a significant analgesic effect of a remifentanil infusion compared with saline. There was more response to current testing.”
Quantitative Assessment of Differential Sensory Nerve Block After Lidocaine Spinal Anesthesia

Liu, S., Kopacz, D.J., Carpenter, R.L.  Department of Anesthesiology, Virginia Mason Medical Center, Seattle, WA

Background

"Recent technology allows for quantitative and selective measurement of A beta (Aβ), A delta (Aδ), and C fiber nerve transmission. To gain further insight into the physiology of differential block after lidocaine spinal anesthesia, we quantitatively measured function of these different fibers over time and correlated these measurements with regression of anesthesia to pinprick, touch, cold, and tolerance of tetanic electrical current (equivalent to surgical incision)."

Methods

"Six volunteers received lidocaine spinal anesthesia with 50 mg of lidocaine (5% in dextrose). Cutaneous current perception thresholds (CPT) at 2000 Hz, 250 Hz, and 5 Hz which stimulate Aβ, Aδ, and C fibers, respectively, were determined at L2-L3 (medial aspect above knee) prior to and then every 10 minutes after spinal anesthesia. Dermatomal levels to pinprick, touch, and cold were assessed every 5 minutes after spinal anesthesia. Tolerance to tetanic electrical stimulus, equivalent to surgical incision, was assessed at L2-L3 every 10 minutes after spinal anesthesia."

Results

"Differential block was demonstrated by the sequential return of sensation to touch, pinprick, and cold at L2-L3. Recovery of function of Aβ, Aδ, and C fibers correlated with return of sensation to touch (R²=0.7, p=0.03), pinprick (R²=0.75, p=0.02), and cold (R²=0.67, p=0.04) respectively. Loss of tolerance of surgical anesthesia corresponded to return of Aβ CPTs to baseline, whereas CPTs for Aδ and C fibers were still elevated above baseline (p=0.025)."

Conclusions

"Differential sensory block during spinal anesthesia is due to different recovery profiles of Aβ, Aδ and C fibers. Return of Aβ CPTs to baseline correlated with duration of surgical anesthesia as assessed with an electrical stimulation model."
Effects of electrical stimulation at different frequencies on perception and pain in human volunteers: Epidural versus intravenous administration of fentanyl

Liu, S.S., Gerancher, J.C., Bainton, B.G., Kopacz, D.J. and Carpenter, R.L.
Virginia Mason Medical Center, Seattle, WA

Abstract

"This study was performed to determine whether epidural fentanyl produced segmental sensory changes to electrical stimulation at different frequencies. Eight healthy volunteers received fentanyl 1 µg/kg both intravenously and epidurally in a randomized, double-blind, cross-over fashion. Perception thresholds and amount of current required to elicit moderate pain (pain stimulation) at 5, 250, and 2000 Hz stimulation were measured at ipsilateral dermatomes C2 and L2 at 0, 5, 15, 30, 45, and 60 minutes after injection. Perceptions to 5, 250, and 2000 Hz stimulation were unaffected by either intravenous or epidural fentanyl (p>0.08). Intravenous fentanyl increased pain stimulation at both 5 and 250 Hz at both dermatomes (p<0.004) and thus did not produce segmental analgesia. In contrast, epidural fentanyl increased pain stimulation only at the L2 dermatome and only at 5 Hz (p=0.005). We conclude that an epidural bolus of fentanyl results in segmental spinal analgesia to transcutaneous electrical stimulation only at specific frequencies. Furthermore, pain produced by stimulation at 5 Hz may have a different pharmacology than pain produced by 250 Hz stimulation."
Computer Controlled Lidocaine Infusion for the Evaluation of Neuropathic Pain after Peripheral Nerve Injury


Background

"Systemic lidocaine has been reported to be effective in treating several neuropathic pain syndromes. Few reports relate plasma lidocaine concentration to analgesia and the available studies have been complicated by labile plasma lidocaine concentrations. We utilized a computer controlled infusion pump (CCIP) to target and maintain stable plasma lidocaine concentrations and study the effect of intravenous lidocaine on 1) pain sources, 2) current perception thresholds, 3) side effects, and 4) pain distribution in patients suffering from peripheral nerve injury pain."

Methods

"This study utilized a randomized double-blind placebo controlled design. Eleven patients suffering from neuropathic pain after a peripheral nerve injury received both a lidocaine and saline infusion in separate study sessions. The order of the study sessions was randomized and separated from each other by one week. The CCIP was programmed to target plasma lidocaine concentration of 0.5, 1, 1.5, 2, and 2.5 \( \mu \text{g/ml} \), each held for 10 minutes. Pain scores and pain distribution was assessed in the painful area, and electrical current perception thresholds (CPT) of the ring finger were measured using a cutaneous perception threshold Neurometer (Neurometer CPT, Neurotron, Inc., Baltimore, MD). Plasma lidocaine concentrations were measured at 4 and 9 minutes after each step increase in infusion and correlated with the observed effects."

Results

"Saline infusion had no effect. However, with lidocaine there was a significant plasma concentration dependent decrease in pain scores starting at 1.5 \( \mu \text{g/ml} \). This effect typically corresponded with a decrease in the size of the receptive field to which the pain was referred. For the electrical stimulus, there was no significant effect on cutaneous perception at 2000 Hz stimulation at the highest concentration examined, however, there was a significant increase in thresholds at 250 Hz (starting at 1.5 \( \mu \text{g/ml} \)) and 5 Hz (starting at 1.0 \( \mu \text{g/ml} \)) stimulation. There were no serious side effects."

Discussion

"The computer controlled delivery of intravenous lidocaine results in relatively stable plasma concentrations which allows a more thorough evaluation of the relationship between plasma concentration and patient response."
Quantitative Assessment of Differential Sensory Blockade After Lumbar Epidural Lidocaine

Wallace, M.S., 1  Tay, B., 2  Irving, G. 3

1  Assistant Clinical Professor, 2  Pain Fellow, 3  Associate Clinical Professor
University of Texas, Houston Medical School, Dept. of Anesthesia

Introduction

"Differential epidural blockade is frequently used in the evaluation of chronic pain syndromes, however, it has been met with much controversy. 1 With the crude sensory measurements used in the human studies, it is difficult to determine which fibers are blocked. Recent technological advances allow for the quantitative measurement of the functional integrity of both large and small diameter sensory fibers using a Current Perception Threshold (CPT) quantitative sensory testing device. 2,3 We used this device to evaluate the existence of a differential blockade after the administration of epidural lidocaine."

Methods

"8 patients suffering from lower abdominal (1 subject) or lower extremity pain (7 subjects) received both lumbar epidural saline (control) and lidocaine...Serial CPTs and sensation to touch, pinprick, and cold at the following sites on the right side were measured at the: 1) mastoid process, 2) umbilicus, 3) anterior knee, 4) great toe; cephalad anesthetic level to touch, pinprick, and cold; and pain scores using a visual analog scale."

Results

"The administration of saline epidurally had no effect on any measures. The administration of 10 milliliters of 2% plain lidocaine epidurally caused an increase in all CPTs at the umbilicus and the knee reaching a statistical significance at 5 Hz for the umbilicus only. There was no effect on CPTs or sensory measures seen at the mastoid process. There was a significant decrease in touch, pinprick, and cold sensation at the umbilicus and knee."

Conclusion

"After epidural lidocaine, it appears possible to demonstrate a differential neural blockade utilizing a Current Perception Threshold device whereas it is not possible with crude sensory measurements. Further studies may allow for better utilization of the CPT device in the management of the pain patient."
Autonomic and peripheral neuropathy in primary biliary cirrhosis: evidence of small sensory fibre damage and prolongation of the QT interval

Kempler, P., Váradi, A., Kádár, É., Szalay, F.
I. Dept. of Medicine, Semmelweis University, Budapest, Hungary

Excerpt

"Hendrickse et. al. found abnormalities of autonomic and peripheral nerve function in primary biliary cirrhosis (PBC). We confirm their findings and report on small sensory fibre damage and prolongation of QT interval in PBC. Thirteen patients were examined (mean age, 60.3; range, 41-73 years; all females) with clinical, biochemical and histological evidence of PBC. Controls (C) were 14 healthy women (mean age, 55.9; range, 41-68 years). The five standard tests of cardiovascular autonomic function - heart rate response to deep breath (HRDB), standing (30/15 ratio) and Valsalva manoeuvre as well as blood pressure responses to standing and sustained handgrip - were evaluated. Corrected QT interval (QTc) were determined with Bazett's formula. Sensory neuropathy was assessed by the Neurometer® CPT (Neurotron, Incorporated, Baltimore, USA). This method provides a simple, non-invasive and quantitative measure of peripheral sensory nerve function. Detection thresholds for constant current electric sine wave stimulation were measured at three different frequencies (2 kHz, 250 Hz, 5 Hz). Digital median and peroneal nerves were studied."

"Significant decrease of autonomic function was found in four reflex tests compared to controls (p < 0.01 for HRDB, 30/15 ratio and sustained handgrip, p < 0.01 for Valsalva ratio). Autonomic dysfunction (with one or more abnormal tests) was found in 77% (10/13) patients, similarly to our previous findings. Two patients had one, 5 had two and 3 had three abnormal tests. Current perception threshold (CPT) was significantly higher in PBC at 2 kHz at both sites (p < 0.01 for median and p < 0.05 for peroneal nerves) and at 5 Hz for peroneal nerve (p < 0.05). 9/13 patients (69%) had abnormal CPT values. Five patients had one abnormal parameter while 2, 3, 4 and 5 abnormal parameters were observed equally in one patient. Two kHz CPT values correlate significantly with tests of large fibre function and 5 Hz detection thresholds correlate significantly with tests of small fiber function. Thus, our data confirm the findings of Hendrickse et. al. in respect of large fibre damage and provides further evidence of small sensory fibre dysfunction in PBC. Evaluation of current perception threshold by the Neurometer® CPT may be a simple and comprehensive way of assessing even early abnormalities of peripheral sensory nerve function in patients with PBC."
Baroreflex Sensitivity and Heart-rate Variability in Insulin-dependent Diabetics with Polyneuropathy

Csaba Lengyel, Tamás Török, Tamás Várkonyi, Péter Kempler, László Rudas
First Department of Medicine and Medical Intensive Care Unit, Albert Szent-Györgyi Medical University, H-6701 Szeged, POB 459, Hungary; and First Department of Medicine, Semmelweis University, Budapest

Introduction

“The ATRAMI investigators (February 14, P 478) show that measurement of baroreceptor reflex sensitivity (BRS) is an appropriate way to identify patients after myocardial infarction who were at a high risk of cardiac death or a non-fatal cardiac arrest because of documented ventricular fibrillation. Autonomic imbalance, however, may be associated with an increased risk of sudden death, even without myocardial infarction.”

Methods

“We analyzed the BRS and heart-rate variability (SDNN: standard deviation of normal-to-normal beats) in the resting supine position and after standing up in patients with long-standing insulin-dependent diabetes mellitus (IDDM) with autonomic and sensory neuropathy.”

“We enrolled 12 patients (six women, six men, mean age 47.8 [SD 15.9] years, duration of IDDM 26.8 [13.4] years...Peripheral sensory nerve function was characterized by current perception thresholds measured by a neuro-selective diagnostic stimulator on the peroneal and median nerves, which permits transcutaneous testing at three sinusoidal frequencies (2000, 250, and 5 Hz) of electrical stimulus.”

Results/Conclusion

<table>
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<th>Neuropathy Indices (1.0 = 1.00 mAmpere)</th>
<th>IDDM Patients</th>
<th>Controls</th>
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<td><strong>Median Nerve</strong></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
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<td>250 Hz</td>
<td>3.3 (3.5)</td>
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<td>5 Hz</td>
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<td><strong>Peroneal Nerve</strong></td>
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<td>Mean (SD)</td>
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<td>5 Hz</td>
<td>3.0 (3.3)</td>
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</table>

“...the IDDM patients with polyneuropathy displayed a severely impaired cardiovascular adaptation mechanism. The decreases in heart-rate variability and BRS probably contribute to the poor prognosis of acute myocardial infarction in diabetic patients.”
The Neurometer: Validation and Comparison with Conventional Tests for Diabetic Neuropathy

Masson, E.A., Boulton, A.J.M.
Dept. of Medicine, Manchester Royal Infirmary, Manchester, UK

Abstract

“The Neurometer® CPT is a portable constant current sine wave stimulator, which has recently been advocated for the Quantification of peripheral nerve dysfunction by the measurement of detection thresholds for constant current stimulation. Stimuli are applied through surface electrodes at three frequencies and a forced choice method is used to determine the minimum amplitude of detection. The possible application of the Neurometer® CPT to the diagnosis and measurement of diabetic neuropathy was evaluated. The preliminary Neurometry results in comparison to those of conventional nerve testing techniques, including thermal and vibration detection thresholds, are discussed. It appears that the device may be a useful screening instrument which could give a fairly comprehensive idea of the functional integrity of different nerve fibre populations, and a full assessment takes only 10 to 15 min, in contrast to conventional alternatives.”

Results

"...Comparison of the Neurometer® CPT with conventional tests of peripheral nerve function, showed significant correlations between current perception threshold for 2 kHz stimulation and measures of large fibre function... Low frequency current perception threshold (5 Hz) correlated significantly with a measure of small fibre function..."

Discussion

"The Neurometer® CPT certainly appears to provide a quick, simple, and pain free non-invasive method of assessing peripheral nerve function...The low variability achieved with the Neurometer® CPT, however, suggests that it may be superior to many conventional tests such as biothesiometry. Neurometry...requires less time than measuring thermal thresholds and electrophysiological assessments. In addition it is not complex, and can probably be operated reliably by inexperienced personnel."
Current Perception Thresholds: A New Method for the Assessment of Peripheral Sensory Neuropathy in Diabetes Mellitus

Ken-ichi Suzuki, M.D., Yien Chung, M.D. Yuka Kobayashi, M.D. & Yosio Goto, M.D.
Department of Internal Medicine, Tohoku Kosei-Nenkin Hospital
Sendai, Japan

Abstract

“The Neurometer® CPT is a portable constant current sine wave stimulator, which has recently been advocated for the Quantification of peripheral nerve dysfunction by the measurement of detection thresholds for constant current stimulation. In order to assess its potential usefulness in the Quantification of diabetic neuropathy, detection thresholds for constant current electric sine wave stimulation were measured at three different frequencies in 29 healthy control subjects and 87 diabetic patients. Significant differences in CPTs of three different frequencies (5Hz, 250Hz, 2000Hz) were found in the diabetic group as compared with those in the healthy control group. We have carried out the first independent assessment of the device in the assessment of diabetic peripheral neuropathy, with comparative data from conventional electrophysiological and objective sensory testing techniques (motor nerve conduction velocity (MCV), sensory nerve conduction velocity (SCV), F-latency, and thermal detection thresholds (TDT)). Non-parametric correlation tests demonstrated a significant relationship between high frequency CPT and tests of large fiber function (250 Hz CPT vs median SCV, r=0.3, p<0.05; 250Hz CPT vs F-latency, r=0.41, p<0.01; 2000Hz CPT vs F-latency, r=0.32, p<0.01). Low frequency CPT correlated with TDT, a measure of small fiber function (r=0.42, p<0.05). Moreover, CPTs of three frequencies were correlated with duration of diabetes. This means that peripheral nerve dysfunction, including small fiber dysfunction and large fiber dysfunction, may progress synchronously with duration. It is concluded that the device may be a simple and comprehensive way of assessing peripheral nerve function and that it provides information about different nerve fiber types.”
A Comparison of Nerve Conduction Velocities and Current Perception Thresholds as Correlates of Clinical Severity of Diabetic Sensory Neuropathy

M.S. Rendell, et. al.
Creighton Diabetes Center, Omaha, NE

Abstract

"Nerve conduction velocities (NCVs) are the standard measurements used to confirm the presence or absence of diabetic neuropathy. NCVs were contrasted with the newer technique of measurement of alternating current perception thresholds (CPTs) in assessing the quantitative level of correlation with severity of diabetic sensory neuropathy. A very detailed, scored neurological history (symptoms) and physical examination, emphasizing sensory assessment, was conducted on 71 individuals with diabetic neuropathy of varying degrees of severity. Sensory and motor NCVs and CPTs at 5, 250, and 2000 Hz of the upper and lower extremities were determined for these individuals. In addition, vibration thresholds (VTs) were measured as a third modality. Twenty eight individuals underwent repeated evaluations at 2, 6, 10 and 12 months after the initial procedures. Using the results of 169 complete evaluations, correlations were determined between physical scores (PS) and symptom scores (SS) and NCVs. NCV correlations with the SS were weaker than with the PS. The strongest of the correlations were found between the PS and motor NCVs of the median nerve (rho=0.29) and the tibial nerve (rho=0.38). Normal NCVs were present in the face of very significant historical and physical abnormality. Correlations of the SS and PS with both VTs and CPTs were higher than with the NCVs. CPTs proved the more effective as predictors of both symptomatic and physical impairment. NCVs appear to lack the resolving power necessary to evaluate subtle differences in clinical state of diabetic sensory neuropathy. The supplementary use of current perception testing may improve the quantitative assessment of this condition."
Prevalence of Hyperesthesia Detected by Current Perception Threshold Test in Subjects with Glucose Metabolic Impairments in a Community

Kiyoshi Takekuma, Fujiko Ando*, Naoakira Niino* and Hiroshi Shimokata*
Dept. of Public Health, Nagoya City University Medical School, Nagoya
*Dept. of Epidemiology, National Institute for Longevity Sciences, Obu, Japan

Objective

“Recent studies reported that hyperesthesia may be an indicator of early diabetic polyneuropathy. Using the current perception threshold (CPT) test, which stimulates peripheral sensory nerve fibers by three different frequencies (2,000, 250, and 5 Hz), we investigated the relationship between hyperesthesia and glucose metabolic impairment in a community.”

Methods

“The number of subjects, aged 40 to 79 years, was 2,074. The CPT values at each frequency were classified into three categories (hyperesthesia, normal, and hypoesthesia). Subjects were also subgrouped into three groups (normal, insulin resistance, and diabetes) according to glucose metabolic status, and those with hypoesthesia at each frequency were excluded in the analyses.”

Results

“The prevalence of hyperesthesia at 2,000, 250, and 5 Hz in male diabetic subjects were 14.1, 15.6, and 7.7%, respectively, and 22.2, 24.5, and 16.4% respectively in female diabetic subjects. In logistic regression analysis adjusted for age, females with diabetes showed a significantly high odds ratio (OR) for hyperesthesia at 2,000 Hz (OR, 2.42; 95% confidence interval (95%CI), 1.18 to 4.97) and 250 Hz (OR, 2.65:95% CI, 1.31 to 5.37). In male diabetic subjects, a significantly high odds ratio for hyperesthesia was seen at 250 Hz (OR, 2.09:95%CI, 1.07 to 4.05).”

Conclusion

“Our results suggested that hyperesthesia may emerge coupled with developing diabetes, supporting the precedent hypothesis.”
Improvement of Sensory Impairment in Patients with Peripheral Neuropathy

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Endocrine Metabolic Medical Center, Redwood City, California

Objective

“To report the findings in 27 patients with peripheral neuropathy (21 with lower extremity sensory impairment associated with diabetic peripheral neuropathy and 6 with other causes), who received treatment with monochromatic near-infrared photoenergy (890 nm) delivered by the Anodyne Therapy System (ATS).”

Method

“All enrolled patients exhibited abnormal sensory perception (either hyperesthesia or hypoesthesia based on a qualifying examination with the Neurometer CPT (current perception threshold) (baseline CPT). The patients received 10 ATS treatments (each lasting 40 minutes) during a 2-week period and then underwent CPT retesting to determine the extent of improvement of sensory impairment in myelinated and unmyelinated sensory fibers of the peroneal nerve.”

Results

“All patients obtained improvement in sensory impairment in comparison with baseline CPT measures, and 16 of the 27 patients achieved normal sensory responses in all nerve fiber subpopulations. Ten patients had been tested previously (initial CPT) and did not exhibit spontaneous improvement in sensory impairment during a mean period of 27 months before baseline CPT. After receiving the ATS Treatments, however, this group of patients showed improvement in comparison with both initial CPT results and baseline CPT.”

Conclusion

“On the basis of the data from this study, the ATS seems to be a safe and effective treatment to improve sensory impairment associated with peripheral neuropathy due to diabetes and other causes.”
Current Perception Threshold and Sympathetic Skin Response in Diabetic and Alcoholic Polyneuropathies

Oishi, M., Mochizuki, Y., Suzuki, Y., Ogawa, K. Naganuma, T., Nishijo, Y., Mizutani, T.
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Objective
“Correlation between current perception threshold and sympathetic skin response was investigated in patients with diabetic or alcoholic polyneuropathy.”

Methods
“Current perception threshold was measured using Neurometer CPT/C, and the sympathetic skin response was measured using Neuropack Σ.”

Patients
“Fourteen patients with diabetic polyneuropathy and 10 patients with alcoholic polyneuropathy were studied.”

Results
“There was a significant negative correlation between the current perception threshold to 5 Hz stimulation and the amplitude of sympathetic skin response.”
“There were no significant correlations between the nerve conduction velocity and the Current Perception Threshold or the amplitude of the Sympathetic Skin Response.”

Conclusion
“Since both current perception threshold to 5 Hz stimulation and sympathetic skin response are related to C fibers, these two are considered to be impaired concurrently in diabetic and alcoholic polyneuropathies.”
Selective activation of primary afferent fibers evaluated by sine-wave electrical stimulation

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Abstract

“Transcutaneous sine-wave stimuli at frequencies of 2000, 250 and 5 Hz (Neurometer) are thought to selectively activate Aβ, Aδ and C afferent fibers, respectively. However, there are few reports to test the selectivity of these stimuli at the cellular level. In the present study, we analyzed action potentials (APs) generated by sine-wave stimuli applied to the dorsal root in acutely isolated rat dorsal root ganglion (DRG) preparations using intracellular recordings. We also measured excitatory synaptic responses evoked by transcutaneous stimuli in substantia gelatinosa (SG) neurons of the spinal dorsal horn, which receive inputs predominantly from C and Aδ fibers, using in vivo patch-clamp recordings. In behavioral studies, escape or vocalization behavior of rats was observed with both 250 and 5 Hz stimuli at intensity of ~0.8 mA (T5/ T250), whereas with 2000 Hz stimulation, much higher intensity (2.14 mA, T2000) was required. In DRG neurons, APs were generated at T5/T250 by 2000 Hz stimulation in Aβ, by 250 Hz stimulation both in Aβ and Aδ, and by 5 Hz stimulation in all three classes of DRG neurons. However, the AP frequencies elicited in Aβ and Aδ by 5 Hz stimulation were much less than those reported previously in physiological condition. With in vivo experiments large amplitude of EPSCs in SG neurons were elicited by 250 and 5 Hz stimuli at T5/ T250. These results suggest that 2000 Hz stimulation excites selectively Aβ fibers and 5 Hz stimulation activates noxious transmission mediated mainly through C fibers. Although 250 Hz stimulation activates both Aδ and Aβ fibers, tactile sensation would not be perceived when painful sensation is produced at the same time. Therefore, 250 Hz was effective stimulus frequency for activation of Aδ fibers initiating noxious sensation. Thus, the transcutaneous sine-wave stimulation can be applied to evaluate functional changes of sensory transmission by comparing thresholds with the three stimulus frequencies.”
Dissociable Brain Activation Responses to 5-Hz Electrical Pain Stimulation: A High-field Functional Magnetic Resonance Imaging Study

Michael T. Alkire, M.D.,* Nathan S. White, B.S.,† Raymond Hsieh, M.D.,‡ Richard J. Haier, Ph.D.§
Dept. Anesthesiology, Univ. Of California Medical Center

Background
To elucidate neural correlates associated with processing of tonic aching pain, the authors used high-field (3-T) functional magnetic resonance imaging with a blocked parametric study design and characterized regional brain responses to electrical stimulation according to stimulus intensity–response functions.

Methods
Pain was induced in six male volunteers using a 5-Hz electrical stimulus applied to the right index finger. Scanning sequences involved different levels of stimulation corresponding to tingling sensation (P1), mild pain (P2), or high pain (P3). Common effects across subjects were sought using a conjunction analyses approach, as implemented in statistical parametric mapping (SPM-99).

Results
The contralateral posterior/mid insula and contralateral primary somatosensory cortex were most associated with encoding stimulus intensity because they showed a positive linear relation between blood oxygenation level–dependent signal responses and increasing stimulation intensity (P1 < P2 < P3). The contralateral secondary somatosensory cortex demonstrated a response function most consistent with a role in pain intensity encoding because it had no significant response during the innocuous condition (P1) but proportionally increased activity with increasingly painful stimulus intensities (0 < P2 < P3). Finally, a portion of the anterior cingulate cortex (area 24) and supplementary motor area 6 demonstrated a high pain–specific response (P3).

Conclusions
The use of response function modeling, conjunction analysis, and high-field imaging reveals dissociable regional responses to a tonic aching electrical pain. Most specifically, the primary somatosensory cortex and insula seem to encode stimulus intensity information, whereas the secondary somatosensory cortex encodes pain intensity information. The cingulate findings are consistent with its proposed role in processing affective–motivational aspects of pain.
Regeneration of Peripheral Nerve Gaps with a Polyglycolic Acid-Collagen Tube

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Objective
The aim of this study was to report by means of objective methods on the effectiveness of a nerve reconstruction procedure using a bioresorbable tube in two patients. Our previous successes in regenerating canine peripheral nerves across long distances (80-mm gaps) using a bioabsorbable tube have led us to investigate the value of such a tube for the treatment of human patients with chronic nerve injuries.

Methods
The device was made from a cylindrically woven polyglycolic acid tube filled with a collagen sponge. It was designed to be resorbed after nerve regeneration. Peripheral sensory nerve defects in two patients with neuroma and pain were reconstructed using this tube. Patient 1 (a 62-year-old man) had a 20-mm defect of the proper digital nerve, and Patient 2 (a 56-year-old woman) had a 65-mm defect of the superficial peroneal nerve.

Results
After surgery, both patients recovered from the unpleasant sensations and intolerable pain. In Patient 1, functional recovery was objectively identified at 2 months, and conduction velocity of the nerve recovered to 49.1 m/s. In Patient 2, conduction velocity of the nerve was determined to be 16.9 m/s at 5 months. Current perception threshold testing indicated that sensory nerve function had been recovered by 65 days after surgery.

Conclusion
This work represents the first precise clinical evaluation, performed under objective evaluation criteria, of sensory recovery achieved using a nerve tube, suggesting that the use of a polyglycolic acid-collagen tube has the potential to become a viable alternative to conventional autografting for the repair of peripheral nerve defects.
Current Perception Threshold Testing in Fabry’s Disease

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Taipei, Taiwan

Abstract

“We investigated 16 patients with Fabry’s disease (eight hemizygous men and eight heterozygous women) in one family. We used constant current perception threshold (CPT) testing, which evaluated three major sensory nerve fiber populations, to assess subjective complaints of pain and paresthesia. We also examined clinical and biochemical features and compared the values to CPTs and nerve conduction studies (NCS) in detecting the sensory neuropathy. Our results showed that CPT testing at low frequencies (5 and 250 Hz) was significantly more sensitive than at a higher frequency (2kHz) and NCS in detecting sensory neuropathy in patients with Fabry’s disease.”

Discussion

“...abnormal current perception was higher in frequencies at 5 Hz and 250 Hz (37.5% and 50%, respectively) than 2 kHz (0%). CPT testing has some advantages. It is easy to perform and can provide a multimodal diagnostic evaluation by testing three major sensory nerve fiber sub-populations within each test site. Furthermore, lower frequencies (5 Hz and 250 Hz) appear to be the most effective in detecting involvement of C and A\textsubscript{s} fibers respectively. Also, range analysis of CPT testing detected both abnormally low (hyperesthetic) and abnormally high (hypoesthetic) CPT values when compared with healthy groups. Testing is useful in subjects with Fabry’s disease who have spontaneous burning pain, paresthesia or hyperesthesia.”...”Because selective involvement of smaller myelinated and unmyelinated fibers occurs in Fabry’s disease, neurological examination and standard NCSs are usually normal. Large myelinated fiber functions are usually preserved despite the fact that median nerve compression at the wrist is more frequent in these patients than in healthy subjects. This is consistent with our findings that compound action potentials, sensory nerve action potentials, and conduction velocities were all within the reference ranges.

The sensitivity of CPTs can be enhanced by testing at multiple body sites and with all three frequencies (5, 250, and 2000 Hz) of stimuli. Testing at more than one location allows the assessment of within site and between site ratios, which are extremely sensitive to early stages of peripheral neuropathy. Combining all modalities including range and ratio analyses can significantly increase the sensitivity to detect peripheral sensory impairment in diabetic and uremic neuropathies but did not do so in our patients with Fabry’s disease”
Unmyelinated Fibre Pathology in Diabetic Patients with Mild Neuropathy

A. Veves, R. Malik, C. Townsend, S. Thompson and A.J.M. Boulton. Manchester Royal Infirmary and University of Aberdeen, UK

Abstract

"We studied the unmyelinated fibre pathology in sural nerve biopsies of 15 diabetic patients (mean age 47 years, 8 type 1, mean duration of diabetes 16.3 years) and compared them with 8 age-matched controls. The results were also related to neuropathy symptom score (NSS) and quantitative sensory testing including current perception threshold (CPT) assessed with a Neurometer. There was no difference in the mean unmyelinated fibre density between diabetic patients and controls (50511 fibres/mm² ± 6084 SE vs 56059 ± 5054) but the fibre diameter in diabetic patients was smaller (0.521 μm ± 0.034 vs 0.876 ± 0.18, p< 0.001). An increase was found in the unassociated Schwann cell profile density (36205 ± 4039 vs 8905 ± 1105, p< 0.0001), the total Schwann cell profile density (61393 ± 4472 vs 44805 ± 3616, p< 0.02) and the % of unassociated Schwann cell profile density (58.11 ± 4.25 vs 20.83 ± 3.09 p< 0.0001). A positive correlation was found between NSS and the unassociated Schwann cell profile density r = 0.55, p< 0.05), unmyelinated fibre density and CPT at 250 Hz r = 0.58, p< 0.05) and fibre diameter and CPT at 2 kHz r = 0.59, p< 0.05). No correlation existed between any unmyelinated fibre pathology and myelinated fibre density, warm thermal threshold, vibration perception threshold and electrophysiology. We conclude that unmyelinated fibre pathology with increased degeneration rates and axonal atrophy are present in patients with early neuropathy and that CPT may be of use in assessing this abnormality."
Current Perception Threshold: an Adjunctive Test for Detection of Acquired Demyelinating Polyneuropathies

Daniel L. Menkes, Michael R. Swenson and Howard W. Sander
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Abstract

"Current Perception Threshold (CPT) evaluation quantifies the sensory threshold to transcutaneous electrical stimulation of three sensory fiber subtypes: A-beta (2000 Hz), A-delta (250 Hz) and C fibers (5 Hz). Demyelinating polyneuropathies tend to affect larger myelinated fibers before smaller unmyelinated fibers, and they usually begin at the proximal nerve roots or terminal axons, due to relative weakness of the blood-nerve barrier in these locations. Axonal polyneuropathies tend to affect smaller fibers before larger fibers, in a distal to proximal gradient. Ten patients with demyelinating polyneuropathy and ten patients with axonal polyneuropathy underwent CPT testing. CPT comparisons were made with regard to side-to-side asymmetries, fiber type involvement, and the ratio of fiber types involved. The C2, lateral antebrachial cutaneous, and sural distributions were examined bilaterally. Demyelinating polyneuropathies were detected with 50% sensitivity and 100% specificity. This diagnostic sensitivity is similar to that of published criteria based upon motor nerve conduction. CPT testing can distinguish demyelinating from axonal polyneuropathies. It may be particularly helpful in patients with predominantly sensory symptoms in whom EMG/NCS data may be equivocal, or in patients who decline EMG/NCS studies."
Age and Gender Differences in Skin Sensory Threshold Assessed By Current Perception in Community-Dwelling Japanese

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Abstract

"The purpose of this study was to investigate age and gender differences in current perception thresholds (CPT) in Japanese citizens. CPT values at frequencies of 2000, 250 and 5 Hz reflect different types of peripheral sensory nerve functions. Since there have been only a limited number of reports which investigated CPT values in community-dwelling people, little is known about variations with age and gender. The present study therefore concentrated on a large population of 1632 individuals (men; 818 mean age ± standard deviation 59.4 ± 10.9, women; 814, 59.4 ± 11.1) in a Japanese community. Significant gender differences in CPT values at 250 and 5 Hz were observed. Multiple comparisons among 4 age groups (40s, 50s, 60s, and 70s) showed age-related differences in CPT values at 2000 and 250 Hz in both genders. However, age and gender interactions with reference to CPT values appeared to be different between these latter two frequencies. At 5 Hz, only men showed age-related variations. These results indicated gender differences in fiber-specific aging changes."
Neuropathy with Anti-Myelin-Associated Glycoprotein Antibodies; Quantitative Sensory Testing and Response to Intravenous Immunoglobulin

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Introduction

"The neuropathy associated with Anti-MAG antibodies is typically demyelinating and predominately sensory. The role of quantitative sensory testing in the evaluation and treatment of patients with this disease has not previously been investigated."

Objectives

"To characterize the sensory changes in neuropathy associated with Anti-MAG antibodies by QST, and determine the response to therapy with intravenous human immunoglobulins (IVIg)."

Methods

"Ten patients with Anti-MAG neuropathy were evaluated clinically and by QST, measured at the large toe at 3 stimulation frequencies: 2000 Hz, 250 Hz, and 5 Hz (Neurometer CPT/C, Neurotron, Inc.). Four of the patients were examined following a 3 month course of treatment with IVIg. Three of the four had muscle weakness in addition to the sensory loss."

Results

"All ten patients had clinical evidence for large fiber sensory loss with impairment of position and vibration. In all ten, QST values at 2000 Hz were above the normal range (613-999, mean 892; normal range 179-523, mean 322, S.D. 110). At 2 50 Hz, QST values in 8 of 10 patients were above the normal range (195-538, mean 323; normal range 44-208; mean 125; S.D. 52) At 5 Hz, QST values in 3 of 10 patients were above the normal range (59-375, mean 145; normal range 18-170; mean 73, S.D. 34). Following IVIg treatment, there was improvement of QST scores in all 4 patients who received treatment. There was also improvement in strength in the 3 treated patients who manifested weakness."

Conclusions

"QST in patients with Anti-MAG neuropathy is consistent with a characteristic pattern of large fiber sensory loss. Therapy with IVIg can improve both sensory and motor functions."
Fifth Scientific Meeting of the International Society for Magnetic Resonance in Medicine

Vancouver, April 1997.

fMRI Mapping of CNS Activations Following Noxious Heat and Electrical Stimuli

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Introduction

“We have recently demonstrated that fMRI activation in the CNS can be reproducibly measured following controlled noxious heat stimuli. Our results are in agreement with those emission tomography (PET). The aim of this study was to determine fMRI activation by electrical stimuli and compare it with activation produced by noxious heat (46C).”

Method

“Eight normal right-handed male volunteers (ago: 33.5 ± 7.7) were used for the electrical and six of the eight for noxious heat stimuli... For the electrical protocol a commercial stimulator (Neurometer, Neurotron Inc.) was modified to be MRI-comparable. Current was delivered to the dorsum of the left hand with gold plated electrodes (Goldtrode, Neurotron Inc.). Three different frequencies were used: 5, 250 and 2000Hz. Current levels (mA) necessary to produce noxious stimulus were determined by psychophysical testing before scanning and they were matched to produce a visual analog scale (VAS) score of 7 (0-10) for each frequency... The location was chosen to overlap that stimulated by the electrodes. 4 epochs of 25 s long of 46C were interleaved with 30 s of neutral (35C) temperature. For all the functional scans subjects had their eyes closed and VAS scores were obtained after each functional scan. For the noxious heat stimulus the VAS scores (0-10) were 8.3 ± 1.5 and for the electrical stimulus: 7.0 ± 0.”

Magnetic Resonance

“The fMRI protocol consists of a sagittal localizer followed by a 3D sagittal SPGR scan (1.2 mm in-plane 2.8 mm thick); 20 slices (7 mm thick) are prescribed perpendicular to the AC-PC line and covering all the frontal lobes to most of the cerebellum. This prescription is used for the following flow-compensated and High Resolution weighed scans. The actual functional scans are taken using an asymmetric spin echo sequence to be sensitive to the BOLD effect. Functional scans are prescribed on the same 20 slices (3.125 mm in-plane, TR/TE= 2.5/70) and 100 images per slice are collected.”

Results and Discussion

“We have found that noxious heat and electrical stimuli activated mostly the same CNS areas as seen in PET studies (anterior and posterior cingulate, somatosensory cortex, thalamus, insulins, frontal lobes). The noxious thermal stimuli have been traditionally accepted as a "natural stimuli", mediated by unmyelinated C-fibers. We observed similar areas of activation using electrical stimuli at 5 Hz. Adaptation to noxious heat was observed and correlates with psychophysical data (VAS scores). Furthermore, it is in agreement with time courses seen in previous studies of peripheral nociceptor adaptation to heat stimuli. However, no adaptation was observed to noxious electrical stimuli. This can be putatively explained by electrical stimuli bypassing peripheral nociceptors and directly stimulating nerve fibers.”
Clinical Neurophysiology Laboratory Tests to Assess the Nociceptive System in Humans

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Department of Neurology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

“This paper presents some currently available neurophysiological tools that are helpful in the clinical setting to evaluate and document neuropathic disturbances that may be associated with pain. The specific tests described in this discussion are quantitative sensory tests (QST’s) autonomic tests (AT’s), micro-neurography (MCNO), and laser evoked potentials (LEP’s). Quantitative sensory testing of the nociceptive system includes the thermal stimulation (TST) and current threshold (CPT) tests.”

“The Current Perception Threshold (CPT) is measured by a microprocessor-controlled electrical neurostimulator and two electrodes coated with conductive gel firmly applied to the skin within the distribution of a cutaneous nerve or dermatome. The stimulator of the commercially available equipment delivers a sinusoidal constant alternating current at three different stimulus frequencies, 5, 250, and 2,000 Hz, and intensities of 0.01 to 9.99 mA. The electrical current stimulates nerve fibers directly because the intensity is far below that required to stimulate the actual receptors in the skin. There is evidence that different stimulation frequencies activate different classes of sensory nerve fibers. The perceived sensation is different for each of the three frequencies of stimulation. MCNG studies have also shown that direct stimulation of single nerve fibers with an intraneural microelectrode results in distinct sensory perceptions. Sinusoidal percutaneous stimulation at a frequency of 5 Hz seems to activate C fibers, the small-diameter slow-conducting axons, which have higher electrical thresholds and require longer stimulus duration. The somewhat larger diameter, faster-conducting Aβ fibers respond best to stimulation at a frequency of 250 Hz. Finally, 2,000 Hz stimulation activates the large, fast conducting Aδ fibers that have the lowest electrical thresholds and require less time for activation.”

“The CPT technique has a high sensitivity (> 92%) for detecting neuropathies when the test includes multi sites and all three frequencies. The coefficient of variation for the CPT in normal subjects and in patients with neuropathy is 5 to 27.5%.”

“Comparisons with nerve conduction studies, TST, vibration threshold studies, and somatosensory evoked potential studies support the neuro-selective nature of this technique. Histopathological and pharmacological studies also provide even further support for the ability of this technique to selectively evaluate the three types of sensory nerve fibers with stimulus frequency variation.”
Current Perception Threshold (CPT) in Syringomyelia

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Abstract

"A feature characteristic of Syringomyelia is a dissociated sensory loss. Damage to the decussating pain and temperature fibers in the anterior commissure leads to a segmental dissociation of sensory disturbances with a sparing of vibration and position senses. This condition of dissociated sensory loss was used as a model to assess the neuroselectivity of the diagnostic Current Perception Threshold (CPT) evaluation."

"Seven patients diagnosed by MRI with cervical syringomyelia (18-56 yrs) were compared with 15 age matched controls (21-60 yrs). Each subject received a neurological clinical evaluation, including the assessment of sensory function. Standardized single-blind forced-choice testing methodology was employed for current perception threshold evaluations (5, 250, and 2000 Hz) that were conducted bilaterally (C6 and C8 dermatome) using a Neurometer® CPT quantitative sensory test device (Neurotron, Inc., Balto., MD)."

"The Syringomyelia subjects' thresholds were significantly elevated in comparison with the controls (5 Hz and 250 Hz (p<0.001). There was no significant difference at 2000 Hz. There was a significant correlation between the clinical assessment of dissociated sensory loss and current thresholds (r=0.73; p<0.01). Current threshold sensitivity was 100% and the specificity was 93%.

"The findings from the study demonstrate current threshold to various stimulus sinusoidal rates to effect different afferent fibers as a measure of dissociated sensory loss."

S.A. Weseley, et. al.
New York Medical College, Valhalla, NY

Abstract

"Normal peripheral nerve conduction is a marker of adequate dialytic therapy in the ESRD population. Decreasing nerve function detected by periodic testing indicates insufficient dialysis. The standard test for the quantitative evaluation of nerve integrity is the nerve conduction test (NCT). A study of 34 dialysis patients proves that the measurement of current perception threshold (CPT) is equally effective to NCT in defining peripheral nerve function (r=0.81, p<0.001). The superiority of the CPT examination is discussed."

Discussion

"Additional considerations for the evaluation of a neurometric procedure include patient compliance and clinical utility. NCT evaluations are routinely available but they are seldom employed on dialysis patients due to poor compliance secondary to its aversive stimulus. In contrast, the CPT stimulus is painless - an aspect of this methodology which is naturally welcomed by patients."

"...the ability to perform the CPT test during a dialysis session makes obtaining a neurological assessment convenient for the patient. The Neurometer device is portable and battery operated, and is therefore, electrically safe and easy to use around the dialysis equipment. These features of the CPT testing procedure will increase patient compliance for neurological assessment, while providing a clinical test that is both reliable and sensitive."
Neurological Complications in Chronic Uremia Management

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Introduction
"Polyneuropathy is one of the most common consequences of chronic renal failure... The majority of patients are asymptomatic, requiring electrophysiological testing to confirm the abnormality. Uremic polyneuropathy is a distal "dying-back" metabolic polyneuropathy... Sensory nerve conduction is apparently more sensitive than motor nerve conduction. The effect of dialysis on uremic polyneuropathy is variable, but signs and symptoms usually stabilize or improve slowly. The trend to short dialysis strategies is a cause for heightened awareness, and "under dialysis" has been an issue in morbidity and mortality among end-stage renal disease (ESRD) patients in the United States. In fact, the health of the peripheral nerve is an important quantitative longitudinal measure of dialysis adequacy in the non-diabetic uremic."

Methods
"...the neuroselective current perception threshold (CPT) routinely in our dialysis population since 1991. The CPT evaluation is conducted with a portable, battery-operated (6V) Neurometer® CPT diagnostic neurostimulator, using a standardized, single-blind, forced-choice testing methodology. CPT is measured bilaterally at the distal phalange of the great toe (peroneal nerve), which is the earliest site for detecting uremic neuropathy, as well as at both the distal phalange of the second finger (median nerve) and the fifth finger (ulnar nerve) to screen for carpal tunnel syndrome. Measurements are made at three frequencies... representing selective stimulation of Types C, B, and A afferent fibers, respectively."

Results
"...as expected, diabetics have significantly more severe neuropathy than do non-diabetics (p < 0.003). Severe neuropathy was highly predictive of 1-year mortality in non-diabetics."

Conclusions
"Monitoring simultaneously the peripheral nerve, as well as markers of somatic and visceral protein stores... should offer the possibility of developing a "risk profile" in the ESRD population."
Current Perception Threshold: Reproducibility and Comparison with Nerve Conduction in Evaluation of Carpal Tunnel Syndrome

J.J. Katims, et. al.
New York Medical College, Valhalla, NY

Abstract

"Neuro-selective current perception threshold (CPT) values quantify peripheral nerve integrity, and provide an index of adequate hemodialysis (HD). Evaluation of polyneuropathy (PN) by CPT correlates with nerve conduction testing (NCT). CPT is convenient, painless and may be performed during HD. Early detection of carpal tunnel syndrome (CTS), a complication of uremia, permits curative intervention. Utility of CPT and NCT measurements in detecting CTS in 29 stable HD patients were evaluated. Reproducibility of seven CPT determinations over 4 weeks was determined in each of 9 HD patients. The coefficient of variation for repeated 2000 Hz CPT measures was 6%. PN was detected by CPT in 92% of the patients and by NCT in 79% (r=0.79, p<0.001). In 38% of the hands there was a CPT impairment in both the median and ulnar nerves of which 25% were symptomatic for CTS. CPTs consistent with CTS (sufficiently greater impairment of the median vs ulnar nerve) were observed in 31% of the hands with combined median and ulnar nerve CPT abnormalities, and 11% were identified with CTS by NCT. The unique ability of the CPT exam to quantify hyperesthesia may account for its superior CTS detection sensitivity. These findings demonstrate that repeated CPT determinations are consistent, and are diagnostic for CTS."

Discussion

"The apparent stability of short-term repeated CPT measures, combined with its extreme sensitivity, enhances its utility for screening and evaluation of CTS and adequacy of dialysis therapy. This is especially important in uremic patients where symptoms resembling CTS often reflect polyneuropathy. Additionally, in contrast with NCT, the CPT technique employs a painless methodology that may be safely applied during dialysis therapy, facilitating compliance for repeat evaluation."
Evaluation of Sensory Function after Median Nerve Decompression in Carpal Tunnel Syndrome Using the Current Perception Threshold Test

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Abstract

“The recovery level for sensory function after carpal tunnel release for the treatment of idiopathic carpal tunnel syndrome (CTS) was assessed with the current perception threshold (CPT) test. Seventeen CTS patients (21 hands) were followed, and the CPTs at the index finger of each patient was measured preoperatively and at 1, 3, and 6 months postoperatively. After carpal tunnel release, there was significant recovery of CPT at all stimulation frequencies, indicating improvement of all sensory functions including sensations of temperature, pain, touch, and vibration.”
Current Perception Thresholds in Vibration-Induced Neuropathy

Youichi Kurozawa and Yoshiro Nasu
Department of Public Health, Tottori University and the Center of Vibration Syndrome, San-in Rosai Hospital, Yonago, Japan.

Abstract

“The authors evaluated the usefulness of Current Perception Threshold (CPT) testing for the assessment of vibration-induced neuropathy (VIN).”

Subjects and Method

“Fifty-nine men... for hand-arm vibration syndrome... officially recognized by the Japanese Ministry of Labor... On the basis of the results of a clinical neurological examination and nerve-conduction test, researchers classified the men according to sensori-neural stages of the Stockholm workshop scales. Stage 2 was defined as intermittent or persistent numbness, as well as reduced sensory perception confirmed by subjective tests for tactile, esthesiometric and vibrotactile perception. Stage 3 was defined as intermittent or persistent numbness with reduced tactile discrimination or impaired nerve conduction.”

"Twenty male volunteers... served as controls.”

Results

“Stage 1-3 groups had significantly increased CPTs at 2000 Hz, compared with the control group. There was a significantly different CPT at 250 Hz between the stage 1 and stage 3 group.”

Discussion

“Nerve-conduction velocity is dominated by the large myelinated fibers... CPT allows for quantitative and selective measurement of three different types of sensory nerve fibers. Large myelinated fibers, small myelinated fibers, and unmyelinated fibers... In the present investigation, the VIN groups had significant increases of CPT of the myelinated fibers, but not for the unmyelinated fibers.”

"Thickness of finger skin is often found in operators who use vibratory tools. This thickness may contribute to the differences in temperature thresholds. Current output of the Neurometer is maintained constantly by a feedback circuit. The CPT test, therefore, is unaffected by skin thickness. The results of our study may support the findings of previous histological findings: demyelination is found predominantly in the peripheral nerves in the hands of men exposed to hand-arm vibration.”

"We conclude, therefore, that the CPT evaluation is useful for the assessment of VIN."
Upper Extremity Cumulative Trauma Disorders (UECTDs) Screening Protocol - A Different Perspective

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Abstract

"Recent Bureau of Labor Statistics data revealed that carpal tunnel syndrome and wrist-related cases led all disabling conditions for lost days from work and prolonged recovery periods. In addition repetitive nature tasks led in "lost work days." Meat processing was recognized as a high risk focus. An UECTD management protocol was implemented in a poultry plant (Tyson Foods) of approximately 1100 employees (killing 1.3 million chickens per week). A screening protocol was implemented to identify individual workers experiencing UECTDs. Unique to the process was the emphasis on comparing the 'individual to themselves' rather than to 'normative data' (which may or may not be representative of the worker or the exposure). Screening was performed on a sequential basis to monitor changes from baseline. Screening tests included: hand strength, volumetric measures, sensory changes *, dexterity measures, joint motion, and symptom survey. To date, 1500 workers have been screened with an attendant decrease in upper extremity worker's compensation costs of over $110,000.00 per year. Only one surgery as been performed (on a worker that had fallen out of the screening process). Previously approximately 20 surgeries were performed annually. This paper will present the protocol and ongoing analysis of the population data and its implications for UECTD case management."

* Electrodiagnostic sensory testing by Current Perception Threshold (CPT) evaluation.
The Relationship Between Peripheral Nerve Function and Markers of Lead Dose

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Center for Occupational & Environmental Neurology, Johns Hopkins Hospital*

Objective
“To determine if bone lead with a half life of 25 years, is a better marker of lead dose than blood lead measures that reflect current, average or cumulative lead exposure when predicting peripheral nerve function.”

Background
“The literature reports lead neuropathy at blood lead concentrations above 60 μg/dl but no studies examine the association of peripheral nerve function and measures of cumulative lead exposure.”

Methods
“78 current smelter workers with a mean (SD) age of 44 (8.3) years and employment duration of 20 (5.6) years had Quantitative Sensory Testing** (QST) with current perception threshold using three different stimuli, 2000, 250 and 5 Hz, to the ring finger and second toe. Threshold, established by forced choice method, equaled a stimulus that was consistently felt at one intensity and not at a slightly lower intensity. We examined separate multiple linear regressions with adjustment for covariates, (age, smoking and alcohol use), to determine the contribution of four measures of lead dose: current blood lead (PbB), working lifetime-weighted average blood lead (WABL), working lifetime-integrated blood lead (IBL) and bone lead (PbBn), to QST assessment.”

Results
“Mean (SD) markers of lead dose included PbB 26 (7.1) μg/dl, WABL 42 (8.4) μg/dl, IBL 902 (301.7) μg yr/dl, and PbBn 41 (24.6) μg/(g bone mineral). We found no significant contribution of PbBn, PbB and WABL to QST with linear regression.”

Conclusions
“Bone lead is not associated with peripheral nerve function as measured with QST. Of the other markers of lead dose, IBL, a measure of cumulative lead exposure over years employed, more closely approximates the lead dose to the nerve. A dose effect relationship exists between IBL and QST. The time spent above a PbB concentration of 40μg/dl is the lead dose most critical for predicting QST.”

* This study was supported by the New Brunswick Occupational Health and Safety Commission

** QST testing performed with Neurometer® CPT/C devices
Objective Assessment of Nerve Injury after Greater Saphenous Vein Stripping

D. Akagi, H. Arita, T. Komiyama, S. Ishii, K. Shigematsu, H. Nagawa, T. Miyata

Division of Vascular Surgery, Department of Surgery, and Department of Anesthesiology, Graduate School of Medicine, The University of Tokyo, Japan

Aim
The complication of nerve injury after greater saphenous vein stripping for varicosity is subjective, and a method for objective evaluation has never been established. The aim of this study was to evaluate postoperative sensory changes by quantitative assessment of current perception threshold (CPT), and to clarify the relation between CPT and symptoms.

Patients and Methods.
Between January 2003 and August 2005, 27 limbs in 18 patients were enrolled. Quantitative sensory function was determined through CPT using a Neurometer® (Neurotron, Inc., USA), with which saphenous nerve neural fiber selective minimum sensing values against three electrical stimuli (2000, 250, 5 Hz) were measured. CPT measurements were scheduled on the day before the operation, and 2e7 days, 1, 3, and 6 months after the operation.

Results
An increase in CPT value of more than 20% or decrease to below 50% compared to the preoperative value with at least two stimuli was defined as CPT abnormality. Subjective symptoms were observed in 13 limbs in the early postoperative period, and 10 limbs showed CPT abnormality. In 6 limbs with a CPT increase over 20% with all three stimuli, neurological symptoms continued for 6 months.

Conclusions
CPT evaluation provides an objective indication of neurological symptoms in the lower limb following varicose vein surgery.
Spine 27(14):1567-1570, 2002

A Quantitative Analysis of Sensory Function in Lumbar Radiculopathy Using Current Perception Threshold Testing

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Sapporo Medical University, Sapporo Kiyota Orthopaedic Hospital, Sapporo, Japan

Study Design
“Peripheral sensory functions in patients with radiculopathy resulting from lumbar disc herniation and in control individuals were analyzed using current perception threshold testing.”

Objective
“[T]o evaluate severity as sensory disturbance quantitatively in patients with lumbar radiculopathy.”

Summary of Background Data
“Subjective evaluation of severity as sensory disturbance associated with spinal disorder using conventional methods often is difficult. Current perception threshold evaluation is a recently proposed method for studying peripheral nerve dysfunction. This is a quantitative sensory test for analyzing functions of A-beta, A-delta, and C fibers.”

Method
“In this study 48 patients with lumbar radiculopathy resulting from lumbar disc herniation were examined. The mean age of the patients was 37.9 years. All the patients had pain distribution from the compression of one lumbar nerve root (L5 or S1), and unequivocal unilateral disc herniation of the corresponding level was shown by magnetic resonance imaging. Eleven healthy volunteers were used as control subjects. Their mean age was 38.2 years. Current threshold evaluation using a Neurometer device was performed at three frequencies: 2000, 250, and 5 Hz. The stimulus sites were located on the dorsal side of the first metatarsus (the L5 dermatome) and the dorsal side of the fifth metatarsus dermatome). These sites were investigated on both legs in all the patients and control subjects. The intensity of pain was scored using a visual analog scale.”

Results
“In the control group, there were no significant differences in current perception threshold values at any frequency between the left and right legs. In the patient group, the current perception threshold values in the affected legs were significantly higher than those in the contralateral legs at all frequencies. The current perception threshold values in the affected legs in the patient group were significantly higher than those in the control subjects at 2000 and 250Hz, whereas there were no significant differences at 5 Hz. The current perception threshold values in the affected legs were significantly higher in patients with hyperesthesia than in those without hypesthesia at 2000 and 250 Hz, and in patients with severe pain than in those with less pain at 5 Hz.”

Conclusions
“Current perception threshold testing showed that the functions of A-beta, A-delta, and C fibers deteriorated in patients with radiculopathy.”
Dorsal root entry zone microcoagulation for spinal cord injury-related central pain: operative intramedullary electrophysiological guidance and clinical outcome

Scott Falci, M.D., Lavar Best, Ph.D., Rick Bayles, Ph.D.
Daniel Lammertse, M.D. and Charlotte Starnes, R.N., M.S.N.

Department of Neurosurgery, Physical Medicine and Rehabilitation and Neuroscience Laboratory, Craig Hospital, Englewood, Colorado

Object

“Surgically created lesions of the spinal cord dorsal root entry zone (DREZ) to relieve central pain after spinal cord injury (SCI) have historically resulted in modest outcomes. A review of the literature indicates that fair to good relief of pain is achieved in approximately 50% of patients when an empirical procedure is performed. This study was undertaken to determine if intramedullary electrical guidance in DREZ lesioning could improve outcomes in patients with SCI-induced central pain. Additionally, electrical data were used to determine if the spinal cord could be somatotopically mapped with regard to this pain of central origin.”

Methods

“Forty-one patients with traumatic SCI and intractable central pain underwent DREZ lesioning in which intramedullary electrical guidance was conducted. In nine patients, recording of DREZ-related spontaneous electrical hyperactivity guided the lesioning process. In 32 patients, recording of DREZ-induced evoked electrical hyperactivity during transcutaneous C-fiber stimulation (TCS) additionally guided lesioning. The follow-up period ranged from 1 to 7 years. The analyzed electrical data allowed for somatotopic mapping of the spinal cord.”

Conclusions

“Intramedullary electrical guidance of DREZ lesioning substantially improves pain outcomes in patients with traumatic SCI-induced central pain, compared with empiric technique. The best outcome occurs when DREZ-related spontaneous electrical hyperactivity and evoked hyperactivity during TCS are both used to guide the DREZ lesioning procedure. With such guidance, 100% relief of pain was achieved in 84% of patients and 50 to 100% relief of pain in 88%. Somatotopic mapping of the electrical data led to a proposed pain mechanism for below-level pain, implicating the sympathetic nervous system.”

Note: C-fiber stimulation, TCS, was obtained using a Neurometer® CPT/C device 5 Hz stimulus.
Quantitative Analysis of Sensory Functions After Lumbar Discectomy Using Current Perception Threshold Testing

Imoto, K., Takebayashi, T., Kanaya, K., Kawaguchi, S., Katahira, G., Yamashita, T.
Department of Orthopaedic Surgery, School of Medicine, Sapporo Medical University, Sapporo, Japan

Abstract

“A Neurometer device is an electrical nerve stimulator used to determine the current perception threshold (CPT) evoked by stimulating A-beta fibers at 2,000 Hz, A-delta fibers at 250 Hz and C fibers at 5 Hz. CPT evaluation is used for analyzing peripheral nerve dysfunction. In this study, the sensory disturbance of the lower-extremity was quantitatively analyzed using CPT testing before and after lumbar discectomy. In 33 patients (L4/5: 16 and L5/S: 17), as subjective evaluations, tactile sensation and leg pain were assessed before and 2 weeks after surgery. In the subjectively improved group (n = 22), significant decreases in CPT at 2,000 and 250 Hz were noted postoperatively, whereas in the unchanged group (n = 11), no significant changes in CPT at any frequencies was noted. The leg pain improved in all patients. Likewise, CPT at 5 Hz, which stimulated C fiber, decreased significantly for both improved and unchanged groups. CPT measured by a Neurometer is very useful in assessing lower-extremity sensory functions before and after surgery for lumbar disc herniation.”
Current Perception Threshold/Quantitative Sensory Testing and MRI Findings In Patients with Signs and Symptoms of Cervical or Lumbar Disc Herniations: A Correlative Study of the Neurosensory Diagnosis of Discogenic Pain

David J. BenEliyahu, Stephen V. Tartaglia, and Ronald Spinelle Selden, New York

Abstract

“Seventy consecutive patients with clinical signs and symptoms of intervertebral disc syndrome were evaluated with MRI and Current Perception Threshold Quantitative Sensory Testing (CPT/QST). CPT/QST functionally assesses a nerve’s ability to convey sensation. Of the seventy cases, fifty patients had both a positive MRI and positive CPT/QST exam. Of the 50 patients with positive MRI and CPT/QST tests, 42 were level-specific, giving CPT/QST an 84% sensitivity. McNemar’s Chi-square statistical analysis revealed good agreement for the full sample tested. In addition, the full sample had a 95% confidence interval for the probability of level-specific agreement for CPT/QST and MRI in patients with disc herniation. CPT/QST may be a useful tool to help the clinician assess the functional significance of MRI disc findings.”
The Effects of Vertebral Axial Decompression On Sensory Nerve Dysfunction In Patients with Low Back Pain and Radiculopathy

Frank Tilaro and Dennis Miskovich
The Advanced Spinal Institute, Ogden, Utah

Abstract

“Effective non-surgical decompression of the nerve root has not been available to this date. The vertebral axial decompression (VAX-D) therapeutic table has demonstrated an ability to significantly reduce intradiscal pressure to a negative 150mm Hg., allowing for disc decompression. The purpose of this study was to determine if VAX-D therapy could externally decompress the nerve root. Patients with radiculopathy and abnormal sensory function determined by the Current Perception Threshold (CPT) Neurometer® who had received VAX-D therapy were retrospectively studied. CPT readings on 22 peripheral nerves were taken before and after VAX-D therapy. Only patients with initial abnormal CPT readings, symptoms of sciatica, positive SLR, and positive imaging studies were reported on. The results after therapy were as follows: 14/22 nerves (64%) returned to normal function, 6/22 (27%) improved, 1/22 (4.5%) had no improvement and 1/22 (4.5%) showed deterioration. The average CPT grade before therapy was 6.36 and after therapy 2.09 (a score of zero indicates normal function). Overall improvement was 67% (p<0.05). Theoretical considerations regarding the mechanism of action are expounded upon in this paper.”
Introduction

“Toe-to-digit transplantation and digit-to-digit replantation provide excellent models to study possible different patterns of nerve regeneration and functional recovery when donor nerves are the same as or different from recipient nerves. It is reasonable to ask whether the transplanted toe behaves more like a normal finger or a normal toe, and whether the replanted digit can achieve complete functional recovery despite previous reports of poor recovery in sensory nerve function following nerve repair.”

“In our previous studies on the recovery of sensation, nerve conduction, and somatosensory evoked potentials (SEPs) to digital nerve stimulation, the transplanted toe achieved 70-90% of normal sensations, including temperature (cold and warm), pinprick, light touch, and vibration. However, two-point discrimination had the worst recovery with a mean of 2.9 mm for normal finger, 6.2 mm for normal toe, and 9.1 mm for transplanted toe. Nerve conduction and SEP findings indicated persistent impairment of digital nerve function.”

Methods

“Recovery of digital nerve function in toe-to-digit transplantation and digit-to-digit replantation was evaluated by transcutaneous constant current sine wave stimulation at 5-Hz, 250-Hz, and 2000-Hz frequencies to determine the current perception thresholds (CPT).”

Results

“For toe transplantation and digit replantation, the mean interval between injury and surgery was 9 months and 7 h, respectively, while the mean interval between surgery and CPT study was 52 months and 20 months, respectively. Control CPTs evoked by three frequency stimuli were obtained from contralateral corresponding normal finger and normal toe. Normal finger had significantly lower 250-Hz and 2000-Hz CPTs than normal toe, but the 5-Hz CPT was not different between them. Replanted digit achieved nearly complete recovery of these three frequency CPTs when compared to normal finger. In toe transplantation, 2000-Hz CPT was comparable to normal finger, while 5-Hz and 250-Hz CPTs were comparable to normal toe.”

Discussion

“The present findings suggest that the transplanted toe was intermediate between normal finger and normal toe, but more like normal toe than normal finger with regard to detection thresholds of the current-evoked sensation.”
A Correlative Electrophysiologic Study of Nerve Fiber Involvement in Carpal Tunnel Syndrome Using Current Perception Thresholds

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\textsuperscript{b} Department of Orthopaedic Surgery, Meiji University of Oriental Medicine Hospital, Kyoto, Japan
\textsuperscript{c} Department of Mathematics, Kyoto Prefectural University of Medicine, Kyoto, Japan

Objective

“To relate clinical severity of idiopathic carpal tunnel syndrome (CTS) to current perception threshold (CPT).”

Methods

“Subjects were 51 patients with CTS (involving 51 hands), and 50 healthy control subjects (50 hands). Involved hands were grouped into three clinical grades (mild, moderate, severe). Using a neurometer (Neurotron, Baltimore, MD), we investigated the relationship between clinical grade and CPT abnormalities.”

Results

“In the mild CTS group, most hands showed CPT abnormalities only at 2000Hz stimulation. The moderate group included a higher percentage of hands showing abnormalities at both 2000 and 250Hz stimulation increased. The severe group included the highest percentage of hands with abnormal values at all frequencies tested.”

Conclusions

“CPT showed abnormalities appear progressively from ‘higher to lower’ frequency stimulations relative to the increasing severity of CTS.”

Significance

“Sensory nerve fiber dysfunction apparently begins in larger fibers, extending stepwise to smaller fibers as the clinical grade of CTS progresses.”
Abstract

“This study evaluated the possible existence of subclinical sensory nerve defects in residents of blackfoot disease (BFD)-hyperendemic villages in Taiwan characterized by long-term arsenic exposure from drinking water. Eighty-five seemingly normal subjects living in BFD villages and 75 external normal controls without exposure were recruited. All subjects were 30-75 years old, without possible causes of peripheral neuropathy and suffered from no symptoms of peripheral neuropathy. Current perception threshold (CPT) was measured by Neurometer® at the trigeminal, median and superficial peroneal nerves with frequencies of 5, 250 an 2000 Hz. Results showed that the two groups were comparable in age, sex, body height and body weight. However, BFD residents had significantly 1.28-2.23-fold higher CPT than normal controls for all frequencies at the 3 nerves. If the mean values + 3 standard deviation (S.D.) derived from normal controls were used as cutoff points for defining abnormalities, 36 of the 85 (42.4%) residents in the BFD villages had at least one abnormal measurement. Site and frequency preferences were noted in the abnormal CPT of the BFD residents. Longer nerves (superficial peroneal and median nerves) were involved more commonly than shorter one (trigeminal); and lower frequencies (5 and 250 Hz) were more commonly involved than the higher (2000 Hz). Stepwise regression analyses consistently showed that residency in BFD villages was significantly associated with higher CPT values after adjusting for age, sex, body height and body weight. In conclusion, abnormal CPT was observed in seemingly normal subjects without clinical neuropathy in the arseniasis-hyperendemic villages in Taiwan.”
Evaluation of the Neurotoxicity of Paclitaxel and Carboplatin by Current Perception Threshold in Ovarian Cancer Patients

Daisuke Doi, Yujiro Ota, Hideki Konishi, Koichi Yoneyama and Tsutomu Araki
Department of Obstetrics and Gynecology, Nippon Medical School

Abstract
“Objectives: Combination chemotherapy consisting of paclitaxel and carboplatin has recently started to be given as the regimen of first choice for epithelial ovarian cancer. One of its side effects, however, is neurotoxicity, and this neurotoxicity has been reported to be the dose-limiting factor. Since it is necessary to measure the severity of the neurotoxicity objectively and quantitatively, we evaluated it on the basis of Current Perception Threshold (CPT) values, which is easy and non-invasive.”

Method
“Sixteen patients with epithelial ovarian cancer were given paclitaxel (175 mg/m2, 3 hours) and carboplatin (area under the curve of 5) every three weeks, and the CPT values were measured at two sites on the day before and several times after administration.”

Results
“All patients exhibited mild neurotoxicity, but it was never so severe that chemotherapy could not be continued. The CPT values peaked on day 4 during one course of chemotherapy, but decreased thereafter and returned almost to the baseline by three weeks, in the same way as the patients’ complaints. The CPT values decreased with the number of courses, and patients’ complaints gradually increased. The CPT values increased more in the cases previously treated with cisplatin than in the other cases. These changes were seen at 2,000 HZ, which generally corresponds to large, myelinated nerves.”

Conclusion
“There were correlations between the changes in the patients’ CPT values and their degree of neurotoxicity. We expect to be able to predict severe neurotoxicity and evaluate the effect of drug therapy for neurotoxicity by measuring CPT values.”
Neurometer Measurement of Current Stimulus Threshold in Rats

Tetsu Kiso, Yukinori Nagakura, Takashi Toya, Naoyuki Matsumoto, Seiji Tamura, Hiroyuki Ito, Masamichi Okada and Tokio Yamaguchi
Neuroscience Research, Pharmacology Laboratories, Institute for Drug Discovery Research, Yananouchi Pharmaceutical Co., Ltd., Tsukuba, Ibaraki, Japan

Abstract

"We examined the current stimulus threshold in rats with the Neurometer, a device used clinically for measuring perception and pain thresholds. Although many studies have indicated the usefulness of this device in the quantification of nerve dysfunction in patients, we have found no published reports on the use of the Neurometer® CPT in animals. Transcutaneous nerve stimuli of the three sine-wave pulses produced by the Neurometer (at 2000, 250 and 5 Hz) were applied to plantar surface of rats. The intensity of each stimulation at which rats vocalized or were hardly startled was defined as the current stimulus threshold. With repeated stimulation, the thresholds were almost constant. Repeated topical application to the area around the stimulating electrode of a high concentration of capsaicin, which acts on small-diameter fibers, increased the thresholds at 250 and 5 Hz, but did not affect the 2000-Hz threshold. Intravenous morphine (2-5 mg/kg) increased all three thresholds, whereas intrathecal morphine (20 or 80 µg) increased only the 5-Hz threshold. Intravenous injection of a minor tranquilizer, diazepam, at 1 mg/kg raised the thresholds at 2000 and 250 Hz, but did not affect the 5-Hz threshold. Higher dose of diazepam increased all three thresholds. These results suggest that the Neurometer® CPT makes possible selective examination of subsets of nerve fibers that differ in diameter not only in humans but also in animals. The present study in rats, in which we established a method of measurement, may provide helpful suggestions for the interpretation of data in humans."
Effects of Aging on Current Vocalization Threshold in Mice Measured by a Novel Nociception Assay

Finkel, J., Besch, V., Hergen, A., Kakareka, J., Pohida, T., Melzer, J., Koziol, D., Wesley, R., Quezado, Z.
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The National Institutes of Health, Bethesda, Maryland, United States

"Background"
Age-related changes in nociception have been extensively studied in the past decades. However, it remains unclear whether in addition to the increased incidence of chronic illness, age-related changes in nociception contribute to increased prevalence of pain in the elderly. Although a great deal of evidence suggests that nociception thresholds increase with aging, other studies yield disparate results. The aim of this investigation was to longitudinally determine the effect of aging on nociception.

"Methods"
The authors developed a nociception assay for mice using electrical stimuli at 2,000, 250, and 5 Hz that reportedly stimulate Aβ, Aδ, and C sensory nerve fibers, respectively. A system was designed to automate a method that elicits and detects pain-avoiding behavior in mice. Using a Latin square design, the authors measured current vocalization thresholds serially over the course of mice’s life span.

"Results"
For 2,000-Hz (Aβ), 250-Hz (Aδ), and 5-Hz (C fiber) electrical stimuli, current vocalization thresholds first decreases and then increases with aging following a U-shaped pattern (P < 0.001). In addition, average current vocalization thresholds at youth and senescence are significantly higher than those at middle age for the 250-Hz (Aδ) and 5-Hz (C fiber) electrical stimulus (P < 0.05).

"Conclusions"
Using a novel and noninjurious nociception assay, the authors showed that over the life span of mice, current vocalization threshold to electrical stimuli changes in a U-shaped pattern. The findings support the notion that agerelated changes in nociception are curvilinear, and to properly study and treat pain, the age of subjects should be considered."
Bibliography of Selected Neurometer® CPT Related Publications Grouped by Topic and Specialty

This section presents bibliographies of selected scientific publications using Neurometer® technology grouped according to topic and specialty. Additional documents, including a comprehensive bibliography of more than 500 scientific publications utilizing Neurometer® technology as well as additional information about clinical applications, product literature and more is available upon request or on Neurotron’s website at: http://www.neurotron.com/downloads.html.

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71. Hermányi, Zs., Putz, Zs., Berta, B., Tóth, N., Istenes, I., Keresztes, K., Kempler, P. Comparison of Case IV, Medoc, Neurometer, Neurometer Rapid, Calibrated Tuning Fork, Neuropathy Impairment Score (NIS), MTHF Gene Polimorfism Methods to Nerve Conduction Velocity in the Diagnosis of Diabetic


http://www.molecularpain.com/content/1/1/13


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**Evaluation of Nerve Regeneration and Recovery of Function**


**Carpal Tunnel Syndrome (CTS)/Hand (See Occupational Medicine section)**


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**General Publications**


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Neuroselectivity Studies and Neuroselective Neuropathies (also see Neuroselective Ischemia and Compression Publications below)


Studies of Hyperesthesia


Neuroselective Ischemia and Compression Publications


Occupational Medicine / Epidemiology


Podiatry


Toxicology and Pharmacology


Urology & Gynocology


**Review Publications and Editorials**


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March 2007
Abstract Booklet
Incorporating Frequently Asked Questions

NEUROMETER® CPT

Selected abstracts from publications referencing Neurometer® CPT electrodiagnostic neuroselective sensory nerve evaluations are enclosed. A comprehensive bibliography listing hundreds of publications is also included along with answers to many common questions about the device and procedures.

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