Applications in Chronic Pain Evaluation

The TSA-II - NeuroSensory Analyzer

INTRODUCTION

There are numerous disorders of the peripheral and central nervous system that lead to chronic pain states (see pg. 2-4). The pathophysiology of nerve injury in chronic pain can be highly complex and can therefore lead to unpredictable response to treatment courses. Patient history, physical and various standard tools have historically been used to evaluate the nociceptive system, often lacking sensivity and with inherent examiner bias. Imaging tools represent the most commonly used diagnostic tools, although these represent a picture of anatomy, not a measure of nerve function and can be associated with a significant number of false-positives. EMG and nerve conduction testing do not evaluate small-caliber, pain-mediating C and A-delta fibers.

The **TSAII NeuroSensory Analyzer** and Quantitative Somatosensory Testing (QST) enables the user to evaluate specific components of the nociceptive system, including pain-mediating unmyelinated C-fibers. The TSAII allows investigation of the coexistence of pain with both central and peripheral nervous system abnormalities, to include permitting diagnosis of neuropathic pain syndromes. This capability can be extremely useful to the practicing pain physician. As concluded by Stojanovic et al, in Current View of Pain, 1998… "*In the clinical setting, quantitative sensory testing is becoming a clinical standard for evaluation of certain chronic pain conditions*".

Nerves consist of fibers of variable diameter with the thicker fibers having a faster conduction velocity. Three types of fibers are generally recognized in the sensory subclass of nerve fibers, with small-caliber, pain-mediating fibers representing roughly 70% of the peripheral nerve system:

- A-beta fibers, the largest fibers, mediate the sensations of touch and mild pressure, as well as the sensation of position of joints and vibration, at a conduction velocity above 30 m/sec.

- A-delta fibers, smaller than A-beta fibers, mediate the sensation of cold and the first components of the sensation of pain, at a conduction velocity between 2 and 30 m/sec.

- C fibers, the slowest and smallest, mediate the sensation of warmth and the main component of the sensation of pain, at a conduction velocity less than 2 m/sec. In addition, C fibers subserve most of the autonomic peripheral functions.

Medoc Ltd. | 1 Ha'Dekel st. | POB 423 Ramat Yishai 30095 Israel | Office. 972-4-9038800 | Fax. 972-4-9038808 | www.medoc-web.com

Lumbar Radiculopathy

Patients with Low Back Pain quite often have root lesions. Clinical bedside exam is often not sensitive enough to pick up small deficits in sensation. EMG is limited as it relates to large fibers exclusively and is not a test of nerve "function". Imaging is expensive, not always readily available and is associated with a significant number of false positives, as it may show an image of pathology that does not necessarily indicate functional impairment, e.g., mild disk herniation may or may not compress the nerve root. The **TSAII NeuroSensory Analyzer** offers a cost-effective test of nerve function, able to document sensory loss in both small and large fiber sensory nerves. Radicular symptoms and signs result from mechanical, inflammatory or chemical irritation of spinal nerve roots. The most common clinical form results when a bulging or herniated intervertebral disk impinges on a lumbar or sacral root. For example, sciatica refers to the syndrome of pain, dysesthesias and hypoesthesias in the distribution of the sciatic nerve as a result of compression of the L5 or S1 roots. In many instances, there is uncertainty if the cause of a patient's discomfort is secondary to a radiculopathy, neuropathy, spinal cord lesion or is non-neurologic in orgin. The documentation of localized hypoesthesia with the TSAII can assist in the differential diagnosis. The site of nerve compression can be better localized, thereby assisting in interventional therapeutic techniques. Response to therapy and functional improvement over time can be documented. Lastly, the TSAII offers an additional parameter for consideration of surgical intervention. Pre-operative elevated warm detection thresholds (c-fiber) have been shown to be prognostic of poor results following surgical decompression (*Nygaard, O.P. et al, 1998*) ; an indicator of symptom severity (i.e., adjacent nerve inflammation and/or central sensitization).

Chronic Regional Pain Syndrome (CRPS)

Common clinical manifestations of CRPS include spontaneous pain, continuous pain, hyperalgesia and sympathetic dysfunction. Abnormal central processing is characteristic of the disorder. The condition often becomes chronic and can progress to a severely disabled limb. Consequently, properly assessment and treatment ~ if initiated early ~ is particularly important as such intervention can be effective and spontaneous remissions do occur. The **TSAII NeuroSensory Analyzer** provides quantitative documentation of thermal hyperalgesia (i.e., pain induced at non-painful temperatures), a positive sensory phenomenon that implies unusual pathophysiologies such as sensitization of receptors, central hyperexcitability, disinhibition or, possibly, ectopic nerve impulse discharge. Serial testing allows the clinician to monitor change during sympathetic block of alternative interventions. Testing with the TSAII also enables subgroups of CRPS patients to be identified. The erythralgia or ABC syndrome (Angry Backfiring C nociceptors) patient has a warm, red limb which is hyperalgesic to heat on testing. Capsaicin therapy has been reported to be beneficial to some ABC patients. The CCC (triple cold syndrome) patient has a cool limb, which is not perceived as such by the patient, yet is hyperalgesic to low temperature testing. This combination of cold hypoesthesia, cold hyperalgesia and a cold limb characterizes the CCC syndrome. Sympathectomy or sympathetic blocks are not recommended for CCC patients. Multiple authors have suggested that sensory deficits (i.e., hypoesthesia or loss of response to cold/warm detection stimuli, etc.) in the upper quadrant might indicate that central mechanisms, including brain-stim abnormality, are frequently involved in the pathogenesis of CRPS (Rommel et al; Thimineur et al;)

Central Pain Syndromes (CPS)

Quantitative Somatosensory Thermal Testing with the **TSAII NeuroSensory Analyzer** has given clinical insights into the complicated central changes which occur in neurogenic pain. Because of the strong significance of sensory abnormalities for the diagnosis of Central Pain Syndromes, a careful sensory examination is important, able to confirm involvement of spinothalamic pathways. The most affected modalities are temperature and pain, with special attention needing to be paid to temperature sensibility. Sensory loss occurs in lesions of the CNS, e.g., in post-stroke (CVA) pain, in Multiple Sclerosis and with Syringomyelia. Quantitative Sensory Testing (QST) has demonstrated that somatosensory abnormalities occur in virtually 100% of cases of CPS following stroke. A small percentage of patients who have suffered a cerebrovascular accident will develop weeks and even months later, a pain syndrome involving the side of the body initially affected by the stroke. The pain is often spontaneous and so severe that suicide may result. Thermal testing reveals hypoesthesia and hyperalgesia (*Boivie et al*) and can support the diagnosis and assist in the evaluation of therapy, ie., usually analgesics, tricyclic anti-depressants and physiotherapy. The use of QST in Multiple Sclerosis has been described by Hansen et al and others.

Post-Herpetic Neuralgia (PHN)

This pain syndrome follows a localize infection with Herpes Zoster virus. Commonly, the distribution is in a band-like area of the trunk or in one branch of the trigeminal nerve on the head and face. During the acute vesicular stage of the infection most individuals experience pain, but 10-20% will have pain after the skin eruption has resolved. The incidence of PHN increases dramatically with age and can be a debilitating consequence. Patients who express hypoesthesia during the eruptive stage of the disease are prone to develop pain later and it has been claimed that the initiation of early therapy can prevent PHN. Post-herpetic pain is manifest as both thermal hypoesthesia AND thermal hyperalgesia, a combination known as Anesthesia Dolorosa. Thermal testing with the **TSAII NeuroSensory Analyzer** documents both hypoesthesia and hyperalgesia and enables quantitative monitoring of therapeutic efficacy. Utilizing the TSAII, patients who express hypoesthesia during the eruptive stage of the disease are more prone to develop pain later *(Nurmikko et al)* and it has been claimed that the initiation of early therapy can prevent PHN.

Trigeminal & Facial Pain

Pathophysiological mechanisms of trigeminal neuropathic pain after nerve injury involved impaired function of both small unmyelinated fibers and large myelinated fibers. Abnormal temporal summation of pain may involve hyperexcitability of central wide-dynamic range neurons. Reduced heat and cold pain thresholds indicate heat and cold hyperalgesia, which may possibly be explained by sensitization of peripheral C nociceptors. In Idiopathic Trigeminal Neuralgia, altered cutaneous thermal sensation in the form of vibratory, warm and cold detection thresholds are also found in the affected and unaffected adjacent divisions compared to the healthy sides, providing evidence of a combined peripheral and central pathologic abnormality. *Kmberstol et al* focused attention on the use of diagnostic measures (ie., vibration and temperature sensibilibity) which can disclose possible damage to brain and brainstem structures following soft-tissue injury of the cervical spine. The authors went on to say “that such damage can be of diffuse and subtle nature and may not necessarily be detected by gross morphological techniques (e.g., CT or MRI), but would rather require the use of sensitive functional tests based on neurophysiological methods”. In patients with chronic facial pain following dorsolateral medullary infarction, *Fitzek et al* confirmed that ipsilateral facial pain was significantly correlated with lower medullary lesions. Likewise, pain and temperature sensation in the ipsilateral face was decreased in all patients with facial pain but not in patients without pain.

Evaluation of Nerve Blocks

The **TSAII NeuroSensory Analyzer** is utilized to quantify and document response to diagnostic and therapeutic nerve blocks. *Dellemijn et al* showed that a deficit in thermal sensory thresholds correlated with pain relief associated with sympathetic blockade by stellate ganglion block. The authors concluded, “Quantitative thermal sensory testing is a useful tool for documenting blockade of small caliber afferent axons from local anesthetic spread. With stellate ganglion block, careful monitoring of temperature (threshold) changes on both sides of the face and both hands may provide a better index of which patients achieve adequate blockade of sympathetic outflow than simply measuring temperature in the hand ipsilateral to the block”. In a separate study, *Kalman et al* looked at quantitative sensory changes in humans after intravenous regional block (w/mepivacaine). The authors concluded, “the cold receptors and/or their A-delta fibers were selectively depressed after the block. In conjunction with earlier findings, this suggests that intravenous regional block (IVRA) with mepivacine can differentially decrease neurogenic inflammation with little impairment of sensory function”. Published in PAIN, 1991, *Wahren et al* utilized Quantitative Somatosensory Testing before and after regional guanethidine block in patients with neuralgia of the hand; concluding, “The results indicate that quantitative thermal sensory tests, together with clinical evaluation of the nerve trauma, can help to predict which patients will have long lasting pain alleviation after RGB treatment. Post-operatively, the TSAII can also provide assistance in confirming recovery of sensory function.

Painful Neuropathies

Examples of painful neuropathies include diabetic neuropathy, alcoholic and uremic neuropathy and post-herpetic neuralgia. Neuropathies may exhibit both positive and negative sensory phenomena. Positive phenomena are those which are typically produced by excessive neural activity. Positive phenomena are expressed as spontaneous ongoing pains and hyperalgesia and can be documented as thermal hyperalgesia, i.e., abnormal heat-pain thresholds. Negative sensory phenomena are expressed as decreased sensibilities and can be identified and quantitied by testing warm and cold thresholds.

Fibromyalgia

Fibromyalgia is a chronic pain syndrome characterized by generalized pain, tenderness, disturbed sleep and pronounced fatigue. The pathophysiology has been unknown but peripheral as well as central mechanisms have been implicated. Over the last several years, much work has been conducted by leading pain researchers utilizing the **TSAII NeuroSensory Analyzer**, yielding increasing evidence of the TSA's contribution to the characterization of Fibromyalgia. *Lautenbacher et al* showed that patients with fibromyalgia had significantly lower heat pain thresholds than healthy subjects (but similar electrical detection and pain thresholds). Tonic thermal stimuli at painful and non-painful intensities were utilized to induce pain inhibition (See Medoc: "Temporal Summation/Windup"). Pain modulation, produced by a concurrent tonic stimulus in healthy persons, was not seen in the Fibromyalgia group. In a separate study, *Weigent et al* stated, "the higher levels of neural input in Fibromyalgia patients suggests that abnormal thermal pain perception in Fibromyalgia cannot be explained solely by psychiatric illness, producing evidence that abnormalities occur in the functional activity of the brain as well as in neurotransmitter levels among persons with Fibromyalgia. Abnormal thermal pain thresholds were found at multiple anatomic sites in the widespread pain of Fibromyalgia. *Berglund et al* concluded that Fibromyalgia was characterized by aberrant perceptions to cold and heat, with touch unaffected. The authors suggested, "very specific somatosensory profiles obtained by sensory evaluation methods show good potential for clinical diagnostic work".

Headaches

In their paper, "Thermal Sensitivity in Unilateral Headaches", *Becser et al* showed that cervicogenic headache patients had significantly higher warm and cold thresholds than controls, at several cephalic and noncephalic points. Warm thresholds over the mastoid process on the symptomatic side were higher in cervicogenic headache patients compared to other groups. The authors hypothesized a bilateral central sensory dysfunction may be an underlying explanation. *Kleinbohl et al* further noted lowered thermal pain thresholds in headache patients, noting the results were in accordance with models of spinal plasticity contributing to pathological pain states and arguing for the diagnostic value of psychophysical measures of sensitization, such as are evaluated with the **TSAII NeuroSensory Analyzer**. In the Annals of Neurology, 2000, "An Association between Migraine and Cutaneous Allodynia", *Burstein et al* described cutaneous allodynia in certain well-defined regions of the skin during migraine attacks, a previously unreported neurological finding that points to hyperexcitability of a specific central pain pathway that subserves the intracranial sensation.