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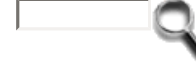
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THE ELECTRODIAGNOSTIC STUDIES (NEUROMETRY) MOSTLY USED IN PAIN COMPLAINT EVALUATION : A BRIEF REVIEW.

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The Quantitative Sensory Testing

A patient is referred quite often for electrodiagnostic evaluation (neurometry) of a wide range of pain complaints. Electrodiagnostic studies are of great interest in the evaluation and localization of peripheral nerve injury. They can differentiate radiculopathy from peripheral neuropathy and the many other causes of acute and chronic pain such as vascular lesions, mechanical or muscular painful diseases, degenerative or inflammatory conditions, myopathies and entrapment syndromes.

Electromyography (EMG) is an examination dedicated to the motor unit study. Motor unit is a neurofunctional entity constituted by a neuron located in the spinal horn and by all the muscle fibers innervated by that axon. Electromyography refers exclusively to needle electrode evaluation of action potentials seen in skeletal muscle at rest and on volition, and hence parallels the definition of ECG and EEG [1]. Nerve Conduction Velocity (NCV) studies refer to motor and sensory unit; sensory unit can be considered as all the sensory peripheral structures that are referred to a single sensory nerve fiber.

A nerve can be affected from different causes of inflammation (neuritis), from different damages with no evidence of inflammation (neuropathy). When pain is experienced along a distribution of a nerve with different etiology (often unknown) we define this clinical condition as neuralgia. When the disturbance of function or the pathologic change occurs in one nerve we refer to mono neuropathy, in several nerves mononeuropathy multiplex; when the damage is symmetrical and bilateral, polineuropathy [2].

Rheumatoid, diabetic, alcoholic, toxic neuropathies, entrapment syndromes are often painful [3]. Injuries to nerves can result in extremely painful conditions such as causalgia, CRPS, PHN, PLP and stump pain, cancer neuropathy [4]. However, when evaluating the patient with acute or chronic pain, neurophysiological tests are the only widely accepted modalities of assessing nerve roots function. Electrodiagnostic studies have shown to be useful in, the diagnosis of different neuropathies such as radiculopathies, entrapment syndromes, peripheral polineuropathies; the neurophysiological assessment allows the pain clinician to localize the lesions and to determine the severity of nerve damage.

THE ELECTRODIAGNOSTIC EXAMINATION

It is quite common that the majority of patients approach the electrodiagnostic examination with a great deal of fear and anxiety. The is mainly due to the fear of needle puncture and/or "electrical shock". Many patients that have been submitted to an EMG study do not want to repeat anymore this examination. Since patient cooperation is mandatory for a successful examination, the electromyographer must be able to deal with the patient's fears. Nowadays the more recent Quantitative Sensory Testing examinations seem to have gained a diffuse acceptance in the pain population. It seems to be due to the use of transcutaneous electrodes in place of needles.

Any kind of electrodiagnostic examination, unlike other studies such as ECG or EEG, cannot be performed in a "blind" and routine manner. Each examination must be individualized according to the clinical picture. A complete history and physical examination must be taken

by the physician performing the electrodiagnostic study. A patient may initially be thought to

have an entrapment neuropathy, but further examination may reveal the presence of a polyneuropathy, radiculopathy, or the like. When abnormalities are found in one extremity, the opposite extremity is also studied. In certain circumstances all the limbs may be examined.

The introduction in clinical practice of the QST has allowed a great deal of information to be obtained on sensory nerve fibers in an atraumatic manner. Even if in many Pain Centers this examination is largely used it remains the need that the results of the examination must then be interpreted in light of the history and clinical

findings.

Somebody can say that we, as pain clinicians, do not have an extraordinary experience in neuro physiology to perform such examination; on the other side we can say also that in many Countries these studies are performed by technicians or by experts in neuromuscular disorders with no particular experience in pain states.

In summary, routine performance of only brief, limited electrical studies is analogous to ordering a limb x-ray and examining only the bones while ignoring the soft tissue structures. Since so much information is to be gained, especially in the evaluation of the patient with chronic pain, the full potential of the electrodiagnostic examination should be utilized [5].

STUDIES ON NERVE CONDUCTION VELOCITY (NCV)

These studies refer to the evaluation of peripheral nerve activity in the extremities. Nerve conduction studies are safe, reliable, and reproducible in assessing peripheral nerve function. They are used to determine the presence and type of neuropathy, to localize lesions, and to determine their severity. The electrical stimulation of a nerve is followed by some measurements in order to determine the nerve's ability to carry the impulse. Stimulation may be obtained either with needle or surface electrodes. When it is necessary to measure deeply placed nerves, such as the sciatic nerve in the gluteal region, near-nerve needle stimulation is used.

With the patient laying on the bed the nerve is charged with a 90 mV transmembrane potential, positive externally. When the negatively applied stimulus exceeds threshold, an action potential is generated. This potential is then self-propagated proximally and distally.

The Pain Clinicians are not involved in motor conduction studies that are generally performed by neurologists or neuro-physiologists for different pathologies, in these studies a nerve is stimulated and the evoked response is recorded from a distal muscle. Our interest in motor conduction studies is mostly related to the fact that the presence of a latency in the nerve conduction can be used to localize a nerve lesion and to assume that a sensory fiber damage may be present as well.

Sensory conduction studies are performed by placing recording electrodes directly over the sensory nerve being examined. The nerve may be stimulated either proximally (antidromic conduction) or distally (orthodromic conduction) to these electrodes, and the time from the onset of the stimulus to the onset of the action potential that is being recorded is measured. The sensory conduction velocity is obtained dividing this time into the distance between the recording and the stimulating electrodes. A reduction in NCV is most commonly associated with disorders of the myelin. However, this may also occur with diseases affecting the large, rapidly conducting axons. Axonal disorders more commonly cause decrease in the amplitude of the evoked motor and sensory responses since fewer fibers are available to contribute to the response.

Sensory nerves commonly studied include the median, ulnar, radial, medial and lateral antebrachial cutaneous, lateral femoral cutaneous, sural, superficial peroneal, and tibial.

Nerve Root Stimulation (NRS), H reflex, and F wave measurements are the mostly utilized examinations of proximal segments at the root and plexus level [5].

Nerve Root Stimulation

Nerve root stimulation may be performed in either the cervical or lumbar region. A

stimulating needle cathode is placed into the paraspinal musculature at the proper level. The anode is placed on the skin. The evoked response is recorded from an appropriate muscle in the limb. To determine abnormality at this level side-to-side latency comparisons are made.

H Reflex

The H reflex, discovered by Hoffman in 1918, it is believed to be the electrical counterpart of the muscle stretch reflex, but it differs in several ways. In infancy, an H reflex can be elicited from most nerves, but after age 2 it can reliably only be found in the tibial nerve. In spinal shock the H reflex may still be present, even in cases of areflexia. The tibial H reflex is normally obtained by stimulating the tibial nerve at the knee with recording from the gastrocnemius or soleus.

The latency measurement between the stimulus and muscular twitch is therefore a measure of the integrity of both the S1 motor and sensory roots. This study is widely utilized for evaluating S1 radiculopathies.

F Wave

The F wave seems to be the result of antidromic conduction of the stimulus in the alpha motor neurons to the spinal cord. As a result they can cause firing of the anterior horn cells. These impulses are then carried orthodromically by the alpha motor neurons, it causes a discharge of the muscle fibers that they innervate. The

same alpha motor neurons may not fire after each stimulus. While the H reflex is identical with each stimulus, the F wave results in a variable response. The F wave is a measurement of motor function only. It can be used in examining proximal nerve function in neuropathy, thoracic outlet syndrome and in radiculopathy. If distal conduction studies are normal but the F wave latency is prolonged, it may be assumed that a proximal lesion exists.

Somatosensory-Evoked Potentials (SEPs)

Somatosensory-Evoked Potentials may be obtained by stimulating a peripheral nerve, usually the median or ulnar at the wrist or the tibial or peroneal at the ankle, and recording wave forms from the contralateral scalp. It is thought that these potentials are carried by sensory fibers in the peripheral nerves and in the dorsal column - lemniscal system centrally. They can therefore theoretically be used to measure function distally or proximally in the peripheral nervous system or in the spinal cord or brain. The main use of the SEPs is in diagnosing multiple sclerosis and for monitoring spinal cord function during spinal surgery. Presently the clinical usefulness of these studies in radiculopathy is very controversial.

Studies in several centers are presently underway to evaluate dermatomal cutaneous stimulation to better localize lesions to a single root, but these studies are still in an experimental stage.

Thermography

Thermography is a very useful and not harmful method, which aids the physician in the evaluation of chronic pain patients. They allow to determine coexistence of pain with both central and peripheral nervous system abnormalities, permitting diagnosis of neuropathic pain syndromes [6].

Thermal emission profile, evaluated by thermography, reflects the degree of vasoconstriction and vasodilation of the skin, which is determined by pathophysiologic, but also physiologic, neural and non-neural processes. Cold patterns may be observed in increased sympathetic outflow, and may be a physiological reflex of pain or a sign of neuro-vegetative pathologies such as sympathetic denervation supersensitivity. A cold pattern is also characteristic of muscular disuse and circulatory pathologies. Hot pattern is seen in case of sympathetic deficit, in inflammatory disease (such as neurogenic inflammation, due to antidromically driven neurosecretion in damaged C-nociceptor terminals) and in focal muscular contracture.

Quantitative Sensory Testing (QST)

Quantitative Sensory Testing (QST) is the use of precisely measured and repeatable sensory stimuli to determine the absolute threshold of sensation within specific somatosensory modalities. The term implies that only one type of stimulus is studied at one time (cold, heat, vibration, electrical stimulus) and that its physical characteristics and intensity are precisely known (degrees, micro volts,...). QST is used to assess a sensory detection threshold (the smallest stimulus that can be detected at least 50% of the time) or other sensory responses from suprathreshold stimulation - e.g., just noticeable differences or abnormal responses (e.g. hypersensitivity)... The stimuli must be precisely controlled in duration, frequency and intensity.

Precise delineation of sensory perception is clearly useful in early detection and for monitoring progression or recovery. It is of less help in differential diagnosis and currently available only in specialized centers. The procedure is painless and inexpensive. Vibration, thermal and pain perception, have been well studied with several commercially available QST devices. Recently function of sensory fibers can be tested with the use of an electrical stimulation applied through the skin.

The principal strengths of QST include simplicity, permitting testing by nonprofessional personnel, and the availability of mean and standard deviation values that are accurate and age-controlled. The procedures are also useful for parametric evaluation of sensory loss in clinical studies involving iatrogenic and metabolic polyneuropathies.

QST is used increasingly to detect and characterize such hypersensitivity phenomena as hyperesthesia, hyperalgesia, or allodynia (pain from stimuli that in healthy persons does not evoke pain).

Quantitative Sensory Testing is the determination of the absolute sensory threshold, defined as the minimal energy reliably detected for a particular modality. QST is a relatively simple procedure that is both noninvasive and non-adversive. It is a logical extension of the sensory portion of the clinical neurological examination. The data obtained from QST can be used in parametric statistical analysis and thus are particularly valuable in screening large populations or in longitudinal evaluations within clinical trials. Recent years have seen the development of a number of relatively inexpensive devices that allow suitable assessment of somatosensory function including vibration, thermal energy and light touch....

As we have said previously today the neurophysiological assessment for chronic pain states usually includes: EMG, nerve root stimulation, nerve conduction velocity, H

reflex, W wave, somatosensory evoked potentials. However a small fiber radiculitis may not have a disc protrusion on MRI and of course would not have a large fiber conduction loss. Quantitative Sensory Test (QSTs) enable an objective, functional evaluation of the entire sensory nerve function [7-8]. Large myelinated (A-beta), small myelinated (A-delta) and unmyelinated C fibers can be evaluated for painless sensory threshold and painful tolerance. It is possible therefore define Current Perception Threshold (CPT) as the minimum amount of painless electrical stimulus that consistently evokes a nerve sensation. Pain Tolerance Threshold (PTT) on the other hand is the maximum amount of electrical stimulus that can be tolerated.

It is important to know that a PTT evokes the pain response from the nerve without causing tissue damage, it is an atraumatic procedure. Both tests are double-blinded automated methodology to selectively evoke responses from the large myelinated, small myelinated and unmyelinated fibers. The CPT evaluation is capable of objectively quantifying sensory abnormalities consistent with polyneuropathy secondary to metabolic conditions (e.g. diabetes), toxicity (e.g. heavy metals), infectious (e.g. AIDS), or hereditary etiologies. Sensory abnormalities consistent with entrapment or compressive neuropathy, radiculopathy, peripheral nerve injuries or CRPS can be documented with the CPT evaluation.

The CPT test is used to identify and localize areas of abnormal function, to determine the severity of the abnormality, to aid in diagnosis and prognosis, to guide and to monitor the different phases of the treatment. Progressive peripheral neuropathy can be characterized by stages of development. The earliest stage is most often sensory hyperesthesia. This is an inflammatory condition that represents for example the neuritis that can precede neuropathy. Hyperesthesia implies irritation or inflammation of a nerve but no loss of function. This condition may precede symptoms or be the most symptomatic.

Progression of the disease may lead to hypoesthesia or, ultimately, to anesthesia. The advanced stages of neuropathy may also be associated with loss of motor nerve function and symptoms of weakness [9-11].

In the typical peripheral nerve we can differentiate the A-beta (large diameter myelinated) fibers that transmit touch, the A-delta (small diameter myelinated) that transmit sharp pain and the C (small unmyelinated fibers) that transmit dull pain, 1/3 of the small unmyelinated C fibers subserve sympathetic function (both afferent and efferent). The A-beta fibers that conduct up to 80 m/s for touch sensation comprise only 5-10% of the total number of fibers, while the A-delta fibers that conduct approximately 20 m/s and convey sharp pain are less than 10% of the peripheral sensory nerve fibers.

Approximately 80% of the number of fibers the peripheral sensory nerve are the unmyelinated C fibers which conduct at approximately 1.5 m/s and convey heat and dull pain. About 30% of these subserve sympathetic function. Tests to evaluate these different types of fibers include: NCV and vibratory tests for large fibers, and thermal perception for small. The CPT and PTT use an electrical stimulus to neuroselectively evaluate each sub-population. Moreover large fibers have numerous ion channels while small diameter fiber have limited surface area and fewer ion channels. The different number of ion pumps is responsible for the low charge threshold of large fibers and high charge threshold of small diameter fibers as well as the brief refractory period of large fibers and long refractory period of small fibers.

Neuroselectivity is achieved using different frequencies of the electrical sine wave stimulus. 2000 Hz delivers less charge more rapidly to evoke responses from the large myelinated fibers (A-beta) while 5 Hz stimulus delivers much more charge in order to evoke responses from the unmyelinated (C) fibers. The main difference between 2000 Hz and 5 Hz stimulation is that large fibers can respond to this rapid stimulus while the unmyelinated fibers require several milliseconds of continuous depolarization to respond. The response that we can evoke in a nerve depends on the electrical charge applied. In order to obtain reproducible measures the current must be kept constant. Differences in skin thickness, edema, trophic skin changes, skin temperature, heart beating and breathing may alter the skin resistance and therefore skin resistance has to be continuously monitored by a feed back loop in order to continuously vary the voltage.

The constant current feature enabled a normative database to be established regardless of skin variations or resistance. The CPT stimulus is a constant alternating current which assures that the stimulus is not modified by variations in tissue impedance. The ability to maintain a constant current despite alterations in impedance is the reason for the high reproducibility of the CPT measurements. These characteristics have been assembled in the Neurometer OR CPT device for QST. They are neuroselective diagnostic constant current stimulators which use a microprocessor controlled stimulus to obtain CPT measures. The test is not painful since the electrical stimulus is administered to the skin using a 1 cm diameter gold plated electrodes. A water based chloride free electrode gel serves as the conductive medium between the electrode and the skin. The electrodes are held in place using a non-conductive tape.

CPT is the minimum amount of transcutaneously applied current that a person can perceive as evoking sensation. Three CPTs are obtained from a body site with three different sine wave stimulation frequencies: 5 Hz, 250 Hz and 2000 Hz. These three

frequencies selectively excite small unmyelinated (C fibers), small myelinated (A-delta) and large myelinated (A-beta) fibers respectively. The CPTs are obtained using a single or double blind forced choice testing procedure which confirms the validity of the responses and reduces examiner bias.

The electrodes can be applied to any cutaneous site depending on the nerve or dermatome distribution that needs to be evaluated. The patients values are then entered into a software program included with the device for analysis and comparison to the established normative values. The equipment is also provided with look-up charts for the rapid screening testing mode to quickly determine if the test results are hyperesthetic, normal or hypoesthetic. Pain Tolerance Threshold is an atraumatic measurement that does not cause stimulus at the electrodes. It is an automated and randomized test first performed at an asymptomatic site. Numerous studies have compared the neuro-selective CPT evaluation with electrodiagnostic methodologies.

It has been shown that CPT abnormalities detected at 2.000 Hz correlate best with tests of large fiber function (A-beta) as demonstrated by the sensory NCV evaluation; 250 Hz CPT abnormalities correlate best with QST of vibratory perception (A-delta) and the 5 Hz CPT abnormalities correlate best with the thermal threshold QST which evaluate small fiber functioning and protective sensation. Vascular pathologies, joint diseases and soft tissue conditions usually do not manifest with cutaneous sensory changes. Ratio abnormalities (PTT/CPT ratio) indicate the early stage of a neuropathy when the nerve is not impaired enough to be classified as hyperesthetic or hypoesthetic.

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RIASSUNTO

Il QST è la valutazione precisa della soglia sensoriale, definita come la minima energia avvertita in modo affidabile per una certa modalità. E' il proseguimento logico della porzione sensoriale dell'esame clinico neurologico. I dati ottenuti dal QST possono essere usati per analisi statistica parametrica e pertanto possono essere utilizzati per studi su vasti campioni di popolazione così come per valutazioni longitudinali all'interno di studi clinici.

SUMMARY

Quantitative Sensory Testing is the determination of the absolute sensory threshold, defined as the minimal energy reliably detected for a particular modality. QST is a relatively simple procedure that is both noninvasive and non adversive. It is a logical extension of the sensory portion of the clinical neurological examination. The data obtained from QST can be used in parametric statistical analysis and thus are particularly valuable in screening large populations or in longitudinal evaluations within clinical trials.

Parole chiave / Key words

Studi elettrodiagnostici, neurometria, QST, valutazione della funzionalità delle fibre sensoriali / Electrodiagnostic studies, neurometry, Quantitative Sensory Testing, assessment of sensory fiber function.

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