The Utility of Clinical Neurophysiological and Quantitative Sensory Testing for Trigeminal Neuropathy

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This article reviews the utility of neurophysiological recordings and quantitative sensory testing (QST) in providing sensitive, quantitative, and objective tests for the diagnosis and localization of damage to the trigeminal nerve. Electromyography and recordings of the masseter reflex and compound muscle action potential evoked by transcranial magnetic stimulation or direct electrical stimulation of the masseteric nerve can be of value in evaluating the function of α motor neurons supplying the muscles of mastication. Orthodromic recording of the sensory action potential and trigeminal somatosensory-evoked potential recording with the near-nerve stimulation technique are sensitive tools for the investigation of trigeminal sensory Aβ afferents, whereas recordings of polysynaptic trigeminal brainstem reflexes and tactile QST are less sensitive. At late stages of recovery, the blink reflex and masseter inhibitory reflex are often normal, but at earlier stages, the blink reflex recording has good prognostic value, and the presence of a reflex response may confirm continuity of the nerve trunk after partial laceration. Trigeminal small-fiber function (Aδ and C) can be studied with thermal QST of the cool, warm, heat pain, and cold pain detection thresholds or with laser-evoked potential recording. Thermal QST may remain abnormal years after axonal damage and aids in the diagnosis of late sequelae of trigeminal nerve injury. In a study of the diagnostic value of neurography, blink reflex and thermal QST, and various commonly used clinical sensory tests, neurophysiologic tests and thermal QST had better sensitivity (50% to 88% vs 40% to 59%) and negative predictive values (78% to 100% vs 70% to 74%) compared to clinical examination, whereas the specificity (55% to 100%) and positive predictive values (48% to 73%) were similar. At 1 year after trigeminal nerve injury, the risk of a false negative finding with clinical sensory testing was 94%, whereas the combination of nerve conduction recordings and thermal QST increased the diagnostic yield to 100% in patients with long-standing postsurgical sensory alteration. In conclusion, clinical neurophysiological recordings and QST improve the diagnostic accuracy for trigeminal neuropathy. J OROFAC PAIN 2004;18:355–359

Key words: neuropathy, neurophysiologic examination, quantitative sensory testing, trigeminal nerve

Detailed history and clinical neurological examination form the basis for making a diagnosis of trigeminal neuropathy. However, it may be difficult or even impossible to diagnose subtle dysfunction and old injuries of the trigeminal nerve by rather crude clinical examination alone. Consequently, conventional clinical sensory testing with qualitative tests, such as measurements

of tactile sensibility, discrimination of brush-stroke direction, and discrimination of sharp from blunt mechanical stimuli, and warm from cold stimuli, has been considered inadequate for definite exclusion of a trigeminal nerve lesion[1] or for follow-up of sensory regeneration.[2,3] Clinical examination does not allow detailed analysis of the type, extent, or nerve fiber profile (Aβ, Aδ, or C fibers) of nerve damage, all of which affect the rate of recovery and final outcome after nerve damage[4,5] and even the risk for development of neuropathic pain.[6] Clinical examination cannot differentiate a total conduction block due to severe focal demyelination of a nerve segment from one due to a total nerve transsection injury. In contrast, an electroneuromyographic examination allows accurate documentation of the state of the nerve and the degree of axonal and/or demyelinating damage and so enables reliable prognosis of recovery and selection of appropriate treatment.

Recent advancements in neurophysiological recording techniques and quantitative sensory testing (QST) provide several sensitive quantitative and objective tests for the diagnostic evaluation and localization of trigeminal neural dysfunction. Although these methods are useful and accurate in the diagnosis of peripheral trigeminal neuropathies of various etiologies and in the evaluation of brainstem pathology and orofacial pain, they are not fully utilized at the moment. This may be in part because of differences in the availability of the tests, but it is also because of the scarcity of studies on the diagnostic value of neurophysiologic tests or QST compared to those on clinical examination. Lack of a "gold standard" for trigeminal nerve neuropathy has also been a problem when evaluating the diagnostic value of various clinical and neurophysiological tests.

This article provides a brief outline of the utility of various neurophysiological and quantitative sensory tests for the examination of the trigeminal nerve and reviews some prospective studies on the diagnostic utility and value of these techniques compared to clinical examination. Although these studies were on iatrogenic trigeminal nerve injury, the main conclusions can be utilized in the diagnosis of trigeminal neuropathies of any etiology.

Neurophysiological Testing and QST of Sensory or Motor Functions of the Trigeminal Nerve

A more detailed description of the various QST and neurophysiological techniques for the examination of the trigeminal nerve can be found in recent reviews.[7–9]

Trigeminal Motor Function

Unilateral weakness of the muscles of mastication and a diminished or absent masseter reflex are difficult to assess clinically. Neurophysiological examination improves the diagnostic accuracy regardless of whether the etiology is in the peripheral or central nervous system. The tests for the investigation of the trigeminal α motor neurons include needle electromyography (EMG) of the muscles of mastication, recordings of the masseter reflex (also evaluating the proprioceptive muscle spindle afferents), and compound muscle action potential (cMAP) evoked from the masseter or temporalis muscles by transcranial magnetic stimulation or by direct electrical stimulation of the masseteric nerve. Combining masseter reflex and needle EMG or cMAP recording enables localization of the dysfunction to the afferent or efferent part of the reflex arc.[7–9]

Trigeminal Aβ Afferent Function

Trigeminal Aβ afferent function can be most accurately assessed with direct orthodromic recording of the sensory action potential (described for the inferior alveolar[10,11] and lingual nerves[12]) or trigeminal somatosensory evoked potential recording with the near-nerve stimulation technique.[13] Because there is considerable interindividual variation, recordings of polysynaptic trigeminal brainstem reflexes mediated via Aβ afferents and the facial and trigeminal α motor neurons are less sensitive in the diagnosis of orofacial symptoms due to peripheral neuropathy.[14] These include the blink reflex recorded from the eye-closing muscles with stimulation of the main sensory branches of the trigeminal nerve and the masseter inhibitory reflex recorded from the masseter muscles with stimulation of the infraorbital or mental nerves.[7–9] At late stages of recovery, the brainstem reflexes are often normal, with the exceptions for total nerve transsection or neuroma-in-continuity.[9,15] Blink reflex recordings have good prognostic value at the early diagnostic workup,[16] and the presence of brainstem reflex responses may confirm continuity of the nerve trunk after partial laceration. All neurophysiological tests for myelinated fiber function are more sensitive to compressing than lacerating peripheral nerve lesions, although the size of the sensory nerve action potential is also an indicator of the amount of axonal damage. Quantitative sensory testing can also be used to assess the function of trigeminal Aβ afferents.[17–19]

Table 1 Diagnostic Value of Clinical Sensory Examination, QST, and Neurophysiological Examination After Iatrogenic Injury to the IAN[14,28]

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
BSD	40	89	64	70
SBD	40	89	64	70
WCD	44	100	73	74
GO	59	73	—	—
TDT	58	56	53	73
CDT	64	100	50	78
WDT	50	100	67	82
BR	59	100	60	85
NCS	88	55	48	100

Data from intraoperative neurophysiological monitoring was used as the "gold standard" of nerve injury when calculating the sensitivity and specificity of the tests done 2 weeks after surgery.[14] The positive predictive values (PPVs) and negative predictive values (NPVs) of the tests were calculated from the subjective sensory outcome (normal or altered sensation) at 1 year.[28]
Clinical sensory tests: BSD = brush stroke directional discrimination (chin); SBD = sharp/blunt discrimination (chin); WCD = warm/cold discrimination (chin); GO = grafting orientation discrimination (lip)
Quantitative sensory tests: TDT = tactile detection threshold (chin); CDT = cool detection threshold; WDT = warm detection threshold
Neurophysiologic examination: BR = blink reflex with mental nerve stimulation; NCS = nerve conduction study.

Trigeminal Small-Diameter Afferent Fiber Function (Aδ and C Fibers)

Trigeminal small-diameter fiber function (Aδ and C) can be studied with noninvasive thermal QST of cool, warm, heat, and cold pain detection thresholds.[14,17–19] Thermal QST is sensitive to axonal injury but rather insensitive to lesions causing mainly demyelination.[20] With an appropriately small thermode, it can be used in any trigeminal distribution,[9,21] but in the authors' experience it is particularly useful in the diagnosis of lingual neuropathy. Because thermal detection thresholds may remain elevated (compatible with clinical hypoesthesia) even years after severe damage with incomplete axonal regeneration, QST is helpful in the diagnosis of late sequelae of trigeminal nerve injury. Application of thermal QST requires proper reference values, because the thresholds may be elevated also on the contralateral homologous distribution after unilateral nerve lesions (probably due to central neuroplastic changes).[22–24] Other methods for studying trigeminal Aδ fiber function include corneal reflex recording and laser-stimulated somatosensory evoked potential recording (referred to as laser-evoked potential, or LEP).[7–9,25] With recent refinement of stimulation settings, trigeminal C-fiber function can also be measured with the LEP technique.[25] Thermal QST and LEP alone do not allow diagnosis of the level of the sensory dysfunction; a lesion anywhere along the pathway from the sensory receptor to the somatosensory cortex or neuroplastic changes subsequent to a peripheral or central lesion[2,3,9,22–24] may lead to alterations of sensory detection threshold. Abnormal perception of thermal stimuli in the form of hyperesthesia or allodynia may also be encountered outside of neuropathic chronic pain conditions.

Diagnostic Value of Neurophysiological and QST Compared to Clinical Examination

In most studies on the diagnostic value of tests for trigeminal nerve neuropathy, the "gold standard" has been the subjective report of sensory alteration. The ability of qualitative clinical tests to document this alteration has often been found to be rather poor.[2,3,6,26] With the use of the results from brain magnetic resonance imaging as the reference, the diagnostic value of recordings of brainstem reflexes has been reported for patients with trigeminal nerve dysfunction.[27] This study yielded a sensitivity of 100%, a specificity of 81%, a positive predictive value of 57%, and a negative predictive value of 100% for the neurophysiologic recordings.[27] These values are rather similar to the results from QST and neurophysiological tests from other studies,[14,20,28] although different endpoints were used in calculating the predictive values (Table 1).

Intraoperative neurophysiological monitoring of the inferior alveolar nerve (IAN) during mandibular surgery has enabled online detection, analysis, and grading of IAN damage.[29,30] Sensory nerve action potentials are ideal for intraoperative monitoring of peripheral nerve function: They are not affected by general anesthesia, and they do not change in reaction to possible central neuroplastic changes,[22–24] but they show clear alteration in response to surgical trauma.[30] A recent prospective follow-up study utilized the data from intraoperative monitoring as a "gold standard" of IAN injury to assess the diagnostic value of IAN neurography, mental nerve blink reflex, tactile and thermal QST, and various clinical sensory tests performed 2 weeks after surgery.[14,20,28] Unfortunately, this is not a perfect gold standard either, as some additional nerve injury may occur immediately after the operation, eg, as a result of postoperative edema. The clinical tests that were done on the lower lip and the chin bilaterally included brush-stroke directional discrimination, sharp/blunt discrimination, warm/cold discrimination, and the grating

orientation test. The neurophysiological tests, tactile QST, and thermal QST showed clearly better sensitivity and, on average, slightly better specificity compared to clinical sensory testing 2 weeks after surgery (summarized in Table 1).[14,20,28] The most sensitive neurography test showed only moderate specificity compared to the function of the nerve at the end of the operation, which may be because of its ability to detect additional postoperative nerve damage.

Further follow-up studies[20,28] have evaluated the sensory recovery after IAN injury and the predictive value of different tests performed at 2 weeks after surgery for the subjective sensory outcome at 1 year. The neurophysiological and QST methods had good negative predictive values (normal test result at 2 weeks reliably indicated normal sensory function at 1 year), whereas the positive predictive values were only moderately reliable, similar to clinical sensory testing (Table 1). All results from the clinical sensory tests had returned to normal by 3 months, and these tests could not verify the subjective sensory alteration thereafter. In contrast, the tactile and thermal QST and neurophysiological tests were able to document subjective sensory alteration and late recovery up to 1 year. At the 1-year examination, the tactile QST and blink reflex were less accurate (yield 50%) than thermal QST (67%) and neurography (94%). This is due to the fact that tactile QST and blink reflex are sensitive to demyelinating injuries that normally recover within 3 to 4 months, whereas thermal QST and neurography are able to detect axonal lesions that recover more slowly and often incompletely.[19] Combining neurophysiological tests and thermal QST increased the diagnostic accuracy to 100% in regard to the ability of the tests to verify the subjective sensory alteration either at the early[13] or the late phase[30] of recovery of IAN injury. For comparison, at 1 year, 14 out of the 15 intraoperatively injured and still symptomatic nerves showed normal results in the clinical tests; this indicates a very high risk of false negative findings (94%) if the diagnosis of trigeminal nerve neuropathy is based solely on conventional clinical examination at a late stage of recovery.

In conclusion, neurophysiological and QST methods are necessary and definitely recommended for the diagnosis of trigeminal nerve neuropathies older than 3 months. They are especially important in cases of litigation after iatrogenic injury. In addition, at the early diagnosis, these methods are useful in determining the severity of nerve damage and the continuity of the nerve as well as in predicting the rate of recovery and the final outcome. They also allow evaluation of small-fiber involvement that plays a role in the development of pain in peripheral neuropathy. In the future, larger studies comparing the diagnostic value of various tools available for the diagnosis of trigeminal neuropathy are needed. For this purpose, iatrogenic trigeminal injuries form a clear and fairly well-defined group of peripheral trigeminal neuropathy. In addition, for thermal QST, standardization of testing protocols between different centers, and further validation of each test, eg, by comparing detection thresholds with intraepidermal nerve fiber density measurements, is required.

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