Psychophysical Assessment of Patients with Posttraumatic Neuropathic Trigeminal Pain

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This article reviews the utility of psychophysical approaches in the assessment of posttraumatic neuropathic trigeminal pain. Methods of quantitative sensory testing are derived from psychophysical principles and provide a widely accepted means for characterizing sensory dysfunction in patients who experience injury to the trigeminal nerve. No published study, however, has sought to compare sensory findings from trigeminal nerve–injured patients who develop neuropathic pain with those from trigeminal nerve–injured patients who remain pain-free. Moreover, sensory testing data from trigeminal nerve–injured patients with pain have been published in only a few reports. As a result, remarkably little is known about sensory factors associated with the development of posttraumatic trigeminal neuralgia. Review of the separate literatures suggests that both trigeminal nerve–injured patients with pain and pain-free trigeminal nerve–injured patients exhibit grossly similar impairments in sensory function. In addition, trigeminal nerve–injured patients with pain may be more likely to report cold allodynia than patients without pain and to exhibit signs of central sensitization such as allodynia to light brushing tactile stimuli and abnormal temporal summation of pain. New studies using state-of-the-art psychophysical methods are needed to search for sensory markers that bear on the development of pain. Moreover, the relationship between psychophysical indices of central sensitization and measures of clinical pain should be addressed to obtain a better understanding of the underlying pathophysiology. J OROFAC PAIN 2004;18:345–354

Key words: allodynia, neuropathic pain, sensitization, sensory testing, trigeminal nerve injury

Contemporary oral and maxillofacial surgical procedures pose a significant risk (up to 100%) of injury to sensory branches of the trigeminal nerve. If injury occurs, sensation may be impaired, but rarely is it lost completely. Quantitative sensory testing (QST) methods based on psychophysical principles have been used to investigate the incidence and severity of neurosensory impairment after different types of maxillofacial surgery and different surgical techniques, the time-course and extent of return of normal sensory function, the disparity in results obtained from different clinical sensory testing and psychophysical procedures, and the impact of sensory alterations on orofacial behaviors and patients' overall satisfaction with treatment.[1–12] In contrast, few QST studies have been reported on patients who develop neuropathic pain after injury to the trigeminal nerve. One reason for this is probably that relatively low numbers of nerve-injured

Table 1 Comparison of Sensory Findings in Trigeminal Nerve-Injured Patients With and Without Pain from Review of the Literature

Variable evaluated by the test	Phenomenon on which test outcomes provide information	Observations from nerve-injured patients with pain	Observations from nerve-injured patients who remain pain-free
Presence of allodynia Dynamic (brush) Punctate (filament) Static (pressure)	Central sensitization: access of pain pathways by Aβ mechanoreceptors Aδ mechanonociceptors Sensitized C-fiber nociceptors	One or more forms likely present in those patients who are hypersensitive to external stimulation	Patients often report dysesthesias; unclear whether these should be considered allodynia
Presence of abnormal temporal summation of pain	Central sensitization: heightened integration of successive noxious inputs by central neurons	Found in many patients	Has not been systematically evaluated
Contact detection sensitivity	Integrity of Aβ mechanoreceptors or central inhibition of mechano-receptors by noxious inputs	Loss of sensitivity in many patients	Loss of sensitivity in many patients
Warmth detection sensitivity	Integrity of C-fiber thermoreceptors	Loss of sensitivity in many patients	Loss of sensitivity in many patients
Cold detection sensitivity	Integrity of Aδ thermoreceptors	No change in sensitivity based on the available data	Loss of sensitivity in some patients
Heat pain detection sensitivity	Integrity of Aδ or C-fiber nociceptors or injury-induced sensitization of C-fiber nociceptors	No change in sensitivity based on the available data	Loss of sensitivity, no change in sensitivity, and increased sensitivity have all been observed
Cold pain detection sensitivity	Integrity of C-fiber nociceptors, injury-induced sensitization of C-fiber nociceptors, or central disinhibition of C-fiber nociceptor input due to loss of Aδ thermoreceptors inputs	Increased sensitivity in many patients	Loss of sensitivity observed in many patients, but increased sensitivity in some patients

patients develop persistent pain; another is that many patients experience pain in difficult-to-test dentoalveolar or intraoral locations.

Compared to the high incidence of sensory impairment after trigeminal nerve injury, the incidence of neuropathic pain (ie, pain initiated or caused by a primary lesion in the nervous system)[13] is relatively low. For example, nerve injury accompanies extraction of teeth, which is experienced by most individuals during their lifetimes. However, permanent neurosensory disturbances seldom occur; the highest incidence, for removal of impacted third molars, is about 1%.[6,14] For patients so affected, alterations in sensation from injury to the inferior alveolar or lingual nerves can be bothersome and unpleasant (dysesthetic). However, few patients meet all of the criteria for a diagnosis of neuropathic pain, ie, persistent, ongoing, episodic, or spontaneously paroxysmal pain in the absence of noxious stimulation.[15] The highest incidence of neuropathic pain (probably about 5%) is associated with pulpal necrosis and endodontic therapies.[16,17] Because the persistent pain in these individuals is largely localized in dentoalveolar and intraoral tissues, psychophysical testing is difficult to perform. Rather, most investigations of neuropathic pain originating from the teeth have focused on the history of inciting events, diagnoses based on anesthetic blocks, and pharmacologic treatments.

No single study in isolation has addressed how sensory function differs in trigeminal nerve–injured patients who develop neuropathic pain and trigeminal nerve-injured patients who remain pain-free. As such, sensory testing data from administration of the exact same procedures do not exist for these 2 groups of patients. Similarities and differences in the sensory function of trigeminal nerve-injured patients with and without pain can only be inferred; such inferences are limited in validity yet provide insight that is unavailable otherwise. The sensory testing approaches employed to date have sought to characterize patients' responses to relatively simple tactile stimuli (moving brush and filament) and controlled thermal stimuli,[10–12,18–20] as shown in Table 1. This table summarizes test outcomes for trigeminal nerve–injured patients with and without pain. These outcomes will be described in greater detail in the text of this article. Limitations of the sensory testing methods are discussed at the end of this article.

Symptoms of Patients with Neuropathic Trigeminal Pain

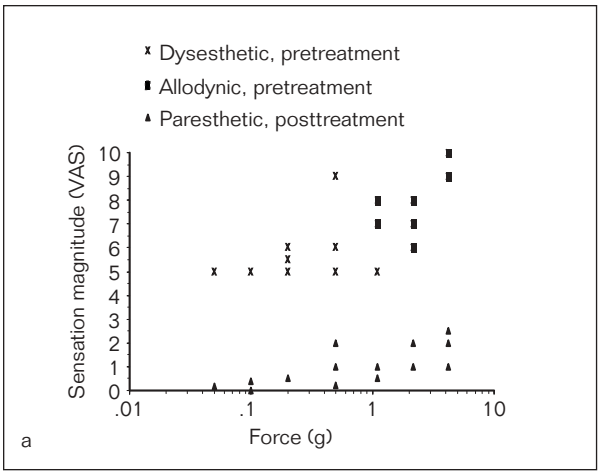
Among the first studies to systematically analyze sensory findings from patients with pain was that of Gregg,[21] in which 84 candidates for microsurgical nerve exploration and repair procedures were studied. The inciting nerve injuries were attributed mainly to third molar surgery, preprosthetic surgery, orthognathic surgery, accidental trauma, and root canal therapy. The timing, quality, and intensity of pain evoked by light touch (5 g) with a small, soft moving brush or with a pin (to detect allodynia and hyperalgesia, respectively), repetitive prick with a pin (15 g, to detect hypoesthesia and anesthesia), and blunt strain-gauge pressure (30 g, to detect hyperpathia or delayed surging pain after moderate pressure) were assessed. In addition, the patients rated their present pain intensity on a visual analog scale (VAS) from 0 (no pain) to 100 (excruciating pain) and described its sensory, affective, and evaluative aspects by completing the McGill Pain Questionnaire. Anesthetic blocks of the injured nerve or sympathetic ganglia were administered to assist in diagnosis.

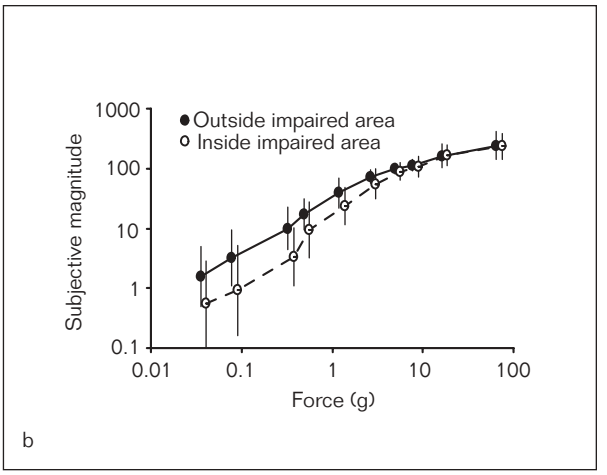
In contrast to pain-free nerve-injured patients, 81% of the 84 patients reported constant pain (with a period of exacerbations noted for most), while 19% reported intermittent or only stimulus-evoked pain. The global pain intensity averaged about 60, which denoted distressing pain. Four symptom components, in combinations of 2 or 3, were found to characterize the main features of the pain. Fifty-one patients (61%) exhibited elements of hyperalgesia (defined as synonymous with allodynia and hyperesthesia) and most often described their pain as "sharp, lacerating, flashing, jumping, stinging, and shooting." Twenty-four patients (29%) exhibited elements of anesthesia dolorosa and described their pain as "numbing, drawing, itching, crawling, annoying, and heavy." These patients had absent or markedly reduced sensation of the applied stimuli. Seventy-one patients (85%) exhibited elements of hyperpathia and described their pain as "dull, sore, tender, aching, gnawing, and radiating." Thirty-five patients (42%) exhibited elements of sympathetically mediated pain and selected from among the following words to describe their pain: hot, burning, nagging, nauseating, lancinating, and agonizing.

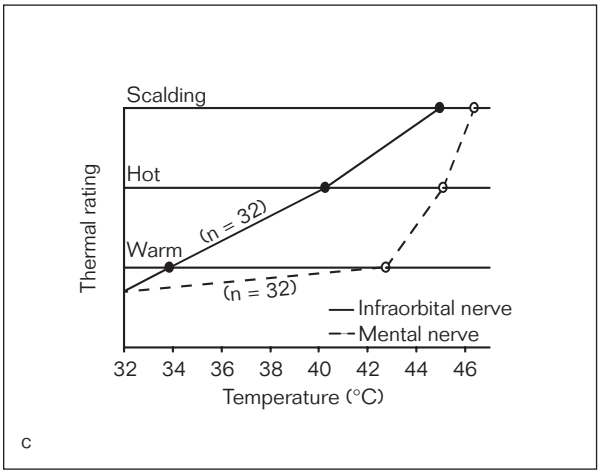
The analysis provided in Gregg[21] established that most patients who develop neuropathic trigeminal pain severe enough to warrant surgical treatment exhibit symptoms similar to those exhibited by patients with spinal neuropathic pain, eg, spontaneous pain (81% of patients) and pain in response to stimuli that are normally nonpainful (61% of patients).[15,20,22] Sensation was not markedly reduced (or absent) in most patients (71% of patients studied by Gregg[21]), and patients could be grossly classified as either "hypersensitive" or "hyposensitive" to externally applied stimuli, which suggests that different mechanisms were associated with the patients' clinical pain. The symptom complexes identified in Gregg[21] are not found in patients without neuropathic pain, although stimulus-evoked dysesthesias to stimulation of the affected tissues are often reported.[1,2,8]

Pain Evoked by Innocuous Mechanical Stimuli

Although roughly one third of patients with neuropathic pain are hyposensitive to externally applied stimuli, the majority are hypersensitive and report pain to stimuli that are normally nonpainful (ie, allodynia). Recent physiological and clinical studies of pain have differentiated allodynia to moving cotton-swab or brush stimuli (dynamic allodynia), to indenting filament stimuli (punctate allodynia), and to blunt pressure stimuli (static allodynia).[19,22] Dynamic and punctate allodynia reflect a state of central sensitization in which signals from Aβ low-threshold and Aδ high-threshold mechanoreceptors, respectively, access trigeminothalamic pain pathways. Only anecdotal examples of data that characterize the pain evoked by different types or intensities of mechanical stimulation in patients with posttraumatic neuropathic trigeminal pain are found in the literature (Fig 1).[16,17,23] In contrast, allodynia in patients with postherpetic neuropathic trigeminal pain has been studied extensively. Studies of these patients demonstrate the usefulness of psychophysical approaches in understanding the mechanisms underlying 1 form of neuropathic pain and provide a model for future studies on posttraumatic trigeminal neuralgia. About 80% of patients with postherpetic neuralgia (PHN) exhibit at least 1 of the 3 types of allodynia, and 50% to 60% of patients exhibit allodynia to low-intensity, moving tactile stimuli.[22,24] Moreover, the intensity of the allodynia correlates with the severity of the patient's clinical pain early in the course of the neuralgia, suggesting that patients' pain may be maintained by different mechanisms throughout its natural course. Based on the limited literature, allodynia may not be observed as frequently in patients with posttraumatic neuralgia as in patients with PHN, and it may be less severe in PHN patients. Its







Figs 1a to 1c *(a)* Subjective intensity and the quality of sensations evoked by filament stimuli applied within the painful area of a patient with neuropathic trigeminal pain. The patient experienced force-independent dysesthesia to forces < 1 g and force-dependent allodynia to forces > 1 g, indicating central sensitization. After treatment with motor cortex stimulation, only mild, force-dependent paresthesia was reported. Reproduced from Meyerson et al[23] with permission from Springer-Verlag. *(b)* Mean ratings (± SE) of subjective touch intensity from pain-free patients with injuries to the inferior alveolar nerves. Reproduced from Essick et al[8] with permission from American Association of Oral and Maxillofacial Surgeons. *(c)* Mean ratings from 16 patients (n = 32 sides) of thermal sensations evoked by stimuli applied to sites innervated by the infraorbital nerve (control) and mental nerve after mandibular preprosthetic surgery. Reproduced from Frost et al[1] with permission from American Association of Oral and Maxillofacial Surgeons.

relationship to the patients' clinical complaints has not been investigated to date.

Perception of Tactile and Thermal Stimuli

To the author's knowledge, only 1 study of QST data from a cohort of patients with posttraumatic neuropathic trigeminal pain has been published. Eide and Rabben[25] studied 15 patients with neuropathic pain secondary to facial trauma, maxillofacial surgery, or dental treatments. All patients reported spontaneous continuous pain, and most patients (73%) additionally reported pain evoked by movement, touch, cold, heat, or psychological stress. Sensory testing was performed within the unilateral painful area on the face and on the contralateral nonpainful, spatially matched site. Thresholds for contact detection were determined with calibrated nylon von Frey filaments applied in an ascending and descending method of limits. Thermal thresholds were determined with a modified Marstock method: The temperature of a contact probe was increased or decreased from baseline skin temperature (32°C) until the patient responded by pressing a button, thereby denoting perception of warmth, cold, heat pain, or cold pain, per the examiner's instructions.

Thresholds for touch detection and warmth perception were higher, on average, on the painful site, denoting tactile and warm hypoesthesia. Thresholds for cold perception and for heat pain perception were comparable on the nonpainful and painful sides. Thresholds for cold pain perception were lower on the painful side, denoting cold allodynia (Fig 2). With the exception of cold pain, these data demonstrate a strong similarity to published data from pain-free patients with injured but nontransected trigeminal nerves.[1–3,8,9,26] For example, using methods similar to Eide and Rabben,[25] Essick et al[8]

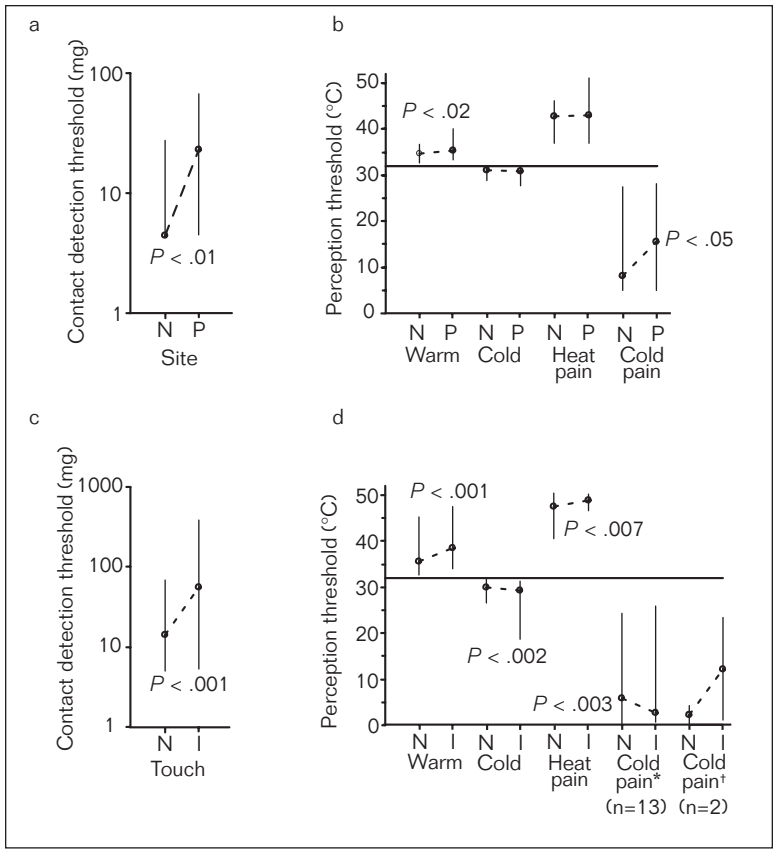


Fig 2 *(top)* Psychophysical threshold data (median and range) from painful (P) and contralateral control (N) sites on the faces of patients with posttraumatic neuropathic pain. *(a)* Contact detection thresholds in mg force. *(b)* Perception thresholds for warm, cold, heat pain, and cold pain. Data taken from Eide and Rabben[25] with permission from Lippincott, Williams and Wilkins. *(bottom) (c and d)* Data from impaired areas on the chin (I) and on adjacent, normal skin sites (N) of pain-free patients with injured inferior alveolar nerves. Cold pain thresholds are plotted separately for patients who did not (n = 13) and did (n = 2) exhibit cold allodynia.[8] *Patients without allodynia. †Patients who demonstrated cold allodynia.

studied 15 patients with injured inferior alveolar nerves. Thresholds from opposite sides of the border of sensory impairment, identified by altered sensitivity to pinprick, were obtained and are plotted in Fig 2 *(bottom)* for comparison with the data from Eide and Rabben.[25]

Detection of Tactile Stimuli

Elevated thresholds for touch perception were observed in patients with and without pain and were interpreted to reflect loss of low-threshold mechanoreceptors (large myelinated Aβ fibers; Figs 2a and 2c). In other studies, tactile detection thresholds have been found to be impaired in the cutaneous distributions of 50% to 70% of trigeminal nerves that were judged to be injured by other criteria.[2,9] In pain-free patients, the subjective intensity of the stimulation is often normal for suprathreshold forces. As illustrated in Fig 1b, the loss in subjective touch intensity for impaired skin sites compared to normal ones decreases as the stimulus force is increased ($P < .001$ for force-by-location interaction). The data were obtained from application of filament stimuli to sites on either side of the border of sensory impairment as mapped by altered sensitivity to pin prick. Although suprathreshold stimuli are perceived to have normal intensity in pain-free patients, they often feel abnormal or paresthetic: Seventy-three percent of the patients studied by Essick et al[8] reported that suprathreshold filaments seemed to stimulate an "island," ie, a greater area of skin than a single point, or felt "dull," "blunt," "flat," "like an eraser," or "numb." These same stimuli evoked discomfort (punctuate allodynia) in pain patients who were hypersensitive to external stimulation (Fig 1a).

The use of contact detection thresholds in the evaluation of pain-free trigeminal nerve–injured patients is supported by many studies. In a recent study, Teerijoki-Oksa et al[9] showed that impairment in contact detection 2 weeks after orthognathic surgery correlates better with the severity of nerve damage, documented intraoperatively using nerve conduction methods, than does impairment in brush-stroke direction discrimination, spatial acuity, or warm/cold or sharp/blunt differentiation. It is unclear, however, whether impairment in touch perception in patients with neuropathic pain correlates with similar electrophysiologic indices of lost innervation. This is because central neural mechanisms associated with pain, as well as loss of peripheral mechanoreceptors, can impair touch

perception. For example, touch perception on the face is impaired by co-localized, experimentally induced pain,[27] and impaired touch perception can be restored to normal in some patients by treatments that alleviate persistent facial pain.[28]

Warmth Perception

Elevated thresholds for warmth perception have been observed, on average, in both patients with and without neuropathic trigeminal pain (see Figs 2b and 2d) and are interpreted to reflect loss of warm-specific thermoreceptors (finely myelinated Aδ and C fibers). Studies of nerve-injured patients often find deficits in warmth perception,[1-3,5,8,9] and thresholds remain elevated for longer periods of time than do those for other basic sensory functions (eg, touch detection) in patients who recover sensation.[3] These 2 findings suggest that tests of warmth perception are more sensitive to nerve injury than other sensory tests. In addition to threshold methods, clinical investigators have instructed patients to report the sensations evoked by slowly rising temperature ramps from 30°C to 50°C. Trigeminal nerve-injured patients with deficits in warmth perception often report explosive, hot sensations because the temperature range from detecting warmth to experiencing scalding heat is greatly reduced (Fig 1c).[1]

In contrast to patients with posttraumatic neuropathic trigeminal pain, patients with postherpetic neuropathic trigeminal pain exhibit lower thresholds for warmth perception (denoting warm hyperesthesia) in painful test sites than in nonpainful test sites.[22] This suggests that nerve damage from viral infection affects sensory function differently than nerve damage from mechanical trauma. In addition, sensory findings from patients with thoracic PHN differ from those of patients with trigeminal PHN. This indicates that sensory findings from damaged spinal nerves cannot be assumed applicable to damaged trigeminal nerves.

Sensitivity to Cold and Heat

Eide and Rabben[25] found that, on average, the threshold for cold pain was lower within painful sites than within nonpainful sites (ie, higher temperatures than normal evoked cold pain), although the percentage of patients affected was not reported (Fig 2b). About 10% to 20% of pain-free patients with long-term sensory deficits after trigeminal nerve injuries provide psychophysical evidence for, or subjective reports of, cold allodynia or hyperalgesia.[2,3,8,26] For example, 2 of 15 patients (13%) in the study by Essick et al[8] demonstrated cold allodynia, whereas 8 patients (53%) exhibited no change and 5 (33%) exhibited cold hypoalgesia (Fig 2d). Increased sensitivity to thermal stimuli is often attributed to injury-induced sensitization of C-fiber nociceptors. However, nerve-injured patients with cold allodynia or hyperalgesia do not necessarily exhibit heat allodynia or hyperalgesia, as evidenced by the patients studied in Eide and Rabben[25] and Essick et al.[8] Alternatively, cold allodynia may result from injury to Aδ cold-specific thermoreceptors. Such an injury can unmask the signals from normal C-fiber nociceptors that are evoked by mild-to-moderate levels of cooling (see Greenspan[19] for discussion). In this situation, increased thresholds for cold perception are predicted.

In contrast to this prediction, neither heat allodynia (supporting sensitization of C-fiber nociceptors) nor cold hypoesthesia (supporting disinhibition) was exhibited by the pain patients studied in Eide and Rabben[25] (Fig 2b). Other studies have variably found impairment in cold and heat pain perception after nerve injury.[3,8,9] For example, in the study by Essick et al,[8] thresholds for both modalities were increased on average (Fig 2d), but analyses of data from individual subjects revealed impairment in only 40% of patients for cold pain and 47% of patients for heat pain. Interestingly, sensitivities to noxious cold and hot stimuli are not altered in painful sites of patients with trigeminal PHN, in contrast to patients with thoracic PHN.[22]

Heat allodynia or hyperalgesia has been documented in some trigeminal nerve–injured patients. For example, Campbell et al[2] instructed patients to rate the intensity of thermal stimuli on a VAS from 0 (no thermal sensation) to 100 (most intense sensation imaginable). The temperature of the stimulus was increased in brief, fixed increments, and ranged from 43°C to 51°C. Pain estimates of 100 in response to temperatures below 45°C were interpreted as evidence of abnormal increased sensitivity to noxious heat. Such responses of maximal pain to temperatures below the typical pain threshold were obtained from 6 (18%) of 34 nerve-injured patients, none of whom was diagnosed with neuropathic pain. Some patients in the study also reported cold hyperalgesia. However, overall, the patients did not consider the neurosensory disturbances "a serious distressing problem."[2]

Temporal Summation of Pain

Similar to mechanical allodynia, abnormal temporal summation of pain is reflective of a state of

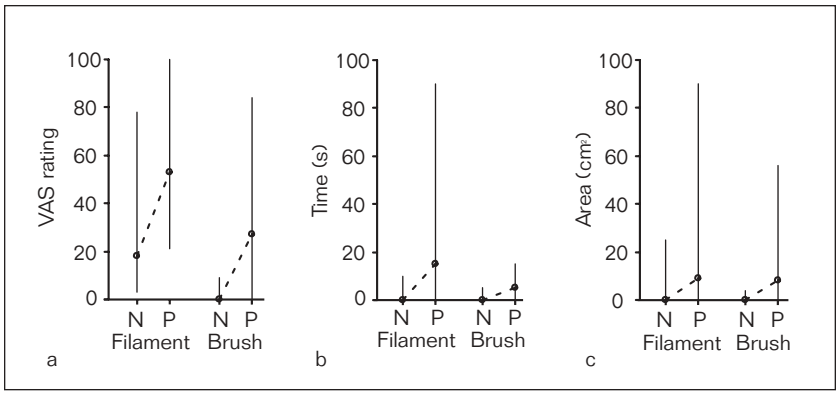


Fig 3 Temporal summation of pain on the painful areas on the face (P) and on the contralateral control sites (N) of patients with posttraumatic neuropathic pain. Median and range of values are shown. *(a)* Maximum increase in pain intensity. *(b)* Persistence of evoked pain after termination of the stimulation. *(c)* Area over which evoked pain radiated from site of stimulation. Median estimates from the painful sides exceeded those from the nonpainful control sides ($P < .005$). Data taken from Eide and Rabben[25] with permission from Lippincott, Williams and Wilkins.

central sensitization that is thought to underlie, in part, ongoing clinical pain in neuropathic pain states.[20,29] Temporal summation refers to the increasing subjective intensity of pain evoked by noxious stimuli delivered in succession. Temporal summation of stimulus-evoked pain was assessed in the patients studied in Eide and Rabben[25] by 2 methods. First, the skin was prodded at 3 Hz for 30 seconds with a stiff filament (marked "6.65 units," corresponding to about 447 g-wt). Second, the vibrating bristles of an electric toothbrush were applied to the skin for 30 seconds. Throughout both modes of stimulation, the patient rated the intensity of the pain on a 100-mm VAS so that the maximum difference in the pain before and during the stimulation could be determined. It was found that on the painful site, the intensity of the temporally summated pain (presumably pricking or burning in nature) increased to a greater extent for both the repeated filament and brush vibration stimulation (Fig 3a). The pain often radiated from the stimulus site and persisted after stimulation (Figs 3b and 3c). Stimulation of the nonpainful site seldom caused discomfort, radiation of a painful sensation, or aftersensation.

Repeated filament and vibrating brush stimuli activate Aβ low-threshold mechanoreceptors and Aδ high-threshold mechanoreceptors.[29,30] The stimuli were not painful initially; however, pain appeared after 5 to 15 seconds and progressively increased in intensity thereafter, which suggests abnormal temporal summation of stimulus-evoked pain.[25] The pain could not be attributed simply to the presence of mechanical hyperalgesia or allodynia, in which case the stimuli would have evoked pain or tenderness-to-touch upon first presentation.[24,30] Abnormal summation of pain was additionally supported by the pain's radiation and persistence and was interpreted to reflect heightened N-methyl-D-aspartate (NMDA)–dependent sensitization of wide dynamic neurons in the trigeminal spinal nucleus that receive converging inputs from myelinated and unmyelinated afferents.[20,29] Consistent with this interpretation, NMDA receptor antagonists have been shown to inhibit the abnormal temporal summation of pain in patients diagnosed with trigeminal PHN and with idiopathic trigeminal neuralgia and to reduce the patients' clinical pain.[29] To the author's knowledge, abnormal temporal summation of pain has not been reported in trigeminal nerve–injured patients who remain pain-free, but it is unclear whether these patients have ever been formally tested for it.

Uses and Limitations of QST

Comparison of the sensory function of nerve-injured patients with and without pain requires QST, a means by which a subject's response to external stimulation can be systematically measured and studied.[10–12,18–22] Of particular relevance to nerve-injured patients are the intensity of stimulation that is detected (threshold estimation) and how suprathreshold stimulation subjectively feels (quantitative and qualitative assessments). Significant

differences in test outcomes compared to control data indicate alterations in sensory function and sensation, respectively. Often these alterations can be attributed to suspected anatomical or functional changes within the peripheral or central nervous systems. However, normal thresholds and normal evoked sensations do not exclude such changes.[3,8,9] This is particularly true when other evidence suggests that the changes are minor or when more than 1 neural mechanism can provide the information needed for normal performance on the tests.

Evaluation of the validity of sensory testing in detecting nerve injury and its central consequences is complicated by the lack of proven or generally accepted "gold standards."[18] Other articles in this issue also make note of this.[10–12] Disappointing results are often attributed to the problems inherent in sensory testing rather than to a lack of understanding of the underlying pathophysiology and its effects on the sensory dimensions being tested. To illustrate, patients' performance on sensory tests correlates poorly with the degree of crushing and stretching nerve trauma observed during orthognathic surgery.[9] This finding indicates that there is no simple obligatory relation between what appears to be nerve damage and altered sensory function, rather than a failure of the sensory testing approaches. Electrophysiologic indices of impaired nerve conduction provide a more objective measure of nerve damage, yet measurement of the same indices 2 weeks after surgery has a diagnostic accuracy of only about 70%.[9] The diagnostic accuracy of sensory tests is generally much less; such tests suffer mainly from poor sensitivity in identifying patients who exhibit impaired nerve conduction intraoperatively.[9] Higher diagnostic sensitivity is obtained from administration of a battery of sensory tests that evaluate different sensory functions.[3,8,9] This is because the probability that some test will specifically target the individual patient's impairment or have sufficient sensitivity is increased. A controversial candidate for gold standard is the patient's subjective report of abnormal stimulus-evoked sensation.[7,8,18] In this case, the diagnostic sensitivity of a test reflects the likelihood that the patient who reports altered sensation will in addition perform abnormally on the test. A battery of tests is administered to characterize the different aspects of sensory dysfunction of the individual patient. Emphasis is placed on understanding the individual patient's altered sensory experiences, rather than detecting peripheral or central neural pathology, which may or may not affect the specific sensory functions targeted by the tests employed.

The validity of some measures of sensory function is established indirectly by their clinical usefulness and their sensitivity to treatments that alter patients' pain. For example, the evaluation of allodynia has proven useful in categorizing patients with neuropathic pain into groups that share common sensory and clinical characteristics, as described in previous sections of this article, or different prognoses for pain management therapies.[21,22,31] Moreover, those with neuropathic pain can be subclassified according to type of pain (eg, posttraumatic versus PHN). Treatments that reduce clinical pain often, but not always, reduce allodynia (Fig 1a) and normalize temporal summation of pain.[20,23,28,29] These observations imply that tests for allodynia and abnormal temporal summation of pain provide meaningful information about neuropathic pain, and in that respect are valid.

It is generally accepted that different sensory tests evaluate the integrity of different classes of primary afferents and the different central neural structures to which they project.[1–3,5,7–10,18–22,24–26,32] Supporting evidence comes from both animal and human studies that demonstrate that different classes of afferents, identified in part by their conduction velocity, are uniquely sensitive to mechanical, warm, cold, and noxious stimulation. Moreover, when the classes are selectively eliminated by local anesthesia or pressure nerve blocks, the sensations associated with the respective classes disappear. Recent findings, however, have demonstrated that strict reliance on this traditional "labeled-line" model to explain sensory abnormalities in nerve-injured patients and patients with neuropathic pain is overly simplistic and flawed. For example, as noted in previous sections, stimulation of afferents that normally subserve touch often produce pain, and stimulation of afferents that produce pain can inhibit touch, even in the absence of nerve damage.[27,32] These observations emphasize the importance of central neural processing and integration of information from different classes of afferents. The reader is referred to Essick,[18] Greenspan,[19] and Price et al[20] for additional information on sensory test outcomes and neural mechanisms.

Poor or insufficient reliability is often cited as a major limitation of QST.[2,3,5,8,9,18] For example, repeated estimates of sensory thresholds often vary 100% or more when measured over periods of weeks or months. Sources of error include normal variations in human sensory sensitivity (often referred to as "central factors"), variations in the subject's response bias, technical variations in test administration, and numeric estimation error inherent in patient-acceptable testing paradigms,

for which only a marginal amount of data is collected. This variability has limited efforts to establish accepted reference values and useful normative limits for individual sensory tests and to determine whether values from, eg, painful and nonpainful sites of the same patient are truly different. It is relevant to the studies of Eide and Rabben[25] and Essick et al[8] discussed in this article (as well as to most other clinical studies) that the threshold values were determined, in part, by the patients' individual criteria for the targeted sensations.[18] These criteria likely varied somewhat from patient to patient. Moreover, should the patients have used different criteria in responding to stimuli applied to painful versus nonpainful sites[25] and to injured versus noninjured sites,[8] differences in the threshold values would have been generated regardless of whether the sites differed in sensitivity. Although within-session shifts in response-bias likely confound the outcomes of tests that require complex decision making, eg, tests of 2-point discrimination,[2,3,7,8] they are less likely for tests that simply measure the detection of stimulation. For example, it is reasonable to assume that most patients report "cold" when the same level of cold is sensed in painful and nonpainful skin sites, or in injured and noninjured sites.

Another problem in the clinical application of sensory testing methods is the exquisite sensitivity of test results to variations in stimulus control and delivery. As an example, thermal sensitivity can be assessed by the ability to discriminate cold and hot objects of nominal temperatures or by the estimation of warm and cold detection thresholds by the use of computer-controlled state-of-the-art instrumentation.[9,18] The diagnostic sensitivity of the latter is appreciably greater than the former.[9] In addition, investigators report differences in the usefulness of sensory tests that are difficult to attribute to any suspected cause. For example, tests based on patients' ability to discriminate direction of motion across nerve-injured skin have been reported to provide both the most[8] and least[3] sensitive measure of sensory impairment in similar populations of trigeminal nerve–injured patients.

All considered, these observations raise concern about the use of psychophysical approaches in the evaluation of patients. However, they also attest to the complexity of the human response to subtle variations in stimulation and testing conditions. Only with a better understanding of this complexity than currently exists can standardized procedures and guidelines for sensory testing be established with confidence.

Conclusions and Future Directions

The findings presented in this article make evident that very little is known about sensory function in trigeminal nerve–injured patients who develop neuropathic pain compared to those who remain pain-free. To properly address this issue, both patient groups should be tested with the same protocols in the same environment. If differences are identified, it should be determined whether they can be attributed to the severity of the injuries or to pre-existing sensory differences in the patients. This can be addressed by multicenter longitudinal studies of patients who undergo elective surgical procedures that entail nerve damage. The aim would be to ascertain whether those patients who developed pain exhibited unique sensory profiles presurgically. For those patients who develop pain, the relationships between measures of pain sensitivity, central sensitization, and the patients' clinical pain should be studied to better understand the underlying pathophysiology, paralleling the approaches that have proven useful in studying patients with PHN. In addition, differences in the sensory function of patients with posttraumatic trigeminal pain and posttraumatic spinal nerve pain should be critically examined for cues that might explain why fewer patients might develop pain after trigeminal nerve injuries.[33] Last, basic research on psychophysical methods is needed to better understand and control those factors that introduce variability in measurements and limit the clinical usefulness of sensory testing.

Acknowledgments

The author's work was supported by NIDCR grant DE07509. The author would like to thank Dr John Zuniga and Dr Mark Hollins for their helpful comments on this manuscript and Mr Raj Prajapati for preparation of the figures.

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