Reliability and Characteristics of Current Perception Thresholds in the Territory of the Infraorbital and Inferior Alveolar Nerves

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Aims: *To estimate the intra- and interrater reliability of current perception threshold (CPT) evaluation, especially within the infraorbital nerve territory (ION) and inferior alveolar nerve territory (IAN) of the orofacial region, and to characterize the CPTs of ION and IAN in the normal population.* **Methods:** *Electrical stimulation (at 2,000 Hz, 250 Hz, and 5 Hz) was applied to ION and IAN to allow for CPT evaluation in 200 subjects, all of whom were healthy, had no systemic diseases, and were free from symptoms and history of neuropathic conditions. Twenty-five of the subjects were evaluated 3 times by 2 examiners to test reliability, and the remaining subjects were evaluated once for normative data.* **Results:** *The intraclass correlation coefficient of CPTs within examiner and between examiners ranged from 0.46 to 0.95. There were no significant differences between right and left sides in CPT evaluation within the ION and IAN territory. Gender and age did not affect the CPT values for ION and IAN in the normal population. There were significant differences between each of the 3 frequency-dependent (2,000 Hz, 250 Hz, 5 Hz) measures within ION and IAN ($P < 0.001$).* **Conclusion:** *Evaluation of CPTs within ION and IAN revealed good intra- and interrater reliability. The study also provided normative data of CPTs of ION, IAN, and the between-site and within-site ratios of CPTs of ION and IAN. This should prove useful in the diagnosis of orofacial neuropathy.*
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Key words: current perception threshold, quantitative sensory test, neuropathic pain, trigeminal nerve

When peripheral somatosensory nerves are damaged by disease or trauma, a small percentage of patients develop symptoms that nearly always include some kinds of pain. Such pains are said to be *neuropathic* because they are believed to be the result of a dysfunctional nervous system. Neuropathic pain ranges from mild and dysesthetic to excruciating. It is unclear how many people suffer from neuropathic pain, but it is conservatively estimated that 0.6% to 1.4% of the total population suffer from this condition.[1] Sensory neuropathies, such as cancer-associated pain, phantom pain, paresthesia after dental extraction, and trigeminal neuralgia, occur frequently in the orofacial region. The earliest stages of neuropathic conditions usually affect sensory nerves, while motor nerves are generally affected in the later stages. Indeed, the presenting complaint of most patients to pain clinics is sensory and not motor in origin.

Neuropathic conditions are usually chronic and often fail to respond to any current therapies. Treatment of the condition causing neuropathy at the earliest stages, when it is limited to the sensory nerves, should provide a better prognosis. Early detection is the key to successful intervention.[2] Therefore, sensory neurologic tests, which allow for early detection, characterization, and follow-up of the condition, are very important. Traditional methods of assessing the sensory nervous system, such as the use of a safety pin, a tuning fork, or a pinwheel, are highly subjective, variable, and prone to examiner bias. This makes their use for longitudinal assessment over time very difficult. Because of this, quantitative sensory tests (QSTs) such as somatosensory-evoked potential, vibratory perception threshold, and thermal perception threshold have been developed. The QSTs can reveal the functional status of myelinated and unmyelinated primary afferents or central somatosensory pathways and their modulation by central summation mechanisms.[3] The QSTs for peripheral nerve integrity provide more clinically relevant information than other physiologic tests such as nerve conduction velocity or electromyographic examination[4] or imaging approaches such as magnetic resonance imaging.

The current perception threshold (CPT) evaluation is one of the QSTs that provides a functional assessment of the somatosensory system. The CPT is the minimum amount of a transcutaneously applied current that an individual consistently perceives as evoking a sensation. The evaluation is painless, noninvasive, and easy to perform. Furthermore, the electrical stimulus has been claimed to selectively excite distinct subpopulations of nerve fibers as a function of sinusoidal frequency.[5–7] The 2,000-Hz stimulus evokes responses attributable to activation of Aβ fibers, the 250-Hz stimulus evokes responses related to Aδ fibers, and the 5-Hz stimulus evokes responses related to C fibers. Thus, CPT evaluation provides selective activation of fiber types, and each of these fiber types has a characteristic neurophysiologic profile. The simplicity and neuroselectivity of CPT evaluation are distinct advantages, and many research centers have used CPT to assess neuropathies.[8]

A few studies have applied a full quantitative sensory testing assessment to the orofacial region. Mechanical, thermal, or electrical stimuli have been used to characterize diseases in the orofacial region such as burning mouth syndrome, trigeminal neuralgia, and temporomandibular disorders.[9–14] But CPT characteristics have not been reported for the orofacial region according to gender and age in a normal population. Although reproducibility should also be taken into consideration before a method is introduced in routine clinical work, no clinical data regarding the reliability of CPT in the orofacial region have been published.

Table 1 Gender and Age Distribution of the 200 Subjects in Experiment 2

Age (y)	Men	Women	Total
10 to 19	20	20	40
20 to 29	20	20	40
30 to 39	20	20	40
40 to 49	20	20	40
50 to 59	20	20	40

Because CPT evaluation appears to be of value in investigations of neuropathic conditions of the orofacial region, the present study addressed intra- and interrater reliability of CPT evaluation, especially within the infraorbital nerve territory (ION) and inferior alveolar nerve territory (IAN) of the orofacial region (experiment 1). In addition, the CPTs of ION and IAN in a normal population were characterized (experiment 2). The findings may provide basic clues in the search for the mechanisms of and treatment modalities for neuropathic conditions in the orofacial region.

Materials and Methods

Subjects

Twenty-five healthy volunteers (16 men and 9 women, 23.6 ± 3.2 years) were included in the reliability tests (experiment 1). Two hundred subjects were selected to examine the effect of age and gender on CPT (experiment 2). The age and gender distribution of this group is presented in Table 1. All of the subjects were healthy, had no systemic diseases, and were without symptoms or a history of neuropathic conditions.

Methods

Tests were performed on the lateral side of the ala of the nose (within the ION) and on the skin under the lower lip (within the IAN) (Fig 1). Electrical stimuli were delivered to the skin through 8-mm-diameter spherical gold-plated electrodes spaced 5 mm apart. The CPT was measured with sine-wave pulses delivered by a constant-current system (Neurometer CPT, Neurotron Inc) at 2,000 Hz, 250 Hz, and 5 Hz. In experiment 1, 2 examiners tested both sides of each territory once each day over a 3-day period in the 25 subjects. For

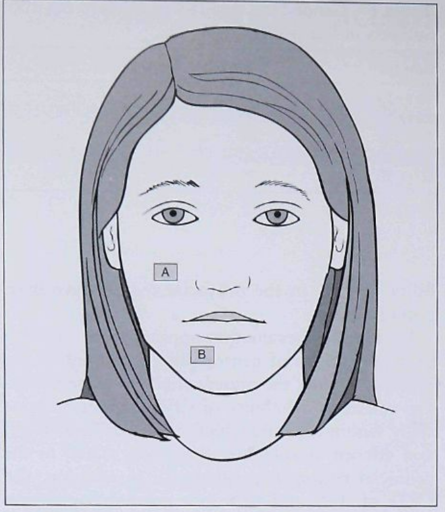

Fig 1 Testing sites. A = infraorbital nerve territory; B = inferior alveolar nerve territory.

Table 2 Intraclass Correlation Coefficients of the Current Perception Thresholds Within and Between Examiners (n = 25)

Frequency/location	Within examiner	Between examiners
2,000 Hz		
Right ION	0.95	0.87
Left ION	0.95	0.71
Right IAN	0.92	0.77
Left IAN	0.90	0.79
250 Hz		
Right ION	0.93	0.62
Left ION	0.83	0.79
Right IAN	0.88	0.74
Left IAN	0.90	0.79
5 Hz		
Right ION	0.83	0.58
Left ION	0.89	0.46
Right IAN	0.88	0.74
Left IAN	0.76	0.75

ION = infraorbital nerve territory; IAN = inferior alveolar nerve territory.

experiment 2, 1 of the 2 examiners tested the randomly selected unilateral side only once in the 200 subjects.

The CPT evaluation was performed as described by Liu et al.[15] The stimulating surface of each electrode was covered by a thin layer of electro-conductive gel held in place with nonconductive adhesive tape. At each frequency, the current was slowly increased from 0.01 mA until the subject reported a sensation. The current was then terminated. A microprocessor-controlled forced choice methodology, which used 6 to 10 cycles of randomly selected real and false stimuli above and below the perception threshold level,[2] was performed in a double-blind manner until the exact CPT value was determined within a 20 µA range. The entire procedure for all 3 frequencies at each site took approximately 5 minutes and was performed in an isolated room to encourage the subject to focus on the stimuli.

Statistical Analysis

The intraclass correlation coefficient (ICC) was calculated to quantify the reliability of the measurements.[16,17] A paired-samples *t* test was performed to investigate the side difference, while an independent-sample *t* test was performed to investigate any gender difference. An analysis of variance (ANOVA) was performed to examine the effects of age on CPTs.

Results

The within-examiner and between-examiners ICC of CPTs ranged from 0.46 to 0.95 (Table 2), revealing good intra- and interrater reliability. No differences were found in CPTs between the right and left sides of ION and IAN of the 25 subjects (Table 3). Therefore, in experiment 2, CPTs were measured on a randomly selected unilateral side in other subjects to characterize CPTs of the normal population.

No gender difference was found in any age group; therefore, the CPTs of men and women were pooled together and analyzed to investigate the effect of age. The CPTs of ION (Table 4) and IAN (Table 5) were not affected by age at any frequency.

The means and standard deviations of CPTs in ION and IAN of experiment 2 are shown in Table

Table 3 Differences in Current Perception Thresholds (Mean ± SD, × 0.01 mA) by Side in the Trigeminal Area (n = 25)

Stimulation	Threshold	Significance
2,000-Hz ION		
Right	93.7 ± 21.6	NS
Left	91.1 ± 22.1	
2,000-Hz IAN		
Right	87.7 ± 22.3	NS
Left	96.3 ± 26.5	
250-Hz ION		
Right	21.0 ± 11.2	NS
Left	19.9 ± 9.5	
250-Hz IAN		
Right	20.8 ± 9.8	NS
Left	22.8 ± 12.7	
5-Hz ION		
Right	11.4 ± 6.9	NS
Left	11.3 ± 6.2	
5-Hz IAN		
Right	11.8 ± 6.6	NS
Left	13.2 ± 6.7	

ION = infraorbital nerve territory; IAN - inferior alveolar nerve territory; SD = standard deviation; NS = not significant.

6. No differences were seen between CPTs of ION and those of IAN at the same frequency. However, there was a significant difference between each of the 3 frequency-dependent CPT measures within each nerve territory. Between-site ratios are presented in Table 7. Within-site ratios of CPTs of ION and IAN are shown in Table 8.

Discussion

Because of its double-blind test possibilities, simplicity, and selectivity, CPT evaluation has been widely employed as a QST for the assessment of various neuropathic conditions.[2,5,6] Since CPT evaluation can be conducted in a double-blind automated testing approach, neither the subject nor the operator controls the actual CPT determination, and neither can influence the test outcome based upon their subjective impressions. No operator interpretation of test results is necessary to determine CPT measurements. Therefore, the CPT evaluation is an objective test, with minimal experimenter bias, for quantifying the functional integrity of sensory nerve fibers or their central somatosensory pathways.

In all kinds of clinical and paraclinical measurements, reliability must be considered in the selection of the appropriate technique and in the establishment of how much change can normally be expected from one measurement to the next. This study was conceived because of the lack of data available in the literature, save for 1 study of the reliability of CPT evaluation in the orofacial region. Goldstein et al[18] performed a test-retest reliability analysis of CPT evaluation over the mental foramen and reported that α values were satisfactory for all frequencies. The ICC is the fraction of variance caused by variation between subjects (range 0 to 1). Thus an ICC value of 1 reflects perfect reproducibility, an ICC > 0.75 generally means "excellent" reliability, while an ICC > 0.4 denotes "good" reliability.[17] In this study, all of the intrarater reliability values of CPTs in ION and IAN were excellent (ICC > 0.75). Although we found less reliability between examiners, 6 of 12 interrater reliabilities were excellent (ICC > 0.75), while the remaining 6 were still good (ICC > 0.4). The high reliability of CPTs, particularly those determined with high-frequency stimulation, is thought to be a result of the ability of the equipment to maintain constant-current output despite alterations in skin impedance.[5] In view of the ICC

Table 4 Characteristics of Current Perception Thresholds (Mean ± SD, × 0.01 mA) in the Infraorbital Nerve Territory According to Age (n = 200)

Age of subject (y)	Threshold		
	At 2,000 Hz	At 250 Hz	At 5 Hz
10 to 19	98.2 ± 34.9	20.5 ± 13.0	11.7 ± 8.9
20 to 29	95.0 ± 24.1	18.6 ± 8.7	9.6 ± 4.9
30 to 39	91.3 ± 23.2	17.6 ± 11.5	9.2 ± 8.0
40 to 49	99.1 ± 24.1	24.8 ± 16.0	13.2 ± 8.5
50 to 59	107.5 ± 26.4	20.8 ± 9.0	10.6 ± 5.2
Significance	NS	NS	NS

SD = standard deviation; NS = not significant.

Table 5 Characteristics of Current Perception Thresholds (Mean ± SD, × 0.01 mA) in the Inferior Alveolar Nerve Territory According to Age (n = 200)

Age of subject (y)	Threshold		
	At 2,000 Hz	At 250 Hz	At 5 Hz
10 to 19	108.6 ± 39.7	21.6 ± 12.6	9.6 ± 7.5
20 to 29	97.6 ± 20.6	21.8 ± 12.5	12.0 ± 6.8
30 to 39	103.7 ± 37.5	24.0 ± 14.0	11.9 ± 9.2
40 to 49	96.4 ± 20.1	22.6 ± 9.7	12.3 ± 7.4
50 to 59	104.0 ± 25.1	23.3 ± 13.1	12.5 ± 10.0
Significance	NS	NS	NS

SD = standard deviation; NS = not significant.

Table 6 Current Perception Thresholds (× 0.01 mA) According to Nerve Territory (n = 200)

Territory/ stimulation	Mean	SD
Infraorbital nerve		
2,000 Hz	98.2	27.1
250 Hz	20.4	12.1
5 Hz	10.9	7.4
Inferior alveolar nerve		
2,000 Hz	102.1	29.9
250 Hz	22.7	12.4
5 Hz	11.7	8.2

SD = standard deviation.

Table 7 Between-Sites Ratios of Current Perception Thresholds (n = 200)

Stimulation	ION/IAN	Significance
2,000 Hz	1.01 ± 0.31	NS
250 Hz	1.07 ± 0.75	NS
5 Hz	1.36 ± 1.55	NS

ION = infraorbital nerve territory; IAN = inferior alveolar nerve territory; NS = not significant.

Table 8 Within-Sites Ratios of Current Perception Thresholds (n = 200)

Territory/ stimulation	Ratio	Significance
Infraorbital nerve		
2,000 Hz/250 Hz	6.63 ± 5.68	$P < 0.001$
250 Hz/5 Hz	2.29 ± 1.39	$P < 0.001$
2,000 Hz/5 Hz	14.2 ± 12.5	$P < 0.001$
Inferior alveolar nerve		
2,000 Hz/250 Hz	5.72 ± 3.18	$P < 0.001$
250 Hz/5 Hz	2.48 ± 1.59	$P < 0.001$
2,000 Hz/5 Hz	14.6 ± 13.8	$P < 0.001$

values obtained from the intra-/interrater analysis, it can be concluded that the use of CPT as a measuring instrument for assessment of the somatosensory system is reliable. Furthermore, our results, showing good reliability of CPTs, are consistent with a previous study.[18]

The procedure of CPT measurement is very simple. A clinician can be taught to perform the test in less than half an hour. Also, the accurate placement of electrodes is not critical because the area of current transmission is fairly large. Therefore, differences in reliability between examiners can be explained by the skill of the operator in inducing the subject to focus on the stimulus. The greatest source of error in CPT testing, as in other QST procedures, is lack of cooperation or, more precisely, lack of attention by the subject. It is critical that the subject focus on the stimulus. The act of increasing the rate of electrical current until the subject reports the first sensation (before the beginning of the microprocessor-controlled double-blind test) also affects CPT. It has been reported that the sensation threshold increases significantly as the rate of current rise is increased; thus, a slowly increasing current yields more accurate and reproducible results than does a rapidly increasing current.[19] Since the double-blind test begins at the level of the first sensation, the rate of increase in the current affects the starting point of CPT evaluation and thus the whole procedure. Therefore, interrater reliability may be improved when the examiners provide a standardized explanation to the subjects and use the same rate of increase in the current to establish a starting point.

In experiment 1, no significant differences were seen between the right and left sides in all CPT values in the trigeminal area (Table 3). Goldstein et al[18] also reported no statistical differences between the right and left sides. Because no significant differences were found, the CPT values of randomly selected unilateral sides were measured in experiment 2.

Some authors report that women are more sensitive than men to stimuli, while others report no difference between men and women.[20–23] They performed their experiments with vibratory, thermal, or mechanical stimuli. Since the thresholds for these stimuli can be significantly affected by various factors such as skin thickness, skin temperature, and the presence of edema, the inconsistent results would seem to be a result of the quality, intensity, and location of stimuli, as well as body size (weight and height) of subjects, rather than of the gender difference itself. We found no gender difference with CPT evaluation of ION and IAN in any age group. Due to the difference in the quality and location of stimuli, it is not meaningful to compare our results to others directly. Our results may provide less distorted information of the gender effect on sensory function because the CPT is known to be unaffected by the above factors.

The effect of age on sensory thresholds has been reported by several authors. These studies also used thermal, vibratory, or mechanical stimuli and are not comparable with our results.[24–28] Only 1 study investigated the effect of aging on CPT values. They reported that CPT findings did not differ significantly between young and old subjects,[29] which is consistent with our results.

The CPT values of ION were not statistically significantly different from those of IAN at each of the 3 stimulus frequencies used in the present study. The similarities between the ION and IAN values may be a result of the nerves belonging to the same cranial nerve (ie, the trigeminal nerve); such characteristics can be used as a diagnostic tool for neuropathies. Between-sites analysis, which includes matched sites and compares CPT values from tests conducted with the same stimulus frequency on different body sites, is recommended for use in clinical practice.[30]

Transcutaneous constant-current sine-wave stimulation at 3 different frequencies has been claimed to activate 3 subpopulations of nerve fibers: unmyelinated C fibers by 5-Hz stimulation, thin myelinated Aδ fibers by 250-Hz stimulation, and large myelinated Aβ fibers by 2,000-Hz stimulation.[31] Some authors have reported indirect evidence of the above selectivity, obtained in various ways.[5–7,32–39] There was a significant difference between each of the 3 frequency-dependent measures within each nerve territory in our results, which may also be considered as indirect evidence for selectivity. The distinct differences in CPT values between the 3 stimulus frequencies suggest the possibility that different types of nerve fibers are involved. The within-site ratio analysis compares CPT values derived from tests conducted with different frequencies on the same body site, permitting each nerve to serve as its own control. The within-site ratio may also be used as a diagnostic tool, as with the between-sites ratio (see above). But validation of the selectivity of CPT evaluation has been questioned.[40] Criticisms include: *(1)* often, the evoked sensations do not mimic sensory perceptions of natural stimuli; *(2)* it is unclear whether receptors or axons of the nerve fibers are directly activated by such stimuli; and *(3)* different functional subtypes of sensory fibers are possibly stimulated simultaneously.[3,40] Further research is needed to determine the degree of selectivity because of the lack of direct evidence.

This study has shown that CPT evaluation is a simple, noninvasive, very reliable method that has many advantages compared to other quantitative sensory testing methods, such as vibratory or thermal threshold evaluation. However, the use of CPT evaluation is limited to nerves close to the skin, since it is impossible to evaluate deeply located nerves. In addition, neuroselectivity still remains to be validated. Most important, as with any neurodiagnostic test, a clinician's interpretation, including a clinical correlation, is essential and necessary for diagnostic purposes. Although our results provide reliability and normative reference values for CPT in a healthy population, further studies should be performed in the orofacial region.

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