Orofacial Thermal Thresholds: Time-Dependent Variability and Influence of Spatial Summation and Test Site

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Aim: *To investigate time-dependent variability and influence of test site and stimulation area size on intraoral cold detection, warmth detection, and heat pain thresholds.* ***Methods:*** *Thirty healthy volunteers (15 women and 15 men) participated. Six extra- and intraoral sites were examined, and cold detection, warmth detection, and heat pain thresholds were measured. Time variability and influence of spatial summation were also studied at one site—the tip of the tongue—three times over a 6-week period. One-way ANOVA for repeated measures and paired sample* t *test compared mean values and SD within and between sites for all thresholds.* ***Results:*** *Several between-site differences were significant (*$P < .05$*). Lowest intraoral thresholds for all stimuli were measured at the tongue site, and at the tongue, thresholds for warmth detection and heat pain, but not cold detection, decreased with increasing size of stimulation area (*$P < .05$*). Overall, thresholds at the tongue site varied nonsignificantly over time (*$P > .05$*).* ***Conclusion:*** *Test site affects orofacial thermal thresholds substantially, whereas time variability and spatial summation on the tongue appear to be modest.* J OROFAC PAIN 2011;25:39–48

Key words: facial pain, neuropathic pain, quantitative sensory testing, reliability, thermal thresholds

Quantitative sensory testing (QST) is used to identify and quantify somatosensory abnormalities, usually in patients with suspected neuropathic pain. A PubMed search on "QST testing" found 69 articles published up to the end of December 2004 and another 120 from January 2005 to March 16, 2009. Interest in QST methods is growing, presumably because equipment is improved and procedures are validated, which makes QST more feasible in a clinical setting and widens the range of applications.[1–3] Svensson et al recommended that chronic intraoral pain patients undergo a comprehensive clinical examination that includes orofacial *and* qualitative and quantitative somatosensory examinations.[4] Recently, the German Research Network on Neuropathic Pain (DFNS) introduced a standardized protocol for assessing somatosensory function at cutaneous test and control sites that takes ~1 hour.[2] Thermal testing parameters are a substantial part of the protocol and are reported to have acceptable reliability on hand as well as on intraoral sites.[5,6] Several factors—such as site, stimulation area size, and time variability—may influence thresholds, and this has not previously been investigated extensively in the oral cavity.[7,8]

Temperature-sensitive afferents supplying the orofacial region are generally reported to be similar to those in other somatic regions.[9] Despite this, various orofacial sites do differ in sensitivity to thermal stimuli.[10,11] Epithelial tissue varies markedly in thickness and degree of keratinization and hydration. Nerve ending density also varies considerably among orofacial sites.[12] Biophysical properties thus influence thermal sensitivity of oral and facial sites.[13,14]

The size of the thermally stimulated area may also affect thresholds; a correlation between perception threshold and stimulation area size was found for several somatosensory measures, including temperature. Spatial summation, which is the phenomenon that an increase in stimulation area size is associated with threshold reduction, has been reported on skin for warmth stimuli,[15,16] for painful heat stimuli,[17,18] and for cold stimuli.[19] Thus, the size of the thermode's stimulation area influences thermal thresholds, which is important to remember when normative values are recorded because thermotesters can vary in size of contact area. If the variation of a thermal threshold can be described as a function of the size of the stimulated area, then threshold values obtained with different thermodes and contact areas can be compared. Extraorally, the magnitude of spatial summation for innocuous and painful heat has been reported to vary according to skin type and skin sensitivity,[20] but current knowledge of intraoral spatial summation is sparse.[8]

Fluctuations over time may also affect threshold determination; for example, Defrin et al[21] and Palmer and Martin[22] observed time-dependent variability of cutaneous thermal thresholds. There appear to be no published reports on intraoral threshold variability over time, and knowledge of the magnitude of such variations is important when considering reliability and applicability in clinical practice.

The aims of this study were to *(1)* compare thermal thresholds between different orofacial sites, *(2)* analyze the relationship between intraoral thermal thresholds and size of stimulation area, and *(3)* investigate time-dependent variability of intraoral thermal thresholds. Thresholds were measured according to the DFNS protocol.

The hypotheses tested were that *(1)* thresholds for perceived warmth, cold, and painful heat vary between different intraoral sites, since the biophysical properties vary in different tissues (gingiva, mucosa),[23] *(2)* thermal thresholds and size of stimulation area are correlated, since the receptive fields of intraoral thermoreceptors have been reported to be small but essentially similar to those of skin,[23] and *(3)* thresholds remain stable over a 6-week period, since cutaneous thermal thresholds have been reported to be relatively stable over a 3-week period.[5] To test the influence of stimulation area and time on thermal thresholds, the tongue—reported to be one of the most sensitive intraoral sites[11,14]—was selected. Because specific pain conditions such as burning mouth syndrome (BMS) affect the tongue, somatosensory testing may provide useful diagnostic information.[24,25]

Materials and Methods

Subjects

Thirty young healthy subjects (mean age 24.9 years, range 20 to 31) participated in the study; 15 were women (mean age 23.5 years, range 19 to 29) and 15 men (mean age 26.3 years, range 22 to 31). All participants were recruited from among students at Malmö University's Dental School. The experimental testing took place from February to April 2007.

Inclusion criteria were good health with no orofacial pain complaints. The exclusion criterion was dental treatment scheduled during the study. In agreement with the 1964 Declaration of Helsinki (2008 revision, www.wma.net), the Regional Ethics Review Board at Lund University approved the study, and all participants signed an informed consent form. Participants received no monetary compensation for study participation.

Study Design

The study comprised three parts:

1. Cold detection (CDT), warmth detection (WDT), and heat pain (HPT) thresholds as described below were compared at six intra- and extraoral sites with the same size of stimulation area.
2. At one intraoral site (the tongue), CDTs, WDTs, and HPTs obtained with five sizes of thermode stimulation areas were compared (see below).
3. At this same site as in part 2, CDTs, WDTs, and HPTs were compared over a 6-week period (see below).

Measurements of Thermal Thresholds. CDTs, WDTs, and HPTs were measured with an MSA Thermotest (Modular Sensory Analyzer, SOMEDIC Sales). All measurements were made with a thermode that was developed especially for intraoral use, with a contact area of 0.81 cm^2. A method of limits was used, with ramped stimuli of 1°C/s, and the procedure ended when the subject pressed a button. The temperature then returned to baseline at a

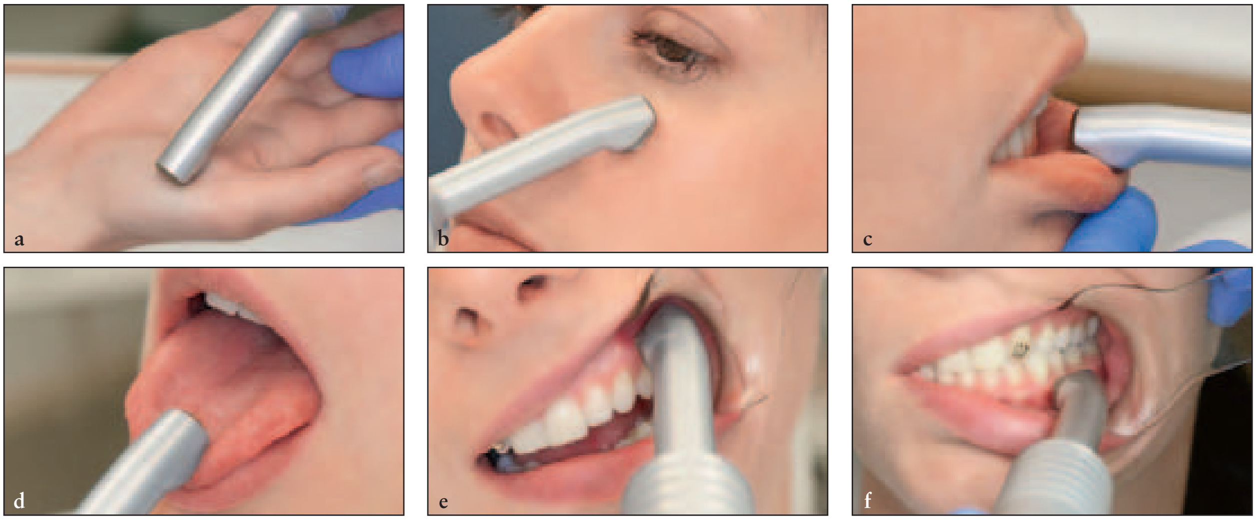

Fig 1 Extra- *(a and b)* and intraoral *(c through f)* sites of thermal stimulation. *(a)* extra-trigeminal site on the hand (thenar eminence), used as a reference point; *(b)* skin area below the left eye (infraorbital skin); *(c)* the mucosa of the lower lip (lip); *(d)* the tip of the tongue (tongue); *(e)* buccal gingiva adjacent to the first upper left premolar (maxillary gingiva); *(f)* buccal gingiva adjacent to the first lower left premolar (mandibular gingiva).

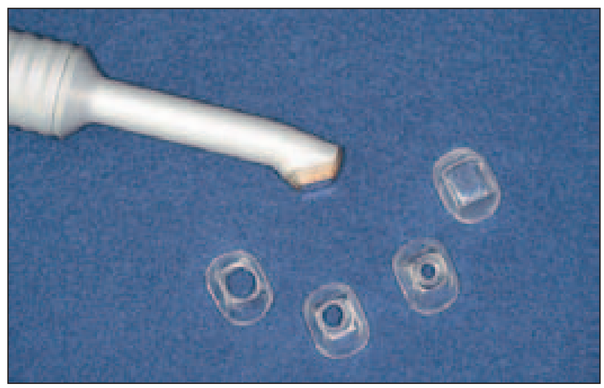

Fig 2 Intraoral thermode and plastic tips for regulating stimulation area size.

rate of 5°C/s. CDT was measured first, followed by WDT and HPT. Three stimuli were given to determine each threshold. The interstimulus interval was randomized at 4 to 6 seconds. During testing, the subject was unable to watch the computer screen. Baseline temperature was set at 32°C for extraoral sites and 37°C for intraoral sites because surface temperature differs between intra- and extraoral tissues[23] and the baseline temperature should be perceived as neutral. Cutoff temperatures were 10°C for cold stimuli and 51°C for warm and hot stimuli. The cold temperature cutoff was set at the thermode's lower measurement limit. Two operators (PE and MP) trained in the investigation procedures made all measurements. The same instructions were given to all subjects at the three examinations. At all examinations, the operator was blinded to previous examination results.

Part 1: Influence of Test Site. Threshold measurements were made at four intraoral and two extraoral sites (Fig 1). These were the mucosa of the lower lip (lip); the buccal gingiva adjacent to the first upper left premolar (maxillary gingiva) and the first lower left premolar (mandibular gingiva); the tip of the tongue (tongue); the skin area just below the left eye (infraorbital skin); and an extratrigeminal point on the hand (thenar eminence, hereafter referred to as thenar), which was used as a reference point. The same operator (PE) examined all subjects once.

Part 2: Influence of Spatial Summation. Four plastic tips that successively reduced the size of contact area were manufactured for the intraoral thermode from 1-mm thick ethylene-propylene copolymer (Essix C+, Ortopro AB), which has a low thermal conductivity coefficient, 0.12 W/m·K, and good insulation properties (Fig 2). Five threshold meas-

Table 1 Mean (and SD) Absolute Threshold Values (°C), and Deviation From Baseline Temperature (Δ°C) for CDT, WDT, and HPT at All Sites

	CDT		WDT		HPT	
Examination site	°C (SD)	Δ°C	°C (SD)	Δ°C	°C (SD)	Δ°C
Intraoral						
Lip	28.1 (3.0)	8.9	43.5 (4.0)	6.5	48.3 (2.3)	11.3
Maxillary gingiva	28.9 (6.2)	8.1	45.9 (2.7)	8.9	47.2 (2.3)	10.2
Mandibular gingiva	29.0 (4.4)	8.0	45.4 (2.2)	8.4	47.4 (2.3)	10.4
Tongue	34.9 (1.4)	2.1	39.1 (1.1)	2.1	46.3 (2.4)	9.3
Extraoral						
Infraorbital skin	30.8 (0.6)	1.2	35.3 (1.6)	3.3	41.0 (4.1)	9.0
Thenar eminence	27.0 (2.8)	5.0	36.6 (2.4)	4.6	45.4 (3.3)	13.4

urements each were made on the tongue for cold, warmth, and heat pain (15 measurements total) with these contact areas: 0.81 cm^2 (uncovered = no plastic tip), 0.50 cm^2, 0.28 cm^2, 0.125 cm^2, and 0.00 cm^2 (fully covered = control). The first four measurements in each series examined the influence of stimulation area size on thermal thresholds. The fourth plastic tip (used in the fifth measurement) fully covered the thermode surface and was used to control for false positive answers and to check the adequacy of the plastic's insulating properties.

In the first 15 subjects, measurements were made with decreasing size of stimulation area and in the last 15 subjects, with increasing stimulation area size. This was done to prevent bias from possible sensitization of the stimulated area. The same operator (PE) made all measurements on the same occasion as for the part 1 measurements. A full examination (parts 1 and 2) took about 45 minutes.

Part 3: Time-dependent Variability. To examine variability over time, tongue measurements of the CDT, WDT, and HPT were made with the uncovered thermode three times: at the first examination and 2 and 6 weeks later. The same operator (MP) made all measurements at 2 and 6 weeks.

Statistical Methods

All variables were continuous, and mean absolute threshold values and SD were calculated. Because baseline temperatures differed between extra- and intraoral sites, mean deviations from baseline (delta values) were calculated and used for all between-site comparisons. For the tongue, measurements made with the uncovered 0.81-cm^2 thermode were used.

One-way ANOVA for repeated measures calculated differences between *(1)* the various sites, *(2)* the three examinations made over 6 weeks (time-dependent threshold variability), and *(3)* measurements obtained with various contact area sizes. When differences were significant, a paired sample *t* test analyzed absolute threshold differences, followed by Bonferroni correction to adjust for multiple comparisons. Independent sample *t* tests calculated gender differences in age distribution. With gender as the grouping factor, the two-way ANOVA for repeated measures analyzed gender differences in thresholds (dependent on site, time, and stimulation area size).

CDTs, WDTs, and HPTs obtained from tongue measurements were plotted against the five sizes of stimulation areas (0.125 to 0.81 cm^2 and the fully covered control tip). For each modality, equations in the form of $y = mx + b$ were calculated to determine m (the slope)—the magnitude of spatial summation. Scatter-dot graphs were drawn to examine spatial summation patterns *(1)* for the group as a whole, *(2)* between the two subgroups stimulated in order of increasing or decreasing size of contact area, and *(3)* between individuals. To examine intraindividual variance between thermal sensitivity on the maxillary and mandibular gingivae, mean values and ranges of threshold differences were calculated for all thresholds.

Distributions of all data were analyzed in Quantile-Quantile plotting. Statistical tests were done two-tailed and at the 5% significance level. All statistical calculations were made using the Statistical Package for the Social Sciences (SPSS, version 16.0 for Windows, IBM).

Table 2 Mean (and SD) Absolute Threshold Values (°C) for CDT, WDT, and HPT of All Stimulation Area Sizes on the Tip of the Tongue (Baseline Temperature was 37°C)

	Area				
	0.81 cm² (SD)	0.50 cm² (SD)	0.28 cm² (SD)	0.125 cm² (SD)	0.00 cm² (SD) (control)
CDT	34.9 (1.4)	35.6 (0.9)	35.3 (1.1)	35.0 (1.4)	14.0 (5.4)
WDT	39.1 (1.1)	39.3 (1.4)	40.2 (1.8)	40.8 (1.6)	48.8 (2.1)
HPT	46.3 (2.4)	47.0 (2.5)	47.6 (2.4)	47.6 (2.4)	51.0 (0)

Results

Thermal Thresholds

All thresholds (CDT, WDT, and HPT) were normally distributed (Table 1).

CDTs. There were significant differences in CDTs between sites (ANOVA, $F_{(5,\ 145)}$ = 32.564; $P < .001$). Intraorally, the lowest CDTs occurred at the tongue. Tongue CDTs were significantly lower than those at all other intraoral test sites ($P < .01$); between-site differences in CDT at all other intraoral sites were nonsignificant. The mean intraindividual difference in CDT between the mandibular and maxillary gingiva was 3.8°C (SD 3.3°C, range 10.3°C). Extraorally, significantly lower CDT values occurred at the infraorbital skin than at the thenar site ($P < .01$).

Comparisons of CDTs between extra- and intraoral sites revealed that the thenar differed significantly from the lower lip ($P < .01$), mandibular gingiva ($P = .03$), and tongue ($P < .01$), whereas the infraorbital skin site differed from all intraoral sites (tongue: $P = .045$; all others: $P < .01$).

WDTs. WDTs differed significantly between sites (ANOVA, $F_{(5,\ 145)}$ = 40.914; $P < .001$). Intraorally, WDTs were significantly lower at the tongue than at all other intraoral sites (all $P < .01$); between-site differences in WDT at all other intraoral sites were nonsignificant. The mean intraindividual difference in WDT between the mandibular and maxillary gingiva was 1.9°C (SD 1.8°C, range 8.2°C). Extraorally, there were no differences in WDT between the infraorbital skin and thenar sites after Bonferroni correction.

Comparisons of WDTs between intra- and extraoral sites showed that the thenar differed significantly from the tongue and maxillary/mandibular gingiva, and infraorbital skin differed from all intraoral sites (all $P < .01$).

HPTs. Between-site differences in HPTs were also seen (ANOVA, $F_{(5, 145)}$ = 14.634; $P < .001$). Intraorally, the HPT was significantly lower at the tongue than the lip ($P < .01$); there were no other significant intraoral between-site differences in HPT. The mean intraindividual difference in HPT between the mandibular and maxillary gingiva was 1.5°C (SD 1.6°C, range 6.8°C). Extraorally, the HPT at the infraorbital skin site was significantly lower than at the thenar ($P < .01$).

Extraoral-intraoral comparisons of HPTs showed that the thenar differed significantly from all intraoral sites (lower lip: $P = .03$; all others: $P < .01$), whereas infraorbital skin HPT only differed from the lower lip ($P = .045$).

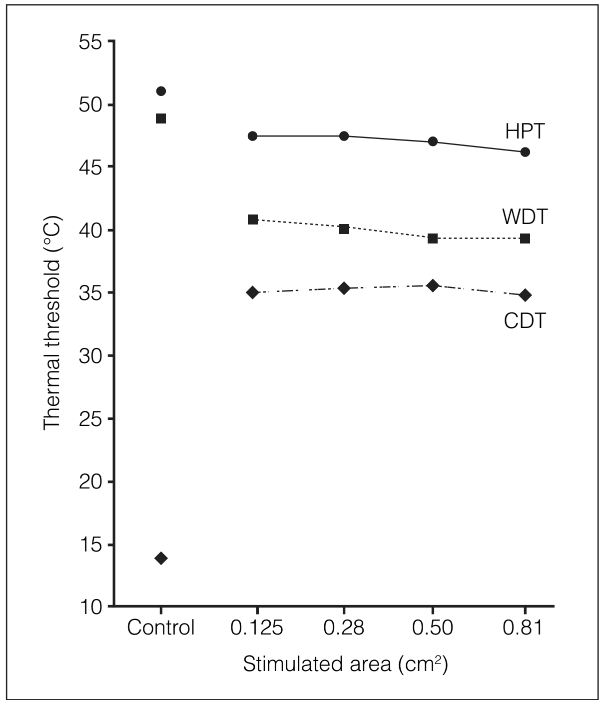

Fig 3 Spatial summation for CDT, WDT, and HPT on the tip of the tongue. When the size of the stimulated area increased, spatial summation was observed for WDT and HPT (decreases in threshold), but not for CDT. Thresholds obtained with fully insulated (control) tip to the far left; the HPT value represents cutoff temperature.

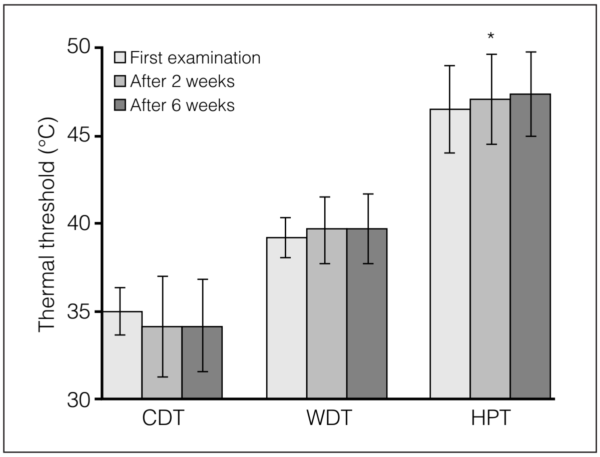

Fig 4 Variability of CDT, WDT, and HPT thresholds on the tip of the tongue over 6 weeks: at first examination and after 2 and 6 weeks. Absolute threshold values and SD (°C) are shown. *Significant difference (after Bonferroni correction) relative to first examination ($P = .018$).

Spatial Summation of Thermal Stimuli

Table 2 lists absolute threshold values for the various stimulation area sizes. WDT and HPT decreased with increasing size of stimulation area, while in general, stimulation area size had little effect on CDT (Fig 3).

During the control measurements of CDT, WDT, and HPT with the fully covered plastic tip, 17 out of 30 subjects reported being able to detect cold (mean CDT: 14.0°C, SD: 5.35°C) and 12 out of 30 subjects, warmth (mean WDT: 48.9°C, SD: 2.12°C). No subject reported heat pain.

CDTs. Interindividual variability in the influence of stimulation area size on CDTs was large. In some individuals, CDT increased with increasing size of stimulation area; in others, the opposite occurred. Stimulation order—whether stimulation occurred in order of increasing or decreasing size of contact area—had no effect on CDTs. Because of this large variability, no linear association between CDT and stimulation area size was observed. CDTs were significantly lower for the 0.50-cm^2 than for the 0.81-cm^2 contact area size, and for the 0.50-cm^2 than for the 0.125-cm^2 area size (both $P = .006$). Comparisons of CDTs between all other area sizes yielded no significant differences. Mean range of intraindividual variation in CDT for the four stimulation area sizes was 0.71°C (SD 0.99°C).

WDTs. All subjects experienced spatial summation of WDT, and magnitude was independent of stimulation order. Interindividual variation was considerable. According to the linear relation ($y = -.5788x + 41.301$), WDT decreases by 0.06°C for every .1-cm^2 increase in stimulation area size. The WDT obtained with the uncovered 0.81-cm^2 thermode differed significantly from the WDTs obtained with the 0.28-cm^2 and the 0.125-cm^2 plastic tips (both $P < .01$), the 0.50-cm^2 tip differed significantly from the 0.28-cm^2 and the 0.125-cm^2 tips (both $P < .01$), and the 0.28-cm^2 tip differed significantly from the 0.125-cm^2 tip ($P = .006$). In these comparisons, the larger area size had the lower WDT. Mean range of intraindividual variation in WDT for the four stimulation area sizes was 1.63°C (SD 1.02°C).

HPTs. With few exceptions, most subjects experienced spatial summation of HPT, and interindividual variation was large. When stimulation occurred in order of decreasing area size, threshold differences between the tips were considerably smaller than when stimulation order was reversed. HPTs obtained with the smaller area sizes varied depending on whether the site had been previously stimulated; recent stimulation of a site with a larger-sized contact area yielded a lower HPT when the site was stimulated with a smaller-sized contact area.

HPT obtained with the 0.81-cm^2 thermode tip at the tongue was significantly lower than HPTs obtained with the 0.50-cm^2 ($P = .024$), the 0.28-cm^2, and the 0.125-cm^2 plastic tips (both $P < .01$); likewise, the HPT obtained with the 0.50-cm^2 tip was lower than the HPTs obtained with the 0.28-cm^2 ($P < .01$) and the 0.125-cm^2 tips ($P = .042$). No significant difference occurred between the two smallest area sizes. When HPTs for all 30 subjects were pooled, irrespective of stimulation order, the linear relation was $y = -.4353x + 48.223$: HPT decreased by 0.04°C for every 0.1-cm^2 increase in stimulation area size. Mean range of intraindividual variation in HPT for the various stimulation area sizes was 1.26°C (SD 1.42°C).

Time-dependent Variability

There was a tendency for thresholds on the tongue tip to be lower in the first round of examinations and higher in subsequent examinations (Fig 4) but overall, the tongue threshold variation over time was not statistically significant. After Bonferroni correction, the only significant difference in any of the three thresholds occurred in HPT—between the first and 2-week examinations ($P = .018$). All threshold variations were in the range of ± 1°C: CDT, 0.95°C (SD 2.23°C); WDT, 0.58°C (SD 1.31°C); and HPT, 0.8°C (SD 1.72°C).

Subjects and Gender Effects

Proportions of men and women were equal at baseline. Mean age for men was significantly higher (*P* = .03) than for women.

No gender-dependent differences in mean thresholds were seen at any site or over time at the tongue site. The relationship between thresholds and stimulation area size on the tip of the tongue differed nonsignificantly between men and women.

Withdrawals

Due to a procedural error during start-up of the thermotesting equipment, the baseline temperature was inadvertently changed for four subjects during the 2-week follow-up examination. These subjects (three men, one woman) were withdrawn from part 3. One subject (a woman) chose not to continue participation after part 1 and 2 for reasons unrelated to the study. All other examinations were completed for all subjects. The five withdrawals did not significantly alter the age or gender distribution of the material.

Discussion

The main findings of this study were that *(1)* thresholds differed markedly between various intraoral sites, *(2)* spatial summation at the tip of the tongue occurred for WDT and HPT but not for CDT, but the variation in stimulation area size-dependent threshold was, in general, modest, and *(3)* the time-dependent variability in threshold measurements at the tip of the tongue was, in general, not significant.

Influence of Test Site

The tongue appears to be particularly sensitive; substantial threshold differences between the tongue and other intraoral sites were found for all thermal stimuli, which agrees with Svensson et al.[26] Thresholds on the lower lip were intermediate in value, more similar to gingival than to tongue thresholds. On the group level, gingival sites differed relatively little between the upper and lower jaws for all stimuli; similarities in innervation probably explain this finding. But on the individual level, some experienced substantial difference between jaws, particularly for CDTs. An earlier study found that when comparing left- and right-side maxillary gingiva in healthy subjects, substantial side-to-side differences in thermal thresholds were also frequent on the individual level, whereas at the group level, there were no significant side-to-side differences.[6]

These findings indicate that some variation in thermal thresholds between the upper and lower jaw and between sides is normal and can be expected within an individual; the normal range of these variations remains to be determined. This is important clinically because QST can be used to investigate therapy-resistant intraoral pain, which is frequently located in the gingival area adjacent to a tooth. The threshold differences between various orofacial sites observed here indicate that if abnormal changes in thermal sensitivity are to be detected, it is essential to establish normative values for the particular site examined *or* for one with similar biophysical properties.

There are several previous reports of thermal threshold differences between various body sites.[15,27] Sensitivity to warmth differs greatly over the surface of the body, but in no other region has it been reported to change so much over a short distance as in the orofacial region. Green[14] reported that sensitivity to warmth changed by a factor of almost four to one over a distance of a few centimeters; from the external (cutaneous) side of the lip to the internal (mucosal) side, the external side being the more sensitive by far.

Green and Gelhard[11] reported extraoral (facial) sites to be more sensitive to warmth than intraoral sites, except for the tip of the tongue, which is also consistent with the present findings. In this study, the tip of the tongue was significantly more sensitive to warmth than the infraorbital skin site, whereas Green[14] found tongue sensitivity to be similar to that of the vermilion lip but lower than that for the infraorbital skin. Methodological differences probably account for this difference in observations. Similarly, the tongue site was more sensitive to cold than any other intraoral site and similar to the infraorbital site.

The present study found no significant differences in threshold values between men and women. Defrin et al reported a similar finding for HPT on the dorsal hand skin,[28] whereas others have found that women in general have lower sensory thresholds—for example, Meh and Denislic, who reported significantly lower heat pain thresholds in women for a range of cutaneous sites, including the face, but found no gender effect in warm-cold difference limen (the temperature interval between perceived warmth and perceived cold).[29]

Influence of Stimulation Area Size

Spatial summation in men and women was similar for all stimuli in the present study. This is consistent with the findings of others; Defrin et al[30] found no gender-related differences in spatial summation to pressure pain, and Lautenbacher and coworkers[31] reported the same for heat pain and pressure pain. The sample size in the present study was too small to achieve adequate power to detect gender-related threshold differences, which if present, may be fairly small; therefore, the present analysis should be judged with caution.

Spatial summation was more pronounced for warmth detection than for painful heat, but the magnitudes of all threshold differences were small. This could be due to the range of contact area sizes, which by necessity was smaller compared to what can be used elsewhere on the body. Heat pain has been reported to differ from warmth in that warmth exhibits considerable spatial summation,[32] but considerable spatial summation to painful heat stimuli has also been demonstrated.[18]

No spatial summation to cold was observed in this study. In contrast, Stevens and Marks[19] found spatial summation to cold stimuli on cheek skin. This could reflect differences in density of cold-sensitive afferent fibers or in biophysical properties between the tissues, or possibly that the range of stimulation area sizes used in the present study was small compared to the range of contact area sizes used in the Stevens and Marks study.

Although threshold variation was small in absolute values, there were statistically significant differences between several area sizes for all modalities. For WDT and HPT, this likely reflects true spatial summation, since the direction (larger areas are associated with lower thresholds) of the relationship between area size and threshold was similar for most subjects and could be described as linear. For CDT, interindividual differences were too large to make such an assumption.

But despite statistical significance, the magnitude of threshold differences was modest. Intraorally, most possible test sites are small by nature, so small thermodes must be used for thermal stimulation. Since spatial summation on the tongue was small for WDT and HPT and inconclusive for CDT with contact areas up to 0.81 cm^2, the impact of stimulation area size seems relatively low compared to the impact of site location. Different thermode sizes for intraoral use, for example, SOMEDIC and Medoc probes, can be considered essentially equal, and, therefore, results from studies using different thermotesters are possible to compare.

The present study used a set of manufactured plastic tips to reduce the size of stimulation area. Because the contact surface between tissue and thermode for the 0.50-, the 0.28-, and the 0.125-cm^2 stimulation areas comprised part thermoconducting material and part plastic, it was necessary to ascertain that the plastic actually insulated the subject's tissue from the covered part of the thermode. The fully covered control tip resulted in markedly higher CDTs and WDTs, compared to when the thermode was partially or fully uncovered. Some subjects did report that they could feel cold and warmth (but not heat pain) during control testing; but in these subjects, control tip thresholds still differed significantly from thresholds measured with a partially or fully uncovered thermode.

Because control tip thresholds were further from baseline temperature and took longer to reach than exposed thermode thresholds, stimulation times were longer. Control tip stimulation caused a build-up of heat (or cold) in the material, and after enough time, the temperature level was within the range of detection for some subjects. This implies that when using the 0.50-, 0.28-, and 0.125-cm^2 tips, some thermal build-up will also occur, which theoretically could affect threshold levels. The authors consider this risk to be minimal, since a threshold that is measured with a fully insulated thermode occurs only after radically prolonged stimulation—the threshold level difference is such that before the heat (or cold) accumulating in the plastic reaches a detectable level, the subject will already have responded to the temperature of the exposed area and ended stimulation.

Time Variability

A significant time-dependent variation was only found for HPT, which could possibly be related to the relatively small number of subjects in this study. All three thresholds varied slightly over time. Others have also reported fluctuations in sensory thresholds over time in healthy individuals.[26,29] In this study, differences tended to be largest between the first and the other two examinations; there were no significant differences between the 2- and 6-week examinations. Possibly the presence of a "first session effect" could be the explanation for this. Bushnell and colleagues reported lower thresholds for WDT and HPT when attention to stimuli was high,[33] and James and colleagues reported 16% lower vibration detection thresholds on the first examination than on the second and third ($P < .02$).[34] Also, since one examiner conducted the first examination and another conducted the 2- and 6-week examinations, interexaminer differences cannot be ruled out as a source of the observed time variations. But instructions to subjects were the same for all examinations, and assessments were performed with minimal participation from the examiner—the subjects held the thermode against the tip of their tongue and interrupted stimulation by pressing a button of their own accord; the role of the examiner was mainly that of surveillance during measurement. In addition, the authors have recently demonstrated, using identical testing procedures, acceptable intra- and interexaminer reliability for thermal threshold assessments on the tongue.[6]

All differences over time were in the range of ± 1°C, which can be compared to the spatial summation findings that were in the same range; an important finding may be the fairly large interindividual variation indicated by the SD values, suggesting that, at least for some individuals, thresholds may vary considerably over time. This should be taken into consideration in the clinical situation.

Generalizability

Normative values for intraoral thermal thresholds of various gingival and mucosal sites so far have not been determined. Manrique and Zald measured CDT and WDT at the tip of the tongue and found the thresholds to be higher than those in the present study; methodological differences, particularly their use of a plastic film covering the entire thermode surface, likely account for this difference.[35] Others have reported tongue CDT, WDT, and HPT in the same range as the present findings.[24,36]

The extraoral HPTs in the present study were within the normal ranges reported previously.[29,37] As for WDT and CDT, the thresholds were higher (further from baseline) than the normative values earlier reported[38]; however, in that study, a 50 × 25-mm thermode was used compared to the 9 × 9-mm thermode used in the present study, and spatial summation conceivably could account for the threshold differences. Therefore, the authors believe the present findings are representative for thermal thresholds in the orofacial area.

Limitations and Strengths

Among the limitations of this study, the plastic tips manufactured for spatial summation assessment did not perfectly insulate the probe, which may compromise spatial summation assessment. The interstimulus interval used for HPT was shorter than that used in some other studies to avoid sensitization or habituation,[5,37] which may have affected the HPT levels. Another weakness is that different examiners performed the testing at first and at later examinations, which could affect the time variability analysis as noted above.

A strength of this study relates to its examination of potential sources of variation in current thermal testing methods used, for example, in the comprehensive QST protocol recommended by the DFNS. It is important to realize that there are substantial differences even between intraoral sites not far separated, and intraoral reference values must accommodate this. The fairly small spatial summation and time variability reported in this study will give higher credibility to normative values when such are available.

Conclusions

Intraoral thermal thresholds are affected by site location. If CDT, WDT, and HPT are to be used to disclose somatosensory deficits in various orofacial pain conditions, normative values should be determined for different intraoral sites. Spatial summation on the tongue is small for WDT and HPT and inconclusive for CDT with thermode contact areas of 0.81 cm^2 and smaller. Threshold variability over a 6-week period is modest. Future studies should determine ranges of normal variance for intraoral thermal thresholds at various sites and study the reliability of threshold measurements when somatosensory changes and pain are present.

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References

1. Zaslansky R, Yarnitsky D. Clinical applications of quantitative sensory testing (QST). J Neurol Sci 1998;153:215–238.
2. Rolke R, Magerl W, Campbell KA, et al. Quantitative sensory testing: A comprehensive protocol for clinical trials. Eur J Pain 2006;10:77–88.
3. Backonja MM, Walk D, Edwards RR, et al. Quantitative sensory testing in measurement of neuropathic pain phenomena and other sensory abnormalities. Clin J Pain 2009;25:641–647.
4. Svensson P, Baad-Hansen L, Thygesen T, Juhl GI, Jensen TS. Overview on tools and methods to assess neuropathic trigeminal pain. J Orofac Pain 2004;18:332–338.
5. Wasner GL, Brock JA. Determinants of thermal pain thresholds in normal subjects. Clin Neurophysiol 2008;119:2389–2395.
6. Pigg M, Baad-Hansen L, Svensson P, Drangsholt M, List T. Reliability of intraoral quantitative sensory testing (QST). Pain 2010;148:220–226.
7. Svensson P, Bjerring P, Arendt-Nielsen L, Kaaber S. Variability of argon laser-induced sensory and pain thresholds on human oral mucosa and skin. Anesth Prog 1991;38:79–83.

8. Svensson P, Bjerring P, Arendt-Nielsen L, Nielsen JC, Kaaber S. Comparison of four laser types for experimental pain stimulation on oral mucosa and hairy skin. Lasers Surg Med 1991;11:313–324.
9. Dubner R, Sessle BJ, Storey AT (eds). The Neural Basis of Oral and Facial Function. New York: Plenum, 1978.
10. Essick G, Guest S, Martinez E, Chen C, McGlone F. Site-dependent and subject-related variations in perioral thermal sensitivity. Somatosens Mot Res 2004;21:159–175.
11. Green BG, Gelhard B. Perception of temperature on oral and facial skin. Somatosens Res 1987;4:191–200.
12. Dixon AD. The position, incidence and origin of sensory nerve termination in oral mucous membrane. Arch Oral Biol 1962;7:39–48.
13. Halata Z, Munger BL. The sensory innervation of primate facial skin. II. Vermilion border and mucosa of lip. Brain Res 1983;286:81–107.
14. Green BG. Thermal perception on lingual and labial skin. Percept Psychophys 1984;36:209–220.
15. Kenshalo DR, Decker T, Hamilton A. Spatial summation on the forehead, forearm, and back produced by radiant and conducted heat. J Comp Physiol Psychol 1967;63:510–515.
16. Stevens JC, Marks LE. Spatial summation and the dynamics of warmth sensation. Percept Psychophys 1971;9:291–298.
17. Price DD, McHaffie JG, Larson MA. Spatial summation of heat-induced pain: Influence of stimulus area and spatial separation of stimuli on perceived pain sensation intensity and unpleasantness. J Neurophysiol 1989;62:1270–1279.
18. Staud R, Vierck CJ, Robinson ME, Price DD. Spatial summation of heat pain within and across dermatomes in fibromyalgia patients and pain-free subjects. Pain 2004;111:342–350.
19. Stevens JC, Marks LE. Spatial summation of cold. Physiol Behav 1979;22:541–547.
20. Defrin R, Petrini L, Arendt-Nielsen L. Spatial summation of thermal sensations depends on skin type and skin sensitivity. Exp Brain Res 2009;198:29–36.
21. Defrin R, Shachal-Shiffer M, Hadgadg M, Peretz C. Quantitative somatosensory testing of warm and heat-pain thresholds: The effect of body region and testing method. Clin J Pain 2006;22:130–136.
22. Palmer ST, Martin DJ. Thermal perception thresholds recorded using method of limits change over brief time intervals. Somatosens Mot Res 2005;22:327–334.
23. Miles TS, Nauntofte B, Svensson P (eds). Clinical Oral Physiology. Copenhagen: Quintessence, 2004.
24. Grushka M, Sessle BJ, Howley TP. Psychophysical assessment of tactile, pain and thermal sensory functions in burning mouth syndrome. Pain 1987;28:169–184.
25. Forssell H, Jaaskelainen S, Tenovuo O, Hinkka S. Sensory dysfunction in burning mouth syndrome. Pain 2002;99:41–47.
26. Svensson P, Bjerring P, Arendt-Nielsen L, Kaaber S. Quantitative determinations of sensory and pain thresholds on human oral mucosa by argon laser stimulation. Pain 1992;49:233–239.
27. Stevens JC, Marks LE, Simonson DC. Regional sensitivity and spatial summation in the warmth sense. Physiol Behav 1974;13:825–836.
28. Defrin R, Shramm L, Eli I. Gender role expectations of pain is associated with pain tolerance limit but not with pain threshold. Pain 2009;145:230–236.
29. Meh D, Denislic M. Quantitative assessment of thermal and pain sensitivity. J Neurol Sci 1994;127:164–169.
30. Defrin R, Givon R, Raz N, Urca G. Spatial summation and spatial discrimination of pain sensation. Pain 2006;126:123–131.
31. Lautenbacher S, Kunz M, Strate P, Nielsen J, Arendt-Nielsen L. Age effects on pain thresholds, temporal summation and spatial summation of heat and pressure pain. Pain 2005;115:410–418.
32. Marks LE. Spatial summation in relation to the dynamics of warmth sensation. Int J Biometeorol 1971;15:106–110.
33. Bushnell MC, Duncan GH, Dubner R, Jones RL, Maixner W. Attentional influences on noxious and innocuous cutaneous heat detection in humans and monkeys. J Neurosci 1985;5:1103–1110.
34. James A, Essick GK, Kelly DG, Tappouni H, McGlone FP. Frequency and site-dependent variations in vibration detection thresholds on the face. Somatosens Mot Res 2000;17:349–360.
35. Manrique S, Zald DH. Individual differences in oral thermosensation. Physiol Behav 2006;88:417–424.
36. Renton T, Thexton A, Hankins M, McGurk M. Quantitative thermosensory testing of the lingual and inferior alveolar nerves in health and after iatrogenic injury. Br J Oral Maxillofac Surg 2003;41:36–42.
37. Yarnitsky D, Sprecher E, Zaslansky R, Hemli JA. Heat pain thresholds: Normative data and repeatability. Pain 1995;60:329–332.
38. Yarnitsky D, Sprecher E. Thermal testing: Normative data and repeatability for various test algorithms. J Neurol Sci 1994;125:39–45.