Influence of Test Site and Baseline Temperature on Orofacial Thermal Thresholds

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Aims: *To investigate thermal thresholds of selected orofacial sites, determine if there is a relationship between thermal thresholds at each site, and analyze the influence of two different baseline temperatures on thermal thresholds at the tongue tip.* ***Methods:*** *Thirty healthy men (mean age, 26 years) participated. Cold detection (CDT), warm detection (WDT), cold pain (CPT), and heat pain (HPT) thresholds were measured bilaterally at five orofacial sites (mentum, lower lip, cheek, forehead, and tongue tip). Relations between thermal thresholds at each test site were assessed. Thermal sensitivity of the tongue tip was compared at two different baseline temperatures (32˚C and 36˚C). One-way ANOVA, Turkey post-hoc test, paired* t *test and Pearson's correlation were used for statistical analyses.* ***Results:*** *There was a significant difference for CDT, WDT, and HPT between test sites (ANOVA,* P < *.001) but no significant difference for CPT (*P = *.634). Subjects sensitive to cooling were sensitive to warming at the mentum (*r = *0.379), tongue tip (*r = *0.610), and cheek (*r = *0.431) but not at the other test sites. There was a strong negative correlation between CPT and HPT at all test sites. There was no significant difference for CDT and WDT at the baseline temperature of 36˚C (paired* t *test,* P =*.660), but there was a significant difference at the baseline temperature of 32˚C (*P < *.001). There were no significant differences between CPTs at the two different baseline temperatures (*P =*.773), while a significant difference existed between HPTs (*P = *.034).* ***Conclusion:*** *Thermal thresholds varied between the orofacial test sites, and baseline temperature affected thermal sensitivity of the tongue. Subjects who were relatively sensitive to cold tended to be more sensitive to heat.* J OROFAC PAIN 2013;27:263–270. doi: 10.11607/jop.1030

Key words: baseline temperature, orofacial, quantitative sensory testing, thermal thresholds, trigeminal site

Quantitative sensory testing (QST) is an acknowledged diagnostic tool for the assessment of somatosensory changes caused by nerve lesions of different etiologies, such as polyneuropathy, and is regarded as a useful diagnostic instrument in the assessment of neuropathic pain.[1] The measurement of thermal pain thresholds is an essential part of QST and is reported to have acceptable reliability in the orofacial region.[2–5] The particular test site and the baseline temperature are factors that may influence thermal thresholds.[3,4,6] Temperature-sensitive afferents supplying the orofacial region are generally reported to be similar to those in other somatic regions.[3] Despite this, various orofacial sites do differ in sensitivity to thermal stimuli.[3] Although substantial normative data exist for test sites on the arms, legs, and trunk, relatively few data are available for sites in the orofacial region.[7] The baseline temperature also affects thermal thresholds. Lele reported that the thresholds are

related to the skin temperature and that this relation is different in the case of warm and cold stimuli,[8] but there has not been an extensive investigation of intraoral sites.

The aims of the present study were to *(1)* investigate thermal thresholds of selected orofacial sites, *(2)* determine if there is a relationship between thermal thresholds at each site, and *(3)* analyze the influence of two different baseline temperatures on thermal thresholds at the tongue tip.

Materials and Methods

Subjects

Thirty young healthy men (mean age 26.1 years, range 23 to 32 years) participated in the study. All participants were recruited from students of the Dankook University Dental School, Cheonan, Republic of Korea. Quantitative thermal sensory tests were performed from September to December 2011. Inclusion criteria were the following: good health without any orofacial pain complaint, no peripheral or central lesions or disease of the somatosensory system, and no problems with understanding the QST instructions. The Institutional Review Board at Dankook University Dental Hospital approved the study (IRB No H-1110/008/002), and all participants signed an informed consent form. Participants received no monetary compensation for study participation.

Experimental Design

The study consisted of two experiments:

1. Influence of test site on thermal thresholds. Cold detection (CDT), warm detection (WDT), cold pain (CPT), and heat pain (HPT) thresholds were measured bilaterally at four extraoral and one intraoral sites. These were the mentum (above the mental foramen), the vermilion of the lower lip, the tip of the tongue, the midpoint of the cheek, and the forehead (2 cm above the midpoint of the brow).
2. Influence of baseline temperature on thermal thresholds at the tongue. The temperature of the tongue is approximately 36°C to 37°C, with all intraoral tissues becoming warmer when the mouth is closed.[9] But the temperature of the tongue tip was approximately 32°C to 35.6°C (mean temperature of 34.0°C ± 1.2°C) when the mouth was open for testing in this experiment. So the investigators tested and compared thermal thresholds at another baseline temperature, 32°C, in addition to a 36°C baseline temperature for the tongue tip.

Apparatus

The thermal tests were performed using a TSA II Neurosensory Analyzer (Thermal Sensory Analyzer, MEDOC). TSA II is a computer-controlled device capable of generating and documenting responses to highly repeatable thermal stimuli, such as warmth, cold, heat-induced pain, cold-induced pain, and of delivering quantitative assessment of small-caliber (A-delta and C-fiber) sensory nerve function.[10] A method of limits was used, with ramped stimuli of 1.0°C/s for detection thresholds and 1.5°C/s for pain thresholds that were terminated when the subject pressed a button. For thermal detection thresholds, the ramp back to baseline was 1°C/s, while for thermal pain thresholds the ramp was 10°C/s. Three stimuli were given to determine each threshold, and the mean threshold temperature of three consecutive measurements was calculated. The interstimulus interval was randomized at 4 to 6 seconds for detection thresholds and at 10 seconds for pain thresholds. The contact area of the thermode was 5 mm × 5 mm. Baseline temperature was set at 32°C for extraoral sites and 36°C for the tongue, because the surface temperature differs between intraoral and extraoral tissues, and the baseline temperature should be perceived as neutral.[9,11] Cutoff temperatures were 0°C for cold stimuli and 50°C for warm and hot stimuli.

Procedures

The detection thresholds were defined as the least change from baseline temperature that was detected as cooler or warmer. The subject was asked to press a button as soon as he detected such a change. In the case of pain thresholds, subjects were instructed to "let the stimulus go beyond the initial thermal sensation, and when it starts being painful, press the button." The definition of the sensations was emphasized to each subject throughout the session. The probe was applied perpendicularly and with consistent and comfortable pressure to the test site. All subjects underwent pre-tests on the left mentum a day before the main experiment. The tests were done in the order of first the mentum, then the lower lip, tongue tip, cheek, and finally the forehead, alternating between the right and left sides. CDTs and WDTs were measured first and then CPT and HPT were determined. The subjects were asked to keep their eyes closed throughout the QST procedure. One experienced examiner made all measurements.

Table 1 Absolute Threshold Values (˚C) and Difference from Baseline Temperature (ΔT,˚C) of CDT, WDT, CPT, and HPT for Test Sites (n = 30)

	Thermal threshold							
	CDT		WDT		CPT		HPT	
Test site	Mean ± SD	ΔT	Mean ± SD	ΔT	Mean ± SD	ΔT	Mean ± SD	ΔT
Mentum	30.8 ± 0.4	1.2	35.1 ± 1.1	3.1	15.0 ± 9.4	17.0	44.3 ± 2.4	12.3
Lower lip	31.1 ± 0.4	0.9	33.4 ± 0.6	1.4	16.0 ± 8.1	16.0	43. 8 ± 2.5	11.8
Tongue tip	32.9 ± 1.4	3.1	39.2 ± 1.4	3.2	17.1 ± 8.1	18.9	46.3 ± 2.1	10.3
Cheek	30.6 ± 0.5	1.4	35.0 ± 1.4	3.0	18.3 ± 9.9	13.7	42.3 ± 3.4	10.3
Forehead	30.1 ± 0.5	1.9	35.5 ± 1.8	3.5	17.1 ± 10.7	14.9	44.5 ± 2.8	12.5
One-way ANOVA	$P < .001$[a]		$P < .001$[a]		$P = .634$[b]		$P < .001$[b]	

a: Comparison between differences from the baseline temperature (ΔT,˚C) at all test sites for CDT and WDT.
b: Comparison between absolute threshold values (˚C) at all test sites for CPT and HPT.
The baseline temperature was set at 32˚C for test sites except the tongue tip (36˚C).

Statistical Methods

All variables were continuous, and mean absolute threshold values and SD were calculated. Differences between sides and sites were analyzed by repeated measures one-way ANOVA. When differences were significant, Turkey post-hoc tests were calculated for multiple comparisons. Pearson's correlation was used to find the relationship between thermal detection and pain thresholds. Paired *t* test compared the thermal sensitivity of the tongue tip at two different baseline temperatures. Statistical tests were done at the 5% significance level. All statistical calculations were made using the PASW statistics version 18.0.

Results

Thermal Thresholds for Test Sites

For cool and warm sensations, the decrement or increment in the temperature from baseline temperature (delta value), respectively, was used as the threshold value and absolute values were used for pain thresholds. The factor side was nested under the factor site to eliminate higher-order interactions. As the analyses revealed no statistically significant effects of side for all four thermal sensations, the average value of right side and left side at each test site was used for thermal thresholds.

CDTs. There were significant differences in CDTs between test sites (ANOVA, $P < .001$) (Table 1). The lower lip, mentum, and cheek were more sensitive to cold stimulation than the tongue tip and forehead. There was a significant difference between the tongue tip and the forehead; ie, the tongue tip was the least sensitive for cooling among all the test sites, and extraorally the forehead was the least sensitive for cooling (Fig 1a). The mean difference from baseline temperature ranged from as little as 0.9˚C for the lower lip to as much as 3.1˚C for the tongue tip (Table 1).

WDTs. WDTs differed significantly between sites (ANOVA, $P < .001$) (Table 1). The lower lip with an increment from baseline temperature of 1.4˚C was the most sensitive for warmth, which was a significantly lower delta value compared to the other test sites. However, there were no differences between the other sites, as shown in Fig 1a.

CPTs. There were no significant differences in CPTs between test sites (ANOVA, $P = .634$) (Table 1). The mean threshold for cold pain in the five orofacial sites was 16.7˚C and the SD was 9.22˚C, which was the largest variation among four thermal parameters.

HPTs. Site differences in HPTs were seen (ANOVA, $P < .001$) (Table 1). The cheek was the most sensitive to noxious heat (mean HPT of 42.3˚C), and the tongue tip (with a mean threshold of 46.3˚C) was the least sensitive, as shown in Table 1 and Fig 1b. There was no significant difference among the mentum, lower lip, and forehead.

As shown in Fig 1, all test sites except the tongue tip were more sensitive to cooling than warming, and greater decrements from baseline temperature were required to reach the cold pain threshold than the increments needed from baseline temperature to reach the heat pain threshold for all test sites.

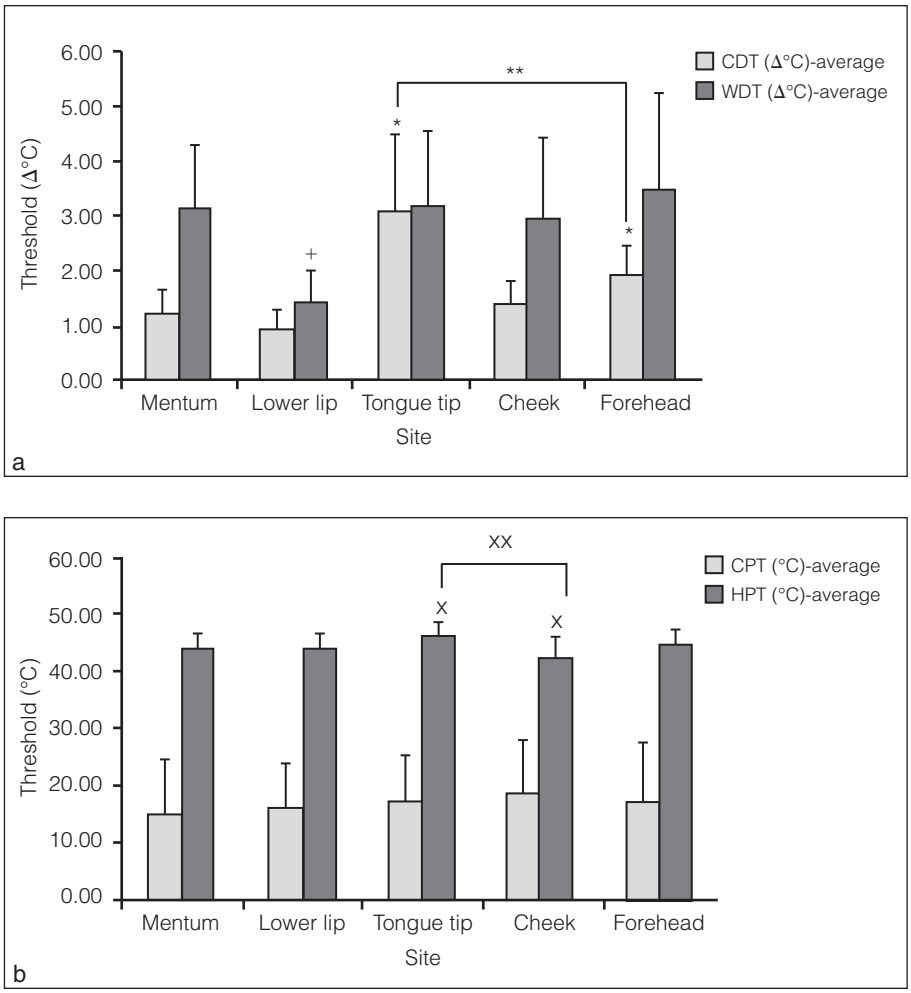

Fig 1 *(a)* Cold and warm difference thresholds and *(b)* cold and heat pain thresholds. The difference threshold is the change from the baseline temperature required to first perceive cool and warmth, respectively. The pain thresholds are the absolute temperatures at which the subjects reported pain first at cold or hot stimuli. *Significant difference relative to other sites on CDT (Δ˚C), **significant difference between the tongue tip and forehead on CDT (Δ˚C), + = significant difference relative to other sites on WDT (Δ˚C), × = significant difference relative to other sites on HPT (˚C), × × = significant difference between the tongue tip and cheek on HPT (˚C) after Turkey post-hoc multiple comparison, $P < .05$). Values reflect mean ± SD.

Relationship Between Thermal Thresholds

The study also tested whether subjects who were relatively sensitive to one of the four thermal sensory thresholds were also relatively sensitive to the others. Table 2 shows significant correlations between thermal thresholds at each test site. It can be seen that subjects who were relatively sensitive to cooling were also relatively sensitive to warming at the mentum ($r = 0.379$, $P < .05$), tongue tip ($r = 0.610$, $P < .01$), and cheek ($r = 0.431$, $P < .05$). However, there were no correlations between CDTs (Δ˚C) and WDTs (Δ˚C) at the lower lip and forehead. There were positive correlations between WDTs (Δ˚C) and HPTs (˚C) at the tongue tip ($r = 0.440$, $P < .05$) and between CDTs (Δ˚C) and HPTs (˚C) at the forehead ($r = 0.446$, $P < .05$). Significant negative correlations were seen between CPTs (˚C) and HPTs (˚C) at all test sites ($r = –0.524$ to $–0.663$, all $P < .01$). No difference in the strength of the correlations was detected between CDTs (Δ˚C) and CPTs (˚C) at all test sites.

Thermal Sensitivity of the Tongue Tip at Two Baseline Temperatures

The change from baseline temperature of 36˚C for detection of warm stimuli (ΔT) applied to the tongue tip was 3.2˚C (SD 1.4˚C) and that for cool stimuli was 3.1˚C (SD 1.4˚C). There was no significant difference in thermal sensitivity for the tongue tip for cool and warm stimuli at baseline temperature of 36˚C (paired t test, $P = .660$) (Table 3). In contrast, at baseline temperature of 32˚C, there was a significant difference between the increment value for detection of warm stimuli (2.2˚C ± 1.3˚C) and the decrement value for detection of cold stimuli (1.2˚C ± 0.5˚C) (paired t test, $P < .001$) (Table 3). Significant differences were seen in CDTs at the tongue tip between the baseline temperature of 32˚C and 36˚C ($P < .001$); WDTs also showed significant differences between the two baseline temperatures ($P < .001$) (Table 3). There were no significant differences between CPTs at the two different baseline temperatures ($P = .773$), while a significant difference existed between HPTs ($P = .034$) (Table 4).

Table 2 Correlations Between Thermal Thresholds for Orofacial Test Sites

Correlation	Test sites
CPT-HPT	Mentum (r = –0.566**), lower lip (r = –0.524**), tongue tip (r = –0.617**), cheek (r = –0.656*), forehead (r = 0.663**)
CDT-WDT	Mentum (r = 0.379*), tongue tip (r = 0.610**), cheek (r = 0.431**)
CDT-HPT	Forehead (r = 0.446*)
WDT-HPT	Tongue tip (r = 0.440*)
WDT-CPT	None
CDT-CPT	None

CDT and WDT: Difference from the baseline temperature (ΔT, ˚C)
CPT and HPT: Absolute value (˚C).
Correlation coefficients and P values are indicated in the table when the significant level is at $P < .05$ (*$P < .05$, **$P < .01$).

Table 3 Comparison Between CDT (ΔT,˚C) and WDT (ΔT,˚C) for the Tongue Tip at Two Different Baseline Temperatures

Baseline temperature	Thermal detection thresholds				
	CDT		WDT		
	Mean ± SD	ΔT	Mean ± SD	ΔT	Paired t test
32˚C	30.8 ± 0.5	1.2 ± 0.5	34.2 ± 1.3	2.2 ± 1.3	$P < .001$[b]
36˚C	32.9 ± 1.4	3.1 ± 1.4	39.2 ± 1.4	3.2 ± 1.4	$P = .660$[b]
Paired t test	$P < .001$[a]		$P < .001$[a]		

CDT and WDT: Difference from the baseline temperature (ΔT,˚C).
a: Paired t tests between CDTs at the baseline temperature of 32˚C and 36˚C, and WDTs at the baseline temperature of 32˚C and 36˚C.
b: Paired t tests between CDT and WDT at the baseline temperature of 32˚C and 36˚C, respectively.

Discussion

Influence of Test Site on Thermal Thresholds

The main finding of this study was that orofacial sites exhibited different thermal thresholds. There are several previous reports of thermal threshold differences between various body sites, including the orofacial region.[3,4,6–8,12–15] Based on the results of the present study, the lower lip appears to be the most sensitive to warming and the tongue tip falls within the range of facial sensitivities for warming. This result agrees with earlier data from Green and Gelhard, which showed that facial regions were significantly more sensitive to warming than oral regions except the vermilion lip and the tongue tip. They also indicated that there were not large differences in sensitivity to cooling between the oral and facial areas.[6] In the present study, the mentum, lower lip, and cheek were significantly more sensitive to cooling than the forehead and the tongue tip, and the tongue tip was least sensitive to cooling than other test sites. Pigg et al reported that the tongue thresholds were significantly higher than the cheek thresholds for CDT, WDT, and HPT, and CPT did not differ between the test sites.[2] In the case of CDT, CPT, and HPT, the data of Pigg et al are consistent with the present findings, but there were no significant differences between the tongue tip and the cheek in WDT in the present study. Matos et al reported that V2 sites (supplied by the maxillary nerve) above the infraorbital foramen are more sensitive for HPT and less sensitive for CDT than V3 sites above the mental foramen (supplied by the mandibular nerve).[16] The present study showed that a V2 site (cheek) is more sensitive than a V3 site (mentum) for HPT. However, there were no significant differences in CDTs between V2 and V3 sites. Methodological differences or ethnicity probably account for these differences in observations.

Table 4 Comparison Between CPT (°C) and HPT (°C) for the Tongue Tip at Two Different Baseline Temperatures

Baseline temperature	Thermal pain thresholds (Mean ± SD)	
	CPT	HPT
32°C	16.8 ± 7.5	45.4 ± 2.7
36°C	17.1 ± 8.1	46.3 ± 2.1
Paired t test	$P = .773$	$P = .034$

CPT and HPT: Absolute value (˚C).
Paired t tests between CPTs (˚C) at the baseline temperature of 32˚C and 36˚C, and HPTs (˚C) at the baseline temperature of 32˚C and 36˚C.

Consistent with the observations of Stevens and Choo[14] and Essick et al,[7] all the test sites except the tongue tip were more sensitive to cooling than warming, and in contrast to warmth, sensitivity to cold varied little among the sites in the present study. The neurophysiological basis for this finding is unclear, but there are a few hypotheses. Lele et al suggested that nonspecific nerve endings for cold stimuli are situated relatively more superficially in the skin than those for warm stimuli.[12] According to Davies et al, the higher thresholds to warmth compared to cold may be related to the small number of warm spots on the skin.[11] On the other hand, Essick et al speculated that facial sites have equal proportions of cool and warm thermoreceptors, but the former are simply more sensitive, requiring less spatial integration for attainment of the threshold.[7] The lower sensitivity for cooling of the tongue tip than extraoral sites might be attributed to the higher baseline temperature of 36°C of the tongue tip, at which the sensitivity to warmth is greater and sensitivity to cooling is less.

In general, detection thresholds varied less than pain thresholds at every site and the variability in the CPTs that were most imprecise and difficult to test was larger than the variability in HPTs. The present study also showed that CPT values were not different among V1, V2, and V3 sites. The high variability in CPTs is well recognized.[7,17–20] Variables such as the criteria on cold pain could influence CPTs, ie, some report an unpleasant cold feeling whereas others show overt pain on noxious cold stimuli.[21] For this reason, their measurement in clinical studies has been eliminated by some investigators.[22] Further study is therefore needed to reduce the inter-individual variations of thermal pain thresholds.

Pigg et al measured CDTs, WDTs, and HPTs at the tongue tip.[3] The temperature change from the baseline temperature to CDTs and WDTs in their study was lower than that in the present study but the HPT was in the same range in both studies. Subjects in the study by Pigg et al were 15 men and 15 women, while all 30 subjects in the present study were men. However, differences in detection thresholds cannot be attributed to sex differences, since it has been reported that sex differences are present only for pain thresholds (especially heat pain) and detection thresholds are independent of sex.[15] In addition, since the ages of the subjects were in the same range and similarly sized thermodes were used in both experiments, age and spatial summation do not likely account for the threshold differences for cool and warmth. However, differences in baseline temperature or ethnic group between both studies may account for the different findings.

The differences in thermal thresholds at orofacial sites could be attributed to variability of the biophysical properties of the skin, such as afferent innervation density, depth of receptors, and variability in the central processing,[3,6–8,23] which would justify that the orofacial sites need their own thermal threshold normative data.

Relationship Between Thermal Thresholds

Essick et al[7] and Stevens and Choo[14] reported that sites that were relatively sensitive to cooling were relatively sensitive to warming and that subjects who were relatively sensitive to warmth were relatively sensitive to cooling. In the present study also, subjects who were more sensitive to nonpainful cool stimuli were more sensitive to warm stimuli at the same test sites except the lower lip and the forehead. One possible interpretation of these findings is that sites in the subject which are abundant in cold receptors also have high density of warm receptors for optimal function.

In the case of pain thresholds, all test sites exhibited significant negative correlations between the thresholds for noxious cold and heat stimuli, as also observed in the study by Essick et al.[7] Thus, it is suggested that subjects' sensitivities to noxious cold stimuli substantially predicted their sensitivities to painful heat stimuli. Significant correlation between CPTs and HPTs can be also explained by criteria for pain being relatively variable among individuals compared to those for cool and warm sensation; ie, individual differences for noxious stimuli in QST are accompanied by differences in pain processing in the central nervous system and reflect individual attitudinal bias for pain.[14,24] Such an interpretation supports the hypothesis of Essick et al[7] that subjects who readily report heat pain are willing to readily report cold pain.

On the other hand, the relationships between nonpainful and painful thermal stimuli were much less compelling, and it is conceivable that subjects' sensitivities to innocuous thermal stimuli poorly predict their sensitivities to noxious thermal stimuli at all test sites except the forehead. However, the forehead exhibited a significant correlation between CDTs (ΔT, °C) and HPTs (°C) in the present study. It is commonly believed that human cold sensation is mediated mainly by Aδ fibers, and the onset of pain sensation and magnitude of pain intensity with an increasing heat stimuli depend on progressive recruitment of the less sensitive C fibers.[9] However, Campero et al found C fibers responding to innocuous cold temperatures in the human hairy skin.[25] This result suggests that those who are sensi-

tive to cold detection might be relatively sensitive to heat pain as well. Another possible explanation is that there are different site-dependent ratios of thermoreceptors for innocuous thermal stimuli to thermonociceptors for noxious thermal stimuli,[7] but further studies are needed to address this.

Influence of Baseline Temperature on Thermal Thresholds of the Tongue

The effect of the baseline skin temperature on the response of warm and cold thermoreceptors to rapid changes in temperature is complex. In general, thermoreceptors respond poorly to changes from baseline temperature at which they are least sensitive.[9] The warmth thresholds are high at low skin temperatures and decrease as the skin temperature rises, while the cold thresholds are low at low skin temperatures and increase when the skin temperature rises above 35°C.[8] That is, warm thermoreceptors are less able to signal increments in temperature at 30°C (a "cool" temperature for warm thermoreceptors) than they are at 35°C. Cold thermoreceptors are less able to signal increments in temperature at 40°C (a "warm" temperature for cold thermoreceptors). In other words, increments are more readily detected at the warmer temperatures and decrements are more readily detected at the cooler temperature.[9,10] Consistent with these findings, the present study found that the baseline temperature influenced the thermal detection threshold for cold and warm, respectively, and cold sensitivity was more affected than warm sensitivity at the lower baseline temperature of 32°C, but there was no significant difference at the higher baseline temperature of 36°C. Further experiments using baseline temperatures above 36°C are needed to confirm the influence of increased baseline temperature on thermal sensitivity. Nonetheless, contrary to the findings for WDTs and CDTs, there were no significant differences in CPTs between baseline temperatures of 32°C and 36°C. The discharge of C-fiber polymodal nociceptive afferents, which are activated by noxious hot and cold stimuli, is relatively unaffected by the baseline temperature of the afferents' receptive field.[9] This suggests that thermal pain thresholds are relatively unaffected by the baseline temperature, although the present study found significant differences in HPTs between the two different baseline temperatures. Further study on the effect of various baseline temperatures on thermal pain thresholds is needed, taking into account the need to obtain baseline temperature measurements at each test site.

Limitations and Strengths

The limitation of the present study is that all subjects were young men, and so the possible influence of sex and age on thermal thresholds could not be evaluated. Further research should consider such factors to obtain normative values of thermal thresholds. There are also relatively few QST data of Asians compared to those of Westerners. Therefore, a strength of the present study is that the findings of normative thermal thresholds of 30 young Asians provides new insights into the influence of ethnicity on thermal thresholds.

Conclusions

Thermal thresholds varied between orofacial test sites. Subjects who were relatively sensitive to cold stimuli tended to be more sensitive to heat stimuli. Baseline temperature affected thermal sensitivity of the tongue. CPT was the most imprecise, with a larger variability than other thermal thresholds. Further studies are needed to address the large variability of CPTs if CPTs are to be used to discriminate cold hyperalgesia or cold hypoalgesia in various orofacial conditions.

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