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ORIGINAL ARTICLE

Quantitative sensory testing (QST) in the orofacial region of healthy Chinese: influence of site, gender and age

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ABSTRACT

Objective: To establish a preliminary thermal and mechanical somatosensory profile using a standardized quantitative sensory testing (QST) to investigate site, gender and age differences in healthy Chinese.

Materials and methods: Twenty younger (age: 20–40 years, 10 men, 10 women) and twenty older (age: 41–61 years, 10 men, 10 women) healthy participants completed the study. Cold detection threshold (CDT), warm detection threshold (WDT), cold pain threshold (CPT), heat pain threshold (HPT), mechanical detection threshold (MDT) and mechanical pain threshold (MPT) were measured at five sites: Left hand, bilaterally at the mental area, tip of tongue and the lower lip mucosa. Mixed model ANOVAs with repeated measures were used to analyze the data.

Results: MDT($p < .001$) and MPT ($p < .05$) were significantly higher on the hand compared to the mental areas. The CDT ($p = .006$) was significantly higher and WDT ($p < .001$) was significantly lower at the tongue compared to lip mucosa and CDT ($p < .001$) was higher at the tongue mucosa than at the mental areas. WDT ($p < .001$) and HPT ($p < .05$) were significantly higher at the tip of the tongue and the lower lip mucosa compared to the mental areas. Significantly lower sensitivity for WDT ($p < .001$) and CDT ($p = .004$) were found in the older group compared to the younger group. Significant gender differences were found with less sensitivity for WDT ($p = .024$) and MDT ($p = .003$) in men compared to women.

Conclusions: Application of standardized QST can provide valuable information of orofacial somatosensory phenotypes in a Chinese population. Age, gender and site are mandatory to control for.

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Introduction

It has been estimated that up to 22% of the population world-wide may suffer from orofacial pain [1]. Orofacial pain conditions can be both recurrent and persistent and include nociceptive, neuropathic and idiopathic subtypes [2,3].

The clinical signs and symptoms often overlap between nociceptive and neuropathic pain conditions, leading to difficulties in differential diagnosis [4,5]. As a reliable, non-invasive psychophysical tool to evaluate the conscious perception of somatosensory stimuli, quantitative sensory testing (QST) has been used to investigate sensory abnormalities in patients with different types of orofacial pain in previous studies [5–9]. The German Research Network on Neuropathic Pain (DFNS) has developed a standardized QST battery for assessment of somatosensory function, and a reference dataset of healthy individuals and patients with various pain conditions have been established [10].

Recent studies have demonstrated the utility and reliability of the standardized QST protocol for the orofacial region [11–13]. For instance, a QST profile at the infraorbital (V2) and mental region (V3) in healthy human has been established [11] and a complete somatosensory profile has been obtained with the use of the standardized QST protocol at intra-oral sites (V2/3) and at the dorsum of the hand (C7) of healthy humans [14]. Intra-oral somatosensory disturbances in atypical odontalgia patients have been examined using healthy individuals as a reference group [12]. Furthermore, QST has demonstrated diagnostic capabilities in temporomandibular disorders (TMD), burning mouth syndrome, atypical odontalgia and idiopathic trigeminal neuralgia [15–18] as well as in elucidating mechanisms of peripheral and central sensitization following third molar surgery [19]. In the diagnosis and understanding of the underlying pathophysiology of orofacial pain, information on the sensory processing is important [5,20]. Since the trigeminal nerve (V) mediates

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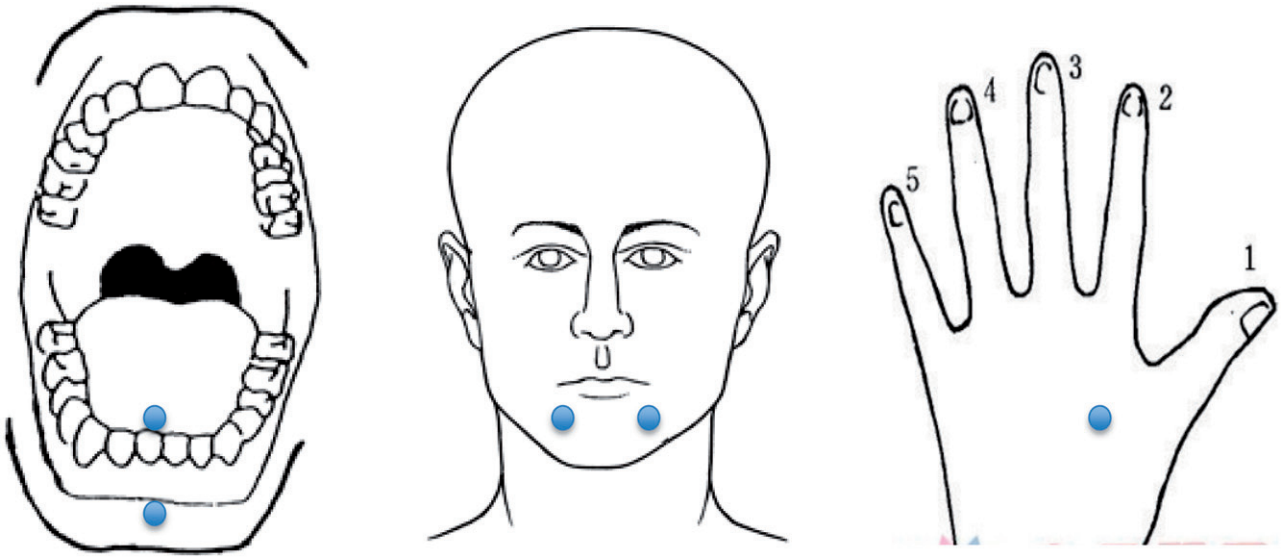

Figure 1. Thermal and mechanical sensory testing was performed at five sites in all participants: at the tip of the tongue, at the mucosa of the lower lip, at the skin on both sides of the mental foramen (V3 L/R) and at the surface of the left hand (C7).

both intra- and extra-oral somatosensory afferent inputs, including nociceptive information from most of the orofacial region, careful assessment is necessary to assist diagnosis [20–23]. However, thermal QST at the intra-oral mucosa has mainly been established in Caucasian populations [14,12,24]. A recent study found that there is, indeed, a significant difference in thermal sensitivity between Caucasian and Chinese populations [25], which may modify the utility of thermal QST in both clinical practice and research studies of orofacial pain in non-Caucasian populations. The aim of the present study was to establish a preliminary thermal and mechanical QST profile at intra- and extra-oral regions comparing with an extra-trigeminal region (hand; C7) and test for site, age and gender differences in healthy Chinese.

Materials and methods

Participants

Twenty younger healthy individuals (age: 20–40 years, mean: 23.7 ± 1.3 years; 10 men, 10 women) and twenty older healthy individuals (age: 41–61 years, mean: 53.0 ± 5.8 years; 10 men, 10 women) participated in the study. None of the participants had prior experience with QST. All experiments were performed in accordance with the guidelines of the local ethics committee at Nanjing (No: PJ2013-013-04).

The inclusion criterion was self-reported health without a history of any kind of orofacial pain problems and willingness to participate in the study. Exclusion criteria included systemic diseases known to be related to orofacial pain, a history of mental disorders, presence of any acute or chronic pain conditions in the head, neck, face and upper limb region, ongoing dental treatment, taking pain medication, antidepressants or non-steroidal anti-inflammatory drugs (NSAIDs) in the last month and the current use of caffeine within 24 h of the day of testing. Informed consent was obtained from all individuals prior to participation.

Study design

Thermal and mechanical sensory testing was performed at five sites in all participants: at the tip of the tongue (Tongue; V3), at the mucosa of the lower lip (Lip; V3), at the skin on both sides of the mental foramen (Mental areas, V3 L/R) and at the surface of the left hand (Hand, C7) (Figure 1). For practical reasons (time, attention of participants, etc.) only six thermal and mechanical test parameters out of the 13 previously described for both intra- and extraoral QST [10] were selected in the present study. All participants were tested at the five sites in a randomized manner by one examiner who had been trained extensively in the use of QST according to the DFNS examination protocol.

Thermal detection and thermal pain thresholds

Thermal quantitative sensory tests were performed using a computerized thermal stimulator (MEDOC TSA-2001 apparatus, Medoc Ltd, Ramat-Yishai, Israel). Two different thermodes were used for the assessments. The contact area of the extra-oral thermode was 30 × 30 mm and the intra-oral thermode was 6 × 6 mm .

Cold and warm detection thresholds (CDT, WDT) were measured first, followed by cold and hot pain thresholds (CPT, HPT). The mean thresholds of three consecutive measurements were calculated. The temperature of the thermode started at a baseline of 32 °C for the extra-oral sites and 37 °C for the intra-oral sites and cooled down or heated up at a rate of 1 °C/s to the lower limit of 0 °C or upper limit of 50 °C. Participants were instructed to press a button on the computer mouse as soon as they perceived the thermal sensation of cold, warm, cold pain, or heat pain following the instructions developed by the DFNS. The procedure then ended and the temperature returned to baseline. The participants were instructed not to look at the computer screen at any time during the testing procedures.

Table 1. Means and SDs of absolute thermal and mechanical QST data from five test sites in a younger ($n = 20$) and older ($n = 20$) group.

			Site				
	Gender	Age	Lip	Tongue	V3 Left	V3 Right	Hand
CDT (°C)	Women	Younger	32.1 ± 0.8	32.7 ± 1.3	31.2 ± 0.4	31.4 ± 0.1	31.2 ± 0.3
		Older	30.2 ± 1.9	32.4 ± 2.1	30.3 ± 0.5	30.3 ± 0.9	29.8 ± 0.9
	Men	Younger	32.4 ± 1.5	32.8 ± 2.8	30.9 ± 0.3	30.6 ± 0.4	29.4 ± 1.8
		Older	30.9 ± 1.3	33.9 ± 1.1	29.5 ± 1.1	30.3 ± 0.8	29.1 ± 2.2
WDT (°C)	Women	Younger	39.4 ± 1.4	39.7 ± 0.7	32.9 ± 0.3	32.8 ± 0.4	33.3 ± 0.8
		Older	43.3 ± 3.0	40.3 ± 0.8	34.0 ± 0.7	34.0 ± 0.9	34.4 ± 1.0
	Men	Younger	42.0 ± 1.6	39.7 ± 1.1	33.6 ± 0.5	34.1 ± 0.9	34.3 ± 0.7
		Older	43.6 ± 3.0	39.6 ± 2.2	34.5 ± 1.8	34.5 ± 1.8	34.4 ± 1.3
CPT (°C)	Women	Younger	23.4 ± 3.0	27.0 ± 1.8	25.2 ± 6.2	23.3 ± 8.0	25.3 ± 4.7
		Older	12.0 ± 10	13.4 ± 8.2	17.1 ± 8.1	17.1 ± 8.1	16.3 ± 8.2
	Men	Younger	17.2 ± 9.0	19.0 ± 8.4	17.7 ± 8.4	17.6 ± 7.8	16.4 ± 7.3
		Older	22.5 ± 9.0	19.5 ± 7.5	23.7 ± 4.9	23.8 ± 6.7	21.6 ± 4.5
HPT (°C)	Women	Younger	44.7 ± 2.0	43.1 ± 2.3	39.3 ± 3.5	40.0 ± 3.4	38.9 ± 2.1
		Older	47.2 ± 2.3	44.6 ± 2.5	41.5 ± 4.3	43.3 ± 4.7	40.3 ± 3.2
	Men	Younger	46.8 ± 2.3	45.1 ± 2.4	41.8 ± 3.3	42.0 ± 3.5	41.7 ± 3.3
		Older	47.3 ± 2.6	45.6 ± 3.3	38.9 ± 3.3	40.6 ± 3.9	39.8 ± 5.3
MDT (mN)	Women	Younger	2.0 ± 0.2	1.8 ± 0.2	2.1 ± 0.3	1.9 ± 0.1	2.6 ± 0.6
		Older	2.1 ± 0.3	2.0 ± 0.3	2.0 ± 0.2	2.0 ± 0.2	3.1 ± 0.3
	Men	Younger	2.1 ± 0.2	2.0 ± 0.1	2.2 ± 0.1	2.2 ± 0.1	3.2 ± 0.2
		Older	2.0 ± 0.1	2.0 ± 0.0	2.0 ± 0.1	2.1 ± 0.1	2.9 ± 0.5
MPT (mN)	Women	Younger	8.6 ± 1.4	10.2 ± 2.6	9.5 ± 2.4	8.9 ± 2.2	15.3 ± 14.0
		Older	11.6 ± 7.1	12.7 ± 9.0	10.9 ± 5.7	10.9 ± 5.7	23.5 ± 13.0
	Men	Younger	12.2 ± 5.4	12.7 ± 6.9	13.7 ± 10.0	12.6 ± 5.9	25.1 ± 15.0
		Older	8.0 ± 0.0	8.0 ± 0.0	8.0 ± 0.0	8.0 ± 0.0	16.0 ± 10.0

Mechanical detection and mechanical pain thresholds

Mechanical detection thresholds (MDT) were measured using standardized Semmes–Weinstein monofilaments with 20 different diameters (North Coast Medical, Canada). The number of each filament (1.65–6.65) corresponds to a logarithmic function of the equivalent forces of 0.008–300 g. The filament was applied vertically to the test sites and the pressure was applied slowly until the filament bowed with a total contact time of about 1 s. To prevent filament slippage, intra-oral examination sites were dried with gauze before testing [14]. To detect the mechanical pain threshold (MPT), weighted pinprick stimuli delivered with a custom made set of seven pinprick stimulators (Aalborg University, Denmark) were used. Each stimulator had a flat contact surface of 0.2 mm that exerted forces of 8–512 mN [26,27]. All pinprick tests were made with the stimulator perpendicularly to the examination site and in a vertical position with the contact time of about 1 s. MDT and MPT were measured using the 'method of limits' technique described by Baumgartner [28]. Five threshold measurements were made, applying series of ascending and descending stimulus intensities. One threshold value was determined by calculating the geometric mean of the five series. The filaments and pin-prick stimulators were disinfected using 75% alcohol after each examination. This procedure is unlikely to cause significant impairment in test performance of the devices.

Statistical analysis

The necessary logarithmic transformation was performed to secure normal distribution of the data. Descriptive statistics were used to summarize all measurements. The mean values and standard deviations of CDT, WDT, CPT, HPT, MDT and MPT in each gender, age group and test site were calculated. The data was analyzed using a multi-way mixed model ANOVA with repeated measures (sites and sides) and between group (age and gender) comparisons. A Bonferroni test was employed for *post-hoc* comparisons. All statistical calculations were performed using the Statistical Package for Social Sciences, version 20 (SPSS, IBM). The significance level was set at .05.

Results

All participants completed the study. The absolute values of all variables CDT, WDT, CPT, HPT, MDT and MPT in the two age groups and for both genders at the five test sites are presented as means and SDs in Table 1.

Side differences

No significant right-to-left side differences were detected for any of the QST parameters ($p > .05$) (Table 3). Therefore, the values from the left and right mental area were combined.

Site differences

Significant site differences were found for CDT, WDT, HPT, MDT, MPT as shown in Tables 2 and 3.

A significant site effect was observed between the left hand and the mental areas. MDT ($p < .001$) and MPT ($p = .002/.001$) at the left hand was higher (less sensitive) than at the mental areas.

At the tip of the tongue and the lower lip mucosa, a significant difference was noted for thermal sensitivity between the lower lip mucosa and the tongue (CDT: $p = .006$, WDT:

$p < .001$) with the tongue being more sensitive than the lower lip mucosa (Table 3).

Furthermore, CDT ($p < .001$) at the tongue mucosa was higher (more sensitive) than at the mental area (Tables 1 and 3). WDTs (Lip: $p < .001$, Tongue $p < .001$) and HPTs (Lip: $p < .001$, Tongue: $p < .05$) were significantly higher (less sensitive) at the tip of the tongue and the lower lip mucosa compared to the mental areas.

Age effects

Significant age differences with higher thresholds (less sensitive) was found for WDT (ANOVA; $p < .001$) and lower thresholds (less sensitive) was found for CDT (ANOVA; $p = .004$) in the older group compared to the younger group (Table 2).

Gender effects

Significant gender differences with higher threshold (less sensitive) was found in men compared to women for WDT (ANOVA; $p = .024$) and MDT (ANOVA; $p = .003$).

Discussion

The present preliminary study demonstrated significant differences in somatosensory sensitivity at different trigeminal test sites and robust age and gender differences were noted in a healthy Chinese population. Further studies can be initiated with standardized QST for better understanding of various orofacial pain mechanisms in the Chinese population.

Site differences

It is a well-established fact that QST parameters obtained in a standardized manner vary significantly between the face, hand and foot [10]. In this study, somatosensory sensitivity was higher at the mental areas (V3 L/R) than at the hand for MDT and MPT in accordance with Rolke et al. [10]. Several reasons may underlie the gross difference in mechanical sensitivity between the trigeminal and spinal regions such as differences in innervation density of the skin, differences in receptor sensitivity [29] and/or differences in biophysical properties for example thickness of the epidermal layers [30].

Site to site differences also exist within the trigeminal region, for example, tactile detection sensitivity, spatial acuity and sensitivity to warmth have been shown to be greater at skin sites located in the midface compared to the lower face [31]. Overall, such site-to-site differences in QST parameters should be recognized when studies are designed and results are compared between clinical trials in different orofacial pain conditions.

Yekta et al. performed QST in 60 healthy volunteers at both sides on the hairy skin of the upper and lower lips and at the anterior lateral two-thirds of the tongue. Thermal sensitivity was higher at the upper lip, followed by the lower lip and the tongue [32]. However, the results from the present study indicated that thermal detection sensitivity at the tongue was higher than at the lower lip mucosa. Moreover, the present results showed significant differences in CDT, WDT and HPT between the intra-oral tongue mucosa and the mental areas. The variation in thermal somatosensory function may include differences in the type of orofacial thermal receptors or their localization in the oral mucosa or facial skin [33]. Overall, these subtle, but significant site-to-site differences within the trigeminal region and between intra- and extra-oral sites further emphasizes the importance of careful description of the anatomical test site and appropriate control when prospective studies are performed in various orofacial pain conditions.

Age differences

In the present study, a significant age effect (decreased sensitivity in older group) was detected only for the thermal detection thresholds (Table 1). Similar results have been reported in a previous study in which decreased thermal detection thresholds (WDT, CDT) were detected whereas thermal pain sensitivity (CPT or HPT) was unchanged with aging [34].

Interestingly, the present study showed no significant differences in MDT or MPT between the younger and older groups. In the oral region, encapsulated sensory corpuscles such as Krause's end-bulbs have been found in monkey fungiform papillae [35], but the influence of aging on these receptors has not been evaluated. Taguchi et al. also found

Table 2. A mixed model analysis of variance (ANOVA) for CDT, WDT, CPT, HPT, MDT and MPT in different gender and age groups at five sites with repeated measures was performed.

	Age		Gender		Site	
	F	p	F	p	F	p
CDT	8.884	.004*	0.638	.426	15.031	<.001*
WDT	14.062	<.001*	5.21	.024*	166.895	<.001*
CPT	2.419	.123	0.264	.608	0.66	.621
HPT	0.607	.438	1.043	.309	15.393	<.001*
MDT	0.002	.961	9.175	.003*	44.145	<.001*
MPT	1.12	.292	0.001	.983	4.631	.002*

*Indicates significant difference ($p < .05$).

Table 3. Differences between test sites.

Site to site	CDT	WDT	CPT	HPT	MDT	MPT
V3L-V3R	1	1	1	1	1	1
Lip-Tongue	0.006*	< 0.001*	1	0.483	0.766	1
Lip-V3L/R	0.672/0.949	< 0.001*	0.513/0.644	<0.001*	1	1
Lip-Hand	0.004*	< 0.001*	0.88	<0.001*	<0.001*	0.001*
Tongue-V3L/R	<0.001*	< 0.001*	1	0.001/0.035*	0.881/1	1
Tongue-Hand	<0.001*	< 0.001*	1	<0.001*	<0.001*	0.005*
V3L/R-Hand	0.786/0.55	1	1	1	<0.001*	0.002/0.001*

*Indicates significant difference ($p < .05$).

that nociceptive behaviors in response to noxious levels of cold and heat were facilitated in aged animals, while mechanical sensitivity measured by von Frey hairs remained unchanged. These discrepancies between the changes in peripheral afferents and the behavioral outcomes might be explained by facilitatory changes in the central nervous system [36].

In this respect, it is interesting to observe that age-dependent decreases in the densities of Meissner corpuscles have been reported in human fingers and toes [37]. Aydoğ also reported the numbers of mechanoreceptors, especially Ruffini receptors, decreased with aging [38]. However, the present study could not demonstrate significant age-related differences in mechanical sensitivity (MDT/MPT) at the dorsum of the hand (C7).

These data suggest that the age effect on the somatosensory function is a stable general trait which is most prominent for thermal than for mechanical QST parameters commonly used as functional measures of somatosensory aging [38]. The underlying mechanisms for such age-dependent changes in somatosensory function may be related to a decrease in density of epidermal nerve fibers with age [39]. Age and ethnicity may be the most common independent factors with an influence on nerve fiber function in general. For example, increasing age is associated with a decrease in motor and sensory (except sural) conduction velocities [40].

In general, the issue of age-dependent changes in specific measures of somatosensory function needs further investigation, but it seems prudent to carefully control for age when QST are compared between groups, for example, in different types of orofacial pain conditions.

Gender differences

In this study, gender differences were observed for MDT and WDT, indicating that men were less sensitive than women to both mechanical and thermal stimuli. A previous study in the trigeminal region examined the sensitivity bilaterally at test sites supplied by the infraorbital (V2) and mental (V3) nerves and demonstrated a significant gender difference with lower CDT (higher sensitivity) for women than for men [11]. Yang et al. tested 70 healthy individuals bilaterally over the infraorbital, mental and hand regions according to the German Research Network on Neuropathic Pain consisting totally of 13 different parameters and revealed that female were more sensitive than male for most of the parameters [41].

Sex-related differences in somatosensory sensitivity may be due to the differences in tissue conformation and thickness, mechanoreceptor densities, skin hydration or temperature characteristics [42]. Indeed, female and male skin may vary regarding biophysical properties; it has been pointed out that female skin appears to have a higher elasticity and extensibility [43]. In addition, hormonal changes during the menstrual cycle may lead to gender differences [44]. Nevertheless, gender seems to be an important factor when evaluating the somatosensory function in orofacial pain conditions also in the Chinese population.

Limitations of the study

The present study was not designed to test variability in QST measures but rather to test for site-to-site differences and the effects of age and gender in a Chinese population. A recent study [25] has demonstrated sizeable differences between Western and Chinese populations and data may not directly be transferred from one population to the other. It should be noted that QST findings also will be sensitive for the number of participants because there are substantial inter-individual variability [45]. The present study tested only 20 participants in each age group which is a relatively small sample size. The results might therefore only be considered as a preliminary profile of somatosensory function but nevertheless clearly indicate the applicability of the QST techniques. Obviously, larger groups would allow for smaller differences to be detected but at compromising the clinical relevance of difference between groups. Future studies may need data from multiple centers and larger cohorts to establish a site, age and gender specific reference base for studies on somatosensory sensitivity in a Chinese population.

Conclusions

The application of thermal and mechanical QST can provide valuable information for a better understanding of the underlying mechanisms of somatosensory phenotypes in healthy Chinese and for further study of sensory dysfunctions in the intra- and extra-oral trigeminal area. The present QST methodology is adequate to be applied in future clinical studies establishing normative values and possibly for mechanism-based profiling of various pain disorders in the intra- or extra-oral areas.

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Disclosure statement

The authors declare no conflicts of interest.

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