Aims: The aims were to compare the sensory thresholds on the tip of the tongue with on the dorsum of the hand, and to investigate the relationship between the sensory threshold and depressive mood with volunteers whose psychological conditions were normal. Methods: Fifty-five subjects (28 women, 27 men) took psychiatric structured diagnostic interview and Self-rating Depression Scale (SDS). In the next step, the quantitative sensory tests (light touch sensation and thermal sensory test) were carried out on the tongue and the hand. Then we investigated the relationship between depressive moods and sensory thresholds on the tongue and the hand using logistic regression model. Result: The sensory thresholds on the tip of the tongues were significantly different from those on the dorsum of the hands. Only on tongue tip, increment of SDS had relation to the thresholds of innoxious thermal stimulation (OR=0.152, 95% CI. 0.049-0.478) and noxious heat stimulation (OR=0.352, 95% CI. 0.169-0.734). Conclusion: This finding might support for the idea that depressive mood had closer association with the tongue of the orofacial areas than the dorsum of the hand.

Key words: Sensory threshold, Tongue, Depressive mood, Structured Diagnostic Interview, Self-rating Depression Scale (SDS)

Introduction

The psychological factors such as emotional condition, depressive state and personality trait were well known to play important role at the onset and aggravation of pain, and at the turning point of pain perception in orofacial region. We often observed a patient whose sensory threshold decreased in oral area and psychological condition was considered as depressive. Feinmann et al. mentioned that in terms of psychological influence the orofacial region was largely effected compared to the other body region. The threshold of simulated pain (thermal or mechanical stimuli) was reported either to decrease or to increase in experimental studies. In recent study, however, many researchers reported the threshold would increase in the patient with major depression.

There were various ways in experimental algetic methods used senses of temperature, a pinprick and electricity esthesia. The quantitative examination methods had been developed to check neuropathies, and to evaluate neurological functions of myelinated nerve (Aβ& Aδ fiber) and unmyelinated nerve (C fiber). There were a lot of reports concerning affecting factors such as sensory factors and emotional factors to sensory threshold. These studies which had been dis-
cussed emotional factor were carried out mainly on hands and feet, and the emotional factors combined with measured sensory thresholds were discussed. On the other hand, there were few reports associating with the emotional factors on orofacial area except for the comparison studies of the orofacial area with other body regions. Although the oral sensitivity was seemed more affected by depressive mood than that in other body area, there were few researches on the association between the pain threshold in the oral area and the depressive mood. We therefore compared the sensory threshold on the tip of the tongue with on the dorsum of the hand, and investigated the association between the pain threshold and the depressive mood in psychologically healthy volunteers. We evaluated the psychological state by a structured interview conducted a psychiatrist to check mental disease and depressed mood in order to exclude a subject with psychologically definite disorder because the self-rating questionnaire was considered insufficient to detect a psychological morbidity. Thereafter the self-rating questionnaire was administered to the appropriate subject to rate the level of depressive mood.

**Materials and Methods**

**Subject**

We recruited 61 Japanese volunteers between ages 17 to 34 during October 2002 to April 2003. Exclusion criteria included the patients who have any medical history of neurological dysfunction in the trigeminal area by trauma or surgery, and stroke or any other neurological impairment, as well as pregnancy and definite mental disorders. Subjects were mainly recruited from the dentist at the Tokyo Medical and Dental University. Using these criteria, 6 subjects were excluded out of 61 volunteers; of those six, four subjects with psychiatric disorders (borderline personality disorder, conversion neurosis, depression, alcoholism) diagnosed by a psychiatrist, while the other two subjects refused to participate. Consequently 55 subjects (28 women, 27 men) were enrolled. The characteristics of the subjects are presented in Table 1. The written informed consents were obtained from all subjects. This study was approved by the local ethics committee of Tokyo Medical and Dental University.

**Psychiatric assessments**

The assessments included the psychiatric history as well as a structured diagnostic interview (Japanese version of Mini International Diagnostic Interview: MINI, ver5.0.0.), to identify psychiatric disorders according to DSM-IV and ICD-10 criteria. With an administration time of approximately 15 minutes, the interview was designed to meet the need for a short but accurate structured psychiatric interview. One of our authors (Y S) conducted the interview for all volunteers. Subjects suffered from psychiatric problems were excluded by this interview. We adopted the Japanese version of the Self-rating Depression Scale (SDS) to measure levels of depressive moods independent of psychiatric diagnosis. The SDS consists of 20 items and measures depressive symptoms over a seven-day period. The Japanese version of this rating scale showed high reliability and validity. Each item is rated from 1(a little of the time) to 4(most of the time); the total SDS can range from 20 to 80, a higher score indicates more severe depression.

**Sensory test**

Sensory testing was carried out in a quiet, air-conditioned room with the subjects relaxed, comfortable and eye closed and mainly in the afternoon. At the first step, subjects were tested to determine their light touch sensations, and secondly the thermal sensory test was conducted. We adopted two types of thermal sensory test. One was reaction time inclusive method (RT-In); the other was reaction time exclusive method (RT-Ex). In RT-In method, the test instrument was put on the body and temperature was continuously changed until the patients felt a warm (or hot) stimulus. In the RT-Ex method, the temperature was not changed during the testing. The sites of stimulation were on the dorsum of the hand in the territory of the radial nerve, and on the tip of the tongue in the territory of mandibular nerve. We choose the dorsum of the hand as a control site because it is practically suitable for the evaluation of sensory thresholds.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
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<tbody>
<tr>
<td>Number of subjects</td>
<td>55</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>49</td>
</tr>
<tr>
<td>Age (median, 25%, 75%)</td>
<td>27(26, 29)</td>
</tr>
<tr>
<td>SDS score (median, 25%, 75%)</td>
<td>33.0(29.0, 36.3)</td>
</tr>
</tbody>
</table>

SDS=Self-rating Depression Score

Table 1. Patient Characteristics
Light touch sensation test
Semmes Weinstein Monofilament (SAKAI Inc, Tokyo JAPAN) was used to measure light touch sensation. The reliability and validity of this device had been established. We used 5 filaments (Filament force: 0.0045-0.1660g) out of the 20 different filaments (Filament force: 0.0045-447.0g). The filament was bend when a calibrated pressure was applied for the tissue. The force was continuously applied by filament for 1 second, and then the filament was removed. The filament was randomly chosen to apply for the tissue and was conducted ten times. We considered that sensory threshold correctly reported when the subjects showed the reactions by the stimuli of 5 (or more) out of 10 filaments. We assigned the 5 filaments numbers 1-5 (Table 2). Each 5 stimuli was applied for the right and left sides to avoid sensitization. Blank stimuli were also applied randomly during the testing.

Thermal sensory test
Thermal stimuli were delivered by pain thermometer (UDH-104, Unique Medical Inc., Tokyo, Japan). The instrument had sufficient reliability and validity for the assessment of thermal threshold. There were two types of the skin contact platinum probes. One was a 2 mm diameter for the tongue tip and the other was a 10 mm square for the dorsum of the hand. The probes were held manually with care in order to minimize mechanical stimuli. Two methods of threshold determination were applied in this thermal testing. The first was reaction time inclusive: RT-In methods, those were dynamic stimuli and called the limit method. The temperature was increased 0.25°C/s and subjects were asked to press the off-switch when they felt first warmth or hot pain. The thresholds were determined from the averaging of three consecutive presentations. The second method was reaction time exclusive: RT-Ex methods, those were static stimuli. In this method thresholds were determined by the reaction time of subjects (within three seconds) when stimulus was applied. The first stimulus temperature was under the skin temperature. We usually applied the probe kept the temperature on 34°C on skin or on tongue, and raise the temperature by every three-degree until the subject felt warmth. From this turning point, we then lowered it by every two-degree until he/she could not feel warm. The threshold would exist between at the upper turning point and at the lower point at which the subject did not feel. We thereafter raised the temperature by every one-degree to detect the threshold at which the subject felt warm again. We decided the average value on three testings as a warm threshold (Thermal Sensitive Thresholds (TST)). We also detected the pain threshold (Thermal Pain Perception Thresholds (TPTh)) provoked by heat with this same procedure. The order of the application of the stimulus was TST on hand, TST on tongue, TPTh on hand and TPTh on tongue. In order to avoid possible sensitization of cutaneous receptors, we used 10 seconds intervals in the TST measurement and 40 seconds intervals in TPTh.

Statistical analysis
No variables had a normal distribution; therefore, the measure of central tendency was shown as the median and 25th and 75th percentiles.

Comparison between hand and tongue
The comparison of sensory thresholds between the dorsum of the hand and the tip of the tongue was investigated with Wilcoxon Matched-paires Singled ranks test.

Association of sensory threshold with depressive mood
We analyzed the association of each sensory threshold with depressive mood with multivariate stepwise logistic regression models. We dichotomized the measured value of each threshold to verify the hypothesis that the values of sensory threshold varied according to the level of a subject’s depressive mood (even in healthy individuals). We gave “0” as the label when the value was equal or less than the median value and “1” when the value was more than the median value. We defined these dichotomized labels as the dependent variable. Independent variables included

Table 2. Numbering of the Semmes Weinstein Monofilament

<table>
<thead>
<tr>
<th>Filament force (g)</th>
<th>Diameter (mm)</th>
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<tbody>
<tr>
<td>1</td>
<td>0.0045</td>
</tr>
<tr>
<td>2</td>
<td>0.0230</td>
</tr>
<tr>
<td>3</td>
<td>0.0275</td>
</tr>
<tr>
<td>4</td>
<td>0.0677</td>
</tr>
<tr>
<td>5</td>
<td>0.1660</td>
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</table>
sex, age and SDS. Also we gave the label of the sex “0” as the men and “1” as the women. The estimated odds ratios for the higher value of dichotomized threshold level (1) were calculated, and the variable was adjusted between independent variables by multivariate stepwise logistic regression models. A P-value of <0.05 was regarded as statistically significant. The data analyses were carried out with SPSS software ver.11.5 for Windows.

**Results**

*Sensory thresholds on the hand vs. the tongue*

The light touch threshold on the tongue tip was significantly lower than that on the dorsum of the hand as shown in Table 3. The thresholds on the tongue tip almost converged on the no.1 of the finest filament while they had much variance on the dorsum of the hand. Regarding thermal test, each thermal threshold (TST RT-In, RT-Ex, TPTh RT-In, RT-Ex) on the tongue tip was significantly higher than that of the dorsum of the hand as shown in Table 3.

**Association of sensory threshold with depressive mood**

The results of multivariate logistic regression analyses were shown in Table 4. The analyses found the significant factors in a few models not only for tongue but for hand. In light touch sensation age-increment was associated with higher thresholds (Table 4-1). In reaction time exclusive thermal sensitive thresholds, the SDS 5 point increment was associated with lower thresholds (Table 4-2). On the other hand, there were no significant variables in the model for hand (Table 4-4).

**Discussion**

There were a lot of reports concerning affecting factors such as sensory factors and emotional factors to sensory threshold. As for sensory factor, it was divided into the general factor and local factor. The general factor included age, gender, standing height, menstrual cycle, body mass index, smoking utility. The local factor included skin temperature, adaptation temperature, temperature changing rate, size of probe and tested site. The anxiety and depressive mood were examined as an emotional factor. This study was the first experimental comparison of the depressive moods to sensory thresholds using the tongue and hand in psychologically healthy subjects. Previous studies had not suggested any baselines as to how the perception thresholds in psychiatrically healthy subjects changed when the depressive mood increased. There had been several studies of sensory testing on normal subjects with depressive mood and on patients suffering from symptoms of depression. Most of these studies, however, used self-reporting questionnaires to rate the depressive mood. There would be possibilities to encounter psychiatrically abnormal patients with mood disorders whose score showed normal range. We therefore considered that it is dangerous to measure psychiatric abnormalities by using only self-rating questionnaires. We rated the SDS after all subjects had a structured diagnostic interview conducted by one psy-

<table>
<thead>
<tr>
<th></th>
<th>hand</th>
<th>tongue</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>light touch</td>
<td>4(3, 4)</td>
<td>1(1, 1)</td>
<td>0.000</td>
</tr>
<tr>
<td>TST RT-In</td>
<td>36.5(35.2, 38.5)</td>
<td>37.9(36.1, 40.1)</td>
<td>0.000</td>
</tr>
<tr>
<td>TST RT-Ex</td>
<td>35.9(34.7, 37.0)</td>
<td>37.6(36.3, 40.4)</td>
<td>0.005</td>
</tr>
<tr>
<td>TPTh RT-In</td>
<td>42.4(39.6, 45.0)</td>
<td>44.3(42.0, 47.1)</td>
<td>0.000</td>
</tr>
<tr>
<td>TPTh RT-Ex</td>
<td>42.7(40.2, 47.0)</td>
<td>45.0(43.3, 46.4)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

TST=Thermal sensitive thresholds; TPTh=Thermal Pain perception Thresholds; RT - In=Reaction time Inclusive; RT-Ex=Reaction time exclusive

Wilcoxon Matched-Pairs Single-Ranks Test
From this interview, subjects suffering psychiatric disorders were excluded. Though the relationship between depressive symptoms and the sensory thresholds of hands had been reported in normal subjects, there was no report concerning the difference of orofacial area and the other part of the body in relation to the depressive mood. The association of both nocuous and innocuous thermal sensory thresholds with SDS on the tongue was greater than those on hand. These results supported the hypothesis that depressive mood affected the orofacial area more than the other physical areas, and suggested that depressed patients might be likely to complain of any uncomfortable feelings in the oral area. Only on the tongue SDS were related to sensory thresholds. So far various quantitative and non-quantitative sensory testing had been applied to orofacial area, and those compared other parts of the body (particularly the hand and forearm and leg) to the orofacial area. Those studies assessed only sensory aspects but emotional aspect. Both the sensory and emotional aspects of sensory thresholds were studied in patients suffering from temporomandibular disorders, and phantom tooth syndrome. Jacobs et al. compared light touch sensation and thermal sensation (warm, cold) on the patients suffering from phantom tooth syndrome with control. They reported that the light touch sensation, as a low mechanical sensory threshold, was significantly lower in the patients than in the control group. Although they reported that the patients were more depressed than the control group, they did not show the direct relationship between decrease of the thresholds and depressive mood. From the investigation on the relationship between depressive symptoms and perception thresholds, Bar et al. and other investigators reported that the patients suffering from major depression showed higher thresholds than the control. In the systematic review, however, Dickens et al. suggested that the depressed patients resulted in decline of clinical pain thresholds. This paradox had not been resolved. With respect to this problem, Geisser et al. suggested that depression was not related to experimental pain in chronic pain patients, but was significantly related to clinical pain in the same sample. The homeostatic or compensatory processes might also reflect important differences of the clinical pain from the experimental pain. Lautenbacher et al. concluded that phasic experimental pain was due to diminished spinal and brainstem transmission and processing; on the other hand endogenous sensation (e.g. clinical complaints of

<table>
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<th>Table 4. Multivariate Logistic Regression Analysis for Sensory thresholds</th>
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<tr>
<td>Factor</td>
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<tr>
<td>--------</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>SDS</td>
</tr>
<tr>
<td>SDS</td>
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<tr>
<td>Sex</td>
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</table>

TST=Thermal sensitive thresholds; TPTh=Thermal Pain perception Thresholds; RT-In=Reaction time Inclusive; RT-Ex; Reaction time exclusive; SDS=Self-rating Depression Score
*Corresponds to 5-point increment, since 1-point increment did not produce meaningful odds ratios
NS=not significant
headaches and stomach pain) was due to insufficient activation of the pain descending inhibitory system. Cassens et al. concluded that a decrease in sustained attention or vigilance, which is more likely to occur in depressive mood than in healthy persons, might have been responsible for the higher threshold. Dickens et al. also mentioned that the attentional impairment seen in depression might be sufficient to reduce the perception of low intensity stimuli. In the brain imaging research compared the reactivity to both noxious and innocuous stimuli between normal subjects and subjects who had recovered from depression, the latter subjects displayed a reduced response in the cerebellum during the anticipation of noxious stimuli compared to innocuous stimuli. The cerebellum is involved in balance, maintenance of muscle tone, and coordination of fine motor movement. A major function of the cerebellum is to compare intended movements with actual movements. A potential action from the spinal cord and the trigeminal nerve controls the balance and movement. The previous report suggested that depressive patients had a damaged cerebellum. From these reports, it seemed that the dysfunction of the cerebellum might cause an increase of experimental sensory thresholds in depressive patients. Our study selected psychiatrically healthy subjects, who felt short of psychiatric disorders. Therefore, the functional impairment (e.g. diminishing spinal and brainstem transmission and processing, showing cerebellum functional abnormalities) resulting from depression was not considered to have occurred in these subjects. We thought this diminishing of perception thresholds to be derived from an insufficient descending inhibitory system, which was the result of an increase of depressive mood.

The SDS had no association with any lower threshold on the hand; however, it associated with lower threshold of two thermal tests for tongue. These results might explain the hypersensitivity in the oral region of some patients with depressive mood in the clinical setting. Although we considered that these thermal thresholds on the tongue might be decreased with an insufficient descending inhibitory system derived from an increasing of depressive moods as previously mentioned, we could not explain the reason why this insufficient system did not lead to a decrease of neither mechanical sensory threshold on the tongue nor any threshold on the hand in our study. There was no report concerning the association of a decrease of thermal sensory threshold on the tongue with depressive mood in previous study. The mechanical sensory threshold on both sites had no association with depressive mood, and the thermal sensory thresholds on the tongue were higher than those on the hand. This suggested that the depressive mood might exert an influence on the thermal sensation rather than the tactile sensation, and on the higher threshold rather than the lower threshold. In the future study, the research should be composed to elucidate these problems.

In this study, the SDS had no association with innocuous light touch thresholds on both tongue and hand. The aging was, however, associated with higher threshold for light touch on the tongue. Regarding to this sensory threshold activated by the large myelinated fiber (Aβ fiber), previous study reported that aging brought a specific decline in the perception of localized lingual pressure. It meant the decrease in the number of type II rapidly adapting receptor units (Morsen's complex). The result of our analysis with logistic regression model showed that the one-year increment of age produced an increase as three times as much of odds ratio with the probability that the subject would belong to the higher threshold group even though the age distribution was very narrow. This result suggested the aging might be a strong effecter on the increase of the light touch threshold on the tongue.

Some other emotional factors except for depressive mood had been discussed for their influence on perception thresholds (e.g. anxiety and catastrophizing). Future studies should include other psychological morbidities in order to investigate the influence of psychological factors more precisely on perception thresholds in the orofacial area.

Acknowledgments

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