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Effects of chewing efforts on the sensory and pain thresholds in human facial skin: A pilot study
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Abstract
The aim of this study was to examine the effect of chewing efforts on sensory and pain thresholds of the orofacial skin of symptom-free subjects. Fourteen healthy volunteers were recruited. Using a stair-case method, the tactile detection threshold (TDT) and the filament-prick pain detection threshold (FPT) on the cheek skin (CS) and the skin overlying the palm side of the thenar skin (TS) were measured before and after chewing gum for 5 min (Time 1: T1) and keeping the jaw relaxed for 5 min (Time 2: T2) as a control.
Both for the test and control situation, the TDT was higher in all measurement sites after 5 min. As for the FPT, the reactions between T1 and T2 were quite opposite: The FPT increased and/or remained stable in T1, while, it decreased at all sites in T2. There were significant session effects (T1-T2) on the FPT at the left CS ($P < 0.01$), right CS ($P < 0.05$) and TS ($P < 0.05$).
The increase of TDT after chewing/no chewing could be due to habituation, while the decrease of FPT observed in the control situation might be due to sensitization, respectively. This potential sensitization, however, was not observed after chewing efforts. Further studies are needed to clarify the modulating effect of masticatory function on the trigeminal sensory system.

Key words: chewing, quantitative sensory testing, habituation, sensitization, descending control system

1. Introduction
Mastication is one of the most common rhythmical behaviors in mammals along with respiration and locomotion. It is now generally accepted that the motor command for the basic pattern of rhythmical alternation of jaw-closing and jaw-opening movements is generated by a neuronal population in the brainstem (the so-called central pattern generator, CPG).\textsuperscript{1,2} Although the basic motor timing could be programmed in a CPG, sensory inputs arising from the movements modify the rhythmic movements reflexly to adapt to environmental demands.\textsuperscript{3-5} As the integration of influences from sensory inputs is necessary to control or fine-tune rhythmical movements, movements of mastication excite several classes of mechanoreceptors; not only muscle spindle (primary and secondary) and periodontal afferents but also skin and mucosal afferents.\textsuperscript{6-8}
Mastication could modulate pain processing with respect to sensory-motor
integration via cortical mechanisms and mastication might drive an opioid descending system through the trigeminal sensory pathway and somatosensory cortex resulting in an antinociceptive effect on chronic pain.9

Farella et al.10 examined the effects of gum chewing on the pressure pain threshold (PPT) and indicated that no significant changes were found for PPT between before and after chewing tasks. However, the effects of chewing on sensory and pain perception of the facial skin have not been investigated up to now.

Consequently, the aim of this study was to examine the effect of chewing efforts on the tactile and tactile pain thresholds in the orofacial skin of symptom-free subjects.

2. Materials and methods

2.1. Subjects

Fourteen healthy volunteers (seven men, seven women, age range 27 to 40 years) were recruited from Nagasaki University staff. All were asymptomatic for pain in the head and neck. As a previous study indicated that pain thresholds were lower in the menstrual phase, women were not tested during their menstrual phase and smokers were excluded.11,12 Informed consent was obtained from all participants. The institutional ethics committee of Nagasaki University Graduate School of Biomedical Sciences approved the study (No. 1181).

2.2. Measurement sessions

Each subject undertook two sessions with 1 week intervals. The order of the sessions was randomized. The subjects were seated comfortably upright in a dental chair. The tactile detection threshold (TDT) and the filament-prick pain detection threshold (FPT) were measured before and after gum chewing for 5 min (Time 1: T1) and keeping the jaw relaxed for 5 min (Time 2: T2) as a control. Chewing was performed unilaterally on the right side.

TDT and FPT were measured 1) on the cheek skin (CS) overlying the central part of the left and right masseter muscles midway between the upper and lower borders and 1 cm posterior to the anterior border, and 2) on the skin overlying
the palm side of the thenar muscle on the point connecting the longitudinal axis of the thumb and index finger (thenar skin: TS). The sequence of the measurement sites was randomized. Semmes-Weinstein monofilaments with 20 different diameters were used (Premier Products, USA). The numbers of the filaments (1.65 to 6.65) correspond to the forces and/or the pressures.13,14 As reported previously,13,14 the pressures (g/mm²) were used in the measurement of the TDT and FPT in this study.

2.3. Tactile detection threshold

At first, TDT was examined. The subjects were instructed to close their eyes during the whole test procedure and to raise their hand as soon as they felt the stimulus on the test site. The filament was applied vertically to the test site and slowly the pressure was increased until the filament bowed. The time needed to bow the filament was standardized to approximately 1.5 s. The stimulus was maintained for approximately 1.5 s and then removed in 1.5 s. Quick applications and bouncing of the filaments against the skin were avoided. At each site, the test started with the pressure of 68.0 g/mm². If the subject raised his/her hand, this was considered a positive response, and the next filament applied was one step lower (47.3 g/mm²). This procedure was repeated with decreasing filament diameters until the subject no longer felt the pressure. This was considered a negative answer. Again, the filament with a higher pressure was applied. This procedure continued until five positive and five negative peaks were recorded and the threshold (TDT) was calculated as the average of these values (pressure). If the subject still had a positive response while applying the lowest pressure (1.45 g/mm²), this pressure was considered the threshold. Two “blank” (placebo) trials were performed after peaks 5 and 10. During these control trials, the filament did not make contact with the tissue. If the subject reported a positive answer, the test was discontinued and the subject was questioned about what kind of stimulus was perceived. The whole procedure was explained again to the subject and afterwards the test was restarted.

2.4. Filament-prick pain detection threshold

After the TDT measurements, the FPT was examined. The stimuli were applied in the same way as for the TDT, but the subjects were instructed to keep their
eyes open and to raise their hand as soon as they felt not only pressure but also pain in the test area. If the subject had no positive response for the highest pressure (439 g/mm²), this value was recorded as the threshold. No placebo stimulus were applied. There was a time lag of 3 min between the measurements on a similar site in order to avoid sensitization. Furthermore, after the examination, the pain intensity experienced at the FPT was assessed on a numeric rating scale (NRS) where 0 cm indicates ‘no pain’ and 10 cm indicates ‘worst pain imaginable’.

2.5. Statistical analysis

Data were not normally distributed, and subsequent analysis was performed with Wilcoxon matched pair test to test the effects of the session and condition. The significance was accepted at $P < 0.05$.

3. Results

Table 1 shows the mean and standard error of mean (S.E.M) of sensory and pain thresholds (TDT and FPT).

Both for the test and control situation, TDT increased in all measurements after 5 min. There were significant effects of experimental condition (before and after 5 min) except the right CS in T2. Significant session effects (T1 - T2) were found at the right CS ($P < 0.05$) (Fig. 1).

For the FPT, it was striking that the reactions between T1 and T2 were quite opposite: in T2, the FPT at all sites significantly decreased after 5 min, while, in T1, the FPT at the right CS significantly increased ($P < 0.01$) and the FPT at the left CS and TS remained stable. There were significant session effects (T1 - T2) on the FPT at the left CS ($P < 0.01$), right CS ($P < 0.05$) and TS ($P < 0.05$) (Fig. 1).

4. Discussion

In clinical practice, the use of sensory tests for both tactile and pain sensation could be helpful in the diagnosis and assessment of orofacial pain.$^{15-18}$

Farella et al.$^{10}$ examined the effects of gum chewing on the pressure pain threshold (PPT) and indicated that no significant changes were found for PPT
between before and after chewing tasks. Morimoto et al.\textsuperscript{19} examined the effect of chewing efforts on facial skin temperature. According to that study, a chewing task for 5 min produced a significant temperature increase of the facial skin and did not return to the initial state even after 30 min. However, the effects of chewing on sensory and pain perception of the facial skin have not been investigated up to now. There is evidence that somatic sensitivity in the orofacial area can be modulated by jaw movements.\textsuperscript{20,21} Kemppainen et al.\textsuperscript{20,21} indicated that opening and closing movements reduced perioral skin sensitivity and tooth pulp-evoked sensations (tooth pulpal detection and pain thresholds). Furthermore, the jaw movement-related attenuation of tooth pulp-evoked sensations was greater for perception thresholds than for pain thresholds.\textsuperscript{21}

In this study, an increase of TDT was found regardless of chewing task. On the other hand, an increase and decrease of FPT were found in T1 (gum chewing) and T2 (control), respectively. The increase of TDT/FPT in the test (T1) and control situation (T2) could be habituation, and the decrease of FPT in the control situation (T2) could be sensitization, respectively. Habituation is a decrease or loss of response following repetitive stimulation, while sensitization illustrates the increased excitability of a reaction produced by trauma and inflammation of peripheral tissues, which can occur peripherally or centrally or both.\textsuperscript{22} In the present findings, sensitization that is the decrease of FPT following repetitive stimulation in T2 was not found after chewing efforts (T1). In fact, the FPT at the right CS in T1 significantly increased, which might have something to do with the effect of unilateral chewing on right side. That is, amount of sensory inputs arising from right side chewing might cause habituation that is the significant increase of FPT at the right CS.

Chewing is not only an oral function but also influences some brain and whole-body functions e.g., cerebral blood flow, body temperature and arousal. For example, the reticular formation in the brainstem and the neural pathways underlying the cortical arousal response known as the ascending reticular activating system (ARAS)\textsuperscript{23} is easily affected by mastication, because sensory inputs arising from masticatory jaw movements might be important input to the ARAS. In fact, Sakamoto et al.\textsuperscript{24,25} provided evidence concerning the effect of mastication on the human brain using fMRI.

As for the interaction between mastication and pain, animal studies showed that the masticatory behavior could modulate pain processing with respect to sensory-motor integration via cortical mechanisms and that mastication might
drive an opioid descending system through the trigeminal sensory pathway and somatosensory cortex resulting in an antinociceptive effect on chronic pain. A neuronal network extending from the frontal cortex and the hypothalamus through the periaqueductal gray matter (PAG) to the rostral ventromedial medulla (RVM) into the medullary and spinal dorsal horn is probably the most powerful descending inhibitory system. Electrical stimulation of PAG or RVM has been shown to reduce the activity of nocireceptive neurons in the spinal trigeminal nucleus. The PAG receives projections from parts of the forebrain such as insular cortex and the amygdala and from specific projection areas. Chiang et al. have shown that the jaw-opening reflex induced by orofacial noxious input can be inhibited by stimulation of the orofacial region in the somatosensory cortex. This powerful endogenous pain-inhibitory system may be a target for pain therapy strategies. Opioids are known to activate inhibitory interneurons in the PAG-RVM system, e.g., enkephalinergic interneurons that are located pre- and postsynaptically to primary afferents. Besides, specific 5-HT receptor agonists and antagonists could thus activate inhibitory interneurons or inhibit excitatory interneurons that are under control of these serotonergic descending neurons. In fact, Mohri et al. revealed that activation of 5-HT neurons by rhythmic behavior of chewing might enhance the 5-HT descending inhibitory pathway and suppress nociceptive responses in humans.

To clarify the involvement of the descending modulatory system and its related neurotransmitters in the masticatory jaw movement, we need further studies from the view points of both clinical and basic research. Animal models of cats, rats and mice could help in this respect.

References

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Figure legends

Fig. 1 - Upper and lower figures show the mean of tactile detection threshold (TDT) and filament-prick pain detection threshold (FPT), respectively. Black circles and squares demonstrate gum chewing (Time 1: T1) and control (Time 2: T2), respectively. TDT and FPT were measured before (pre) and after (post) gum chewing for 5 min (T1) and keeping the jaw relaxed for 5 min (T2) as a control.

**, p < 0.01; *, p < 0.05, showing a significant difference between pre and post. ##, p < 0.01; #, p < 0.05, showing a significant difference between T1 and T2.
Fig. 1

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<tr>
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<th>Gum chewing (T1)</th>
<th>Control (T2)</th>
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<tbody>
<tr>
<td><strong>Left Cheek skin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Right Cheek skin</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Thenar skin</strong></td>
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**Pressures (g/mm²)**

- **TDT**
  - Pre: 1.45
  - Post: 31.5

- **FPT**
  - Pre: 33.1
  - Post: 439

- **Gum chewing (T1)**
  - Pre: **##**
  - Post: **#**

- **Control (T2)**
  - Pre: ***##**
  - Post: **#**

- **Thenar skin**
  - Pre: ****
  - Post: **#**
Table 1 - Sensory and pain thresholds.

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<tr>
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<th>TDT</th>
<th>FPT</th>
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<tbody>
<tr>
<td></td>
<td>pre</td>
<td>post</td>
</tr>
<tr>
<td><strong>Gum chewing (T1)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheek skin (Left)</td>
<td>6.29 (3.47)</td>
<td>9.28 (5.39)</td>
</tr>
<tr>
<td>Cheek skin (Right)</td>
<td>6.18 (4.32)</td>
<td>12.3 (11.8)</td>
</tr>
<tr>
<td>Thenar skin</td>
<td>8.54 (3.27)</td>
<td>15.9 (11.4)</td>
</tr>
<tr>
<td><strong>Control (T2)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheek skin (Left)</td>
<td>5.44 (3.71)</td>
<td>8.63 (5.15)</td>
</tr>
<tr>
<td>Cheek skin (Right)</td>
<td>5.37 (3.10)</td>
<td>6.84 (2.86)</td>
</tr>
<tr>
<td>Thenar skin</td>
<td>9.13 (3.13)</td>
<td>14.9 (9.30)</td>
</tr>
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</table>

Data are expressed as mean (standard error of mean: S.E.M) of the pressure (g/mm²).

TDT = tactile detection threshold, FPT = filament-prick pain detection threshold.

TDT and FPT were measured before (pre) and after (post) gum chewing for 5 min (Time 1: T1) and keeping the jaw relaxed for 5 min (Time 2: T2) as a control.