Effects of chewing efforts on the sensory and pain thresholds in human facial skin: A pilot study

Ichiro Okayasu ^{a,*}, Osamu Komiyama ^b, Noriaki Yoshida ^c, Kumiko Oi ^a, Antoon De Laat ^d

^a Department of Clinical Physiology, Graduate School of Biomedical Sciences, Nagasaki University, 1-7-1 Sakamoto, Nagasaki 852-8588, Japan

^b Department of Oral Function and Rehabilitation, Nihon University School of Dentistry at Matsudo, 2-870-1 Sakaecho-nishi, Matsudo, Chiba 271-8587, Japan

^c Department of Orthodontics, Graduate School of Biomedical Sciences, Nagasaki University, 1-7-1 Sakamoto, Nagasaki 852-8588, Japan

^d Department of Oral and Maxillofacial Surgery, School of Dentistry, Oral Pathology and Maxillofacial Surgery, Catholic University of Leuven, Kapucijnenvoer 7, B-3000 Leuven, Belgium

^{*} Correspondence: Dr Ichiro Okayasu, Department of Clinical Physiology, Graduate School of Biomedical Sciences, Nagasaki University, 1-7-1 Sakamoto, Nagasaki 852-8588, Japan

Tel: +81 95 819 7714 Fax: +81 95 819 7715 E-mail: okayasu@nagasaki-u.ac.jp

The number of pages in the text: 12 The number of tables: 1 The number of figures: 1

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).^{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.³⁻⁵ As the integration of influences from sensory inputs is necessary to control or fine-tune rhythmic 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.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.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.^{20,21} Kemppainen et al.^{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.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.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)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.^{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.9 A neuronal network extending from the frontal cortex and the hypothalamus through the periaqueductal gray matter (PAG) to the rostal ventromedial medulla (RVM) into the medullary and spinal dorsal horn is probably the most powerful descending inhibitory system.²⁶⁻²⁹ Electrical stimulation of PAG or RVM has been shown to reduce the activity of nociresponsive neurons in the spinal trigeminal nucleus.³⁰⁻³⁵ The PAG receives projections form parts of the forebrain such as insular cortex and the amygdala and from specific projection areas. Chiang et al.³⁶ 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.^{37,38} Opioids are known to activate inhibitory interneurons in the PAG-RVM system, e.g., enkephalinergic interneurons that are located preand 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.^{39,40} In fact, Mohri et al.⁴¹ 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, ^{30,32-35,42} rats^{31,36,39,40,43,44} and mice^{3,4,45} could help in this respect.

References

- 1. Lund JP. Mastication and its control by the brain stem. Crit Rev Oral Biol Med 1991; 2: 33-64.
- 2. Nakamura Y, Katakura N. Generation of masticatory rhythm in the brainstem. Neurosci Res 1995; 23: 1-19.
- 3. Okayasu I, Yamada Y, Kohno S, Yoshida N. New animal model for studying mastication in oral motor disorders. J Dent Res 2003; 82 (4): 318-321.
- Okayasu I, Yamada Y. Maeda T, Yoshida N, Koga Y, Oi K. The involvement of brain-derived neurotrophic factor in the pattern generator of mastication. Brain Res 2004; 1016: 40-47.

- 5. Yamada Y, Yamamura K, Inoue M. Coordination of cranical motoneurons during mastication. Resp Physiol Neurobiol 2005; 147: 177-189.
- 6. Appenteng K, Lund JP, Seguin JJ. Intraoral mechanoreceptor activity during jaw movement in the anesthetized rabbit. J Neurophysiol 1982a; 48: 27-37.
- Appenteng K, Lund JP, Seguin JJ. Behavior of cutaneous mechanoreceptors recorded in mandibular division of gasserian ganglion of the rabbit during movements of lower jaw. J Neurophysiol 1982b; 47: 151-166.
- Johansson RS, Trulsson M, Olsson KA, Westberg K-G. Mechanoreceptor activity from the human face and oral mucosa. Exp Brain Res 1988; 72: 204-208.
- Ogawa A, Morimoto T, Hu JW, Tsuboi Y, Tashiro A, Noguchi K et al. Hard-food mastication suppresses complete freund's adjuvant-induced nociception. Neuroscience 2003; 120: 1081-1092.
- Farella M, Bakke M, Michelotti A, Martina R. Effects of prolonged gum chewing on pain and fatigue in human jaw muscles. Eur J Oral Sci 2001; 109: 81-85.
- 11. Isselee H, De Laat A, Bogaerts K, Lysens R. Long-term fluctuations of pressure pain thresholds in healthy men, normally menstruating women and oral contraceptive users. Eur J Pain 2001; 5: 27-37.
- 12. Isselee H, De Laat A, De Mot B, Lysens R. Pressure-pain threshold variation in temporomandibular disorder myalgia over the course of the menstrual cycle. J Orofac Pain 2002; 16: 105-117.
- 13. Levin S, Pearsall G, Ruderman RJ. Von Frey's method of measuring pressure sensibility in the hand: an engineering analysis of the Weinstein-Semmes pressure aesthesiometer. J Hand Surg 1978; 3: 211-216.
- 14. Essick GK. Comprehensive clinical evaluation of perioral sensory function. Oral Maxillofac Clin North Am 1992; 4: 503-526.
- 15. Komiyama O, De Laat A. Tactile and pain thresholds in the intra- and extra-oral regions of symptom-free subjects. Pain 2005; 115: 308-315.
- 16. Komiyama O, Gracely RH, Kawara M, De Laat A. Intraoral measurement of tactile and filament-prick pain threshold using shortened Semmes-Weinstein monofilaments. Clin J Pain 2008; 24: 16-21.
- 17.Okayasu I, Oi K, De Laat A. The effect of tooth clenching on the sensory and pain perception in the oro-facial region of symptom-free men and women. J Oral Rehabil 2009; 36: 476-482.
- 18. Okayasu I, Oi K, De Laat A. The effect of nonfunctional tooth contact on

sensory and pain perception in patient with myofascial pain of the jaw muscles . J Prosthdont Res in press.

- 19. Morimoto T, Takada K, Hijiya H, Yasuda Y, Sakuda M. Changes in facial skin temperature associated with chewing efforts in man: A thermographic evaluation. Archs Oral Biol 1990; 36: 665-670.
- 20. Kemppainen P, Leppanen H, Waltimo A, Pertovaara A. Effects of jaw clenching, jaw movement and static jaw position on facial skin sensitivity to non-painful electrical stimulation in man. Archs Oral Biol 1993; 38: 303-308.
- 21. Kemppainen P, Vaalamo I, Leppala N, Pertovaara A. Changes in tooth pulpal detection and pain thresholds in relation to jaw movement in man. Archs Oral Biol 2001; 46: 33-37.
- 22. McNeill C, Dubner R, Woda A. What is pain and how do we classify orofacial pain?. In: Sessle BJ, Lavigne GJ, Lund JP, Dubner R, editors. Orofacial Pain: from basic science to clinical management, 2nd ed. Chicago. Quintessence; 2008, pp. 3-11.
- 23. Moruzzi G, Magoun HW. Brain stem reticular formation and activation of the EEG. Electroencephalogr Clin Neurophysiol. 1949; 1: 455-473.
- 24. Sakamoto K, Nakata H, Kakigi R. The effect of mastication on human cognitive processing: A study using event-related potentials. Clin Neurophysiol 2009a; 120: 41-50.
- Sakamoto K, Nakata H, Honda Y, Kakigi R. The effect of mastication on human motor processing: A study with CNV and MRCP. Neurosci Res 2009b; 64: 259-266.
- 26. Sessle BJ. Masticatory muscle disorders: Basic science perspectives . In: Sessle BJ, Bryant PS, Dionne RA, editors. Temporomandibular disorders and related pain conditions, Progress in pain research and management, vol.4. Seattle. IASP press; 1995, pp. 47-61.
- 27. Sessle BJ. Acute and chronic craniofacial pain: brainstem mechanisms of nociceptive transmission and neuroplasticity, and their clinical correlates. Crit Rev Oral Biol Med, 2000; 11: 57-91.
- 28. Sessle BJ. Mechanisms of oral somatosensory and motor functions and their clinical correlates. J Oral Rehabil, 2006; 33: 243-261.
- 29. Sessle BJ. What is pain, and why and how do we experience pain?. In: Lavigne G, Sessle BJ, Choiniere M, Soja PJ, editors. Sleep and pain. Seattle. IASP press; 2007, pp. 23-43.
- 30. Andersen RK, Lund JP, Puil E. Excitation and inhibition of neurons in the

trigeminal nucleus caudalis following periaqueductal gray stimulation. Can J Physiol Pharmacol 1978; 56: 157-161.

- 31. Chiang CY, Hu JW, Sessle BJ. Parabrachial area and nucleus raphe magnus-induced modulation of nociceptive and nonnociceptive trigeminal subnucleus caudalis neurons activated by cutaneous or deep inputs. J Neurophysiol 1994; 71: 2430-2445.
- 32. Hayashi H, Sumino R, Sessle BJ. Functional organization of trigeminal subnucleus interpolaris: nociceptive and innocuous afferent inputs, projections to thalamus, cerebellum, and spinal cord, and descending modulation from periaqueductal gray. J Neurophysiol 1984; 51: 890-905.
- 33. Sessle BJ, Dubner R, Greenwood LF, Lucier GE. Descending influences of periaqueductal gray matter and somatosensory cerebral cortex on neurons in trigeminal brain stem nuclei. Can J Physiol Pharmacol 1976; 54: 66-69.
- 34. Sessle BJ, Hu JW. Raphe-induced suppression of the jaw-opening reflex and single neurons in trigeminal subnucleus oralis, and influence of naloxone and subnucleus caudalis. Pain 1981; 10: 19-36.
- 35. Sessle BJ, Hu JW, Dubner R, Lucier GE. Functional properties of neurons in trigeminal subnucleus caudalis of the cat. II. Modulation of responses to noxious and non-noxious stimuli by periaqueductal gray, nucleus raphe magnus, cerebral cortex and afferent influences, and effect of naloxone. J Neurophysiol 1981; 45: 193-207.
- Chiang CY, Dostrovsky JO, Sessle BJ. Role of anterior pretectal nucleus in somatosensory cortical descending modulation of jaw-opening reflex in rat. Brain Res 1990; 515: 219-226.
- Messlinger K, Ellrich J. Processing of nociceptive inputs from different tissues to the spinal trigeminal nucleus and release of immunoreactive substance P. In: Sessle BJ, Nakamura Y, editors. Neurobiology of Mastication: from Molecular to Systems Approach. Amsterdam. Elsevier; 1999, pp.177-188.
- 38. Messlinger K. Migraine: where and how does the pain originate?. Exp Brain Res 2009; 196: 179-193.
- Ellrich J, Messlinger K, Chiang CY, Hu JW. Modulation of neuronal activity in the nucleus raphe magnus by the 5-HT¹-receptor agonist naratriptan in rat. Pain 2001; 90: 227-231.
- 40. Messlinger K, Ellrich J. Meningeal nociception: Electrophysiological studies related to headache and referred pain. Microsc Res Tech 2001; 53: 129-137.

- 41. Mohri Y, Fumoto M, Sato-Suzuki I, Umino M, Arita H. Prolonged rhythmic gum chewing suppresses nociceptive response via serotonergic descending inhibitory pathway in humans. Pain 2005; 118: 35-42.
- 42. Hu JW, Dostrovsky JO, Sessle BJ. Functional properties of neurons in cat trigeminal subnucleus caudalis (medullary dorsal horn). I. Responses to oral-facial noxious and nonnoxious stimuli and projections to thalamus and subnucleus oralis. J Neurophysiol 1981; 45: 173-192.
- 43. Yamamoto T, Matsuo R, Kiyomitsu Y, Kitamura R. Sensory inputs from the oral region to the cerebral cortex in behaving rats: An analysis of unit responses in cortical somatosensory and taste areas during ingestive behavior. J Neurophysiol 1988; 60: 1303-1321.
- 44. Yamamoto T, Matsuo R, Kiyomitsu Y, Kitamura R. Taste responses of cortical neurons in freely ingesting rats. J Neurophysiol 1989; 61: 1244-1258.
- 45. Nishiyori M, Nagai J, Nakazawa T, Ueda H. Absence of morphine analgesia and its underlying descending serotonergic activation in an experimental mouse model of fibromyalgia. Neurosci Lett 2010; 472: 184-187.

Figure legends

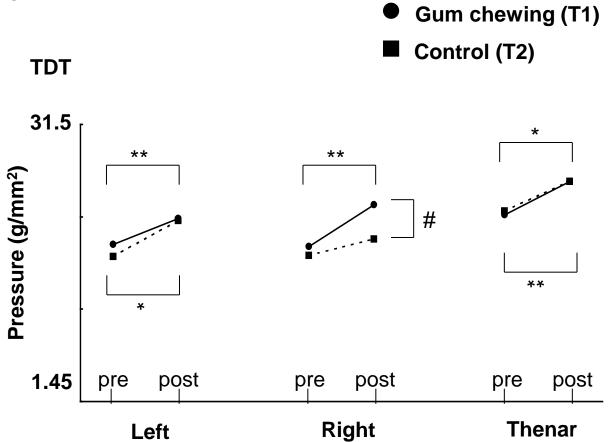
Fig. 1 - Upper and lower figures show the mean of tactile detection threshold (TDT) and filament-prick pain detection threshold (FPT), respectively.

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.

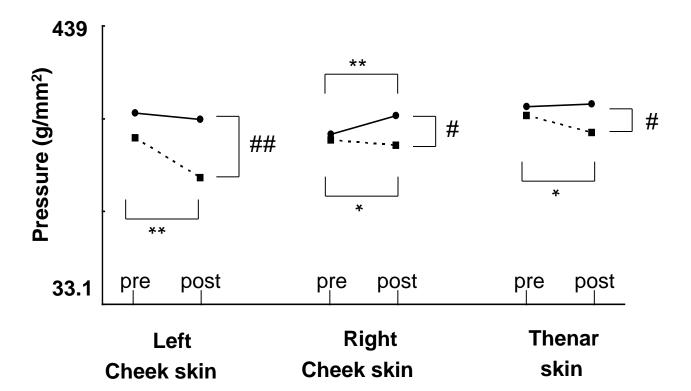
^{##}, p < 0.01; [#], p < 0.05, showing a significant difference between T1 and T2.





Cheek skin

FPT



Cheek skin

skin

	TDT		FPT	
	pre	post	pre	post
Gum chewing (T1)				
Cheek skin (Left)	6.29 (3.47)	9.28 (5.39)	254 (96.7)	238 (103)
Cheek skin (Right)	6.18 (4.32)	12.3 (11.8)	214 (125)	259 (139)
Thenar skin	8.54 (3.27)	15.9 (11.4)	272 (103)	286 (117)
Control (T2)				
Cheek skin (Left)	5.44 (3.71)	8.63 (5.15)	188 (69.2)	111 (45.5)
Cheek skin (Right)	5.37 (3.10)	6.84 (2.86)	199 (131)	179 (121)
Thenar skin	9.13 (3.13)	14.9 (9.30)	240 (93.8)	203 (104)

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.