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Research article

Somatosensory evoked magnetic fields of periodontal mechanoreceptors

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ABSTRACT

To evaluate the localization of responses to stimulation of the periodontal mechanoreceptors in the primary somatosensory cortex, somatosensory evoked fields (SEFs) were measured for stimulation of the left mandibular canine and first molar using magnetoencephalography in 25 healthy subjects. Tactile stimulation used a hand-made stimulus device which recorded the trigger at the moment of touching the teeth.SEFs for the canine and first molar were detected in 20 and 19 subjects, respectively. Both responses were detected in the bilateral hemispheres. The latency for the canine was 62.1 ± 12.9 ms in the ipsilateral hemisphere and 65.9 ± 14.8 ms in the contralateral hemisphere. The latency for the first molar was 47.4 ± 6.6 ms in the ipsilateral hemisphere and 47.8 ± 9.1 ms in the contralateral hemisphere. The latency for the first molar was significantly shorter than that for the canine. The equivalent current dipoles were estimated in the central sulcus and localized anteroinferiorly compared to the locations for the SEFs for the median nerve. No significant differences in three-dimensional coordinates were found between the canine and first molar. These findings demonstrate the precise location of the teeth within the orofacial representation area in the primary somatosensory cortex.

1. Introduction

Tactile sensation in the teeth captures the states of teeth contact and information about occlusal force to control jaw movement during mastication. This tactile sensation is perceived by the periodontal mechanoreceptors. Natural teeth have many periodontal mechanoreceptors located across the periodontal ligaments and monitor information about tooth loads which can detect the temporal and spatial characteristics, hardness, and size of food particles during mastication, and can distinguish dimensions as small as about 20 μm. Additionally, mastication is reported to improve short-term cognitive function [1]. Consequently, the periodontal mechanoreceptors are considered to be important in brain function.

Tactile sensation mediated by the periodontal mechanoreceptors is a very important somatic sensation and various previous studies have used psychophysical methods [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12]. More recent studies have evaluated the sensation of the periodontal mechanoreceptor using functional brain imaging methods. A functional magnetic resonance imaging (fMRI) study using a pneumatic pressure control device showed that significant brain activation was found in the bilateral insular cortices and in the supplementary motor cortex, but no significant brain activation was found in the somatosensory cortex [13]. Other fMRI studies investigated the influence of frequency for stimulation [14] and the relative representation of teeth in the somatosensory cortex [15], which found activation in the primary somatosensory cortex. fMRI investigation of brain activation for tactile stimulation of the incisor tooth investigated the representation of the periodontal mechanoreceptors of the incisor and canine teeth [16, 17]. Activity was recorded in the primary somatosensory cortex but significant difference was found in the representation of the incisor and canine teeth [17].

Tactile sensations are projected to the somatosensory cortex through the Aβ fibers which have high conduction velocity. Therefore, detection of the early cortical responses of periodontal mechanoreceptors requires a method with high spatial and temporal resolution. fMRI does not have

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adequate temporal resolution to detect the early cortical response. Consequently, although the Penfield representation locates the teeth in the primary somatosensory cortex, the exact representation of each tooth type was not specified. Somatosensory evoked fields (SEFs) for the central incisor were detected but the location of the representation of the incisor was not clear [18]. Therefore, the early cortical responses and somatic representations of the periodontal mechanoreceptors of each tooth type are still unclear. Additionally, no studies have evaluated the somatic representations of the periodontal mechanoreceptors of the molar teeth.

Functional brain imaging techniques, especially magnetoencephalography (MEG), can record the early cortical response and estimate the localization of periodontal mechanoreceptors. MEG, a non-invasive brain imaging technique, detects the weak magnetic fields caused by neural activity. Such magnetic fields are not distorted by the scalp structure. MEG has high temporal resolution similar to electroencephalography (EEG), but MEG has higher spatial resolution than EEG. SEFs in response to electrical and tactile stimulation of the oral organs have been investigated by several research groups and revealed the localization of oral organs in the primary somatosensory cortex [19, 20, 21, 22, 23]. Additionally, SEFs for dental pulp were observed and the localization was revealed [24].

Generally, organs with high spatial resolution, especially the fingers, have somatic representation extending over large areas of the primary somatosensory cortex, and the representation of each finger has been mapped [25]. The periodontal mechanoreceptors have high spatial resolution and sensitivity similar to the fingers. Therefore, we hypothesized that each tooth type has a different location in the primary somatosensory cortex similar to the fingers.

To confirm this hypothesis, the present study measured SEFs for the mandibular canine and first molar teeth. The neural source was modeled at peak latency using an equivalent current dipole (ECD) model, which assumes that the measured magnetic field can be most appropriately explained by a single current at one point in the brain. Latency and ECD location were compared between the canine and first molar.

2. Subjects and methods

This article complies with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. This study examined 50 hemispheres of 25 right-handed healthy normal young subjects, 18 males and 7 females aged 20–27 years (mean 22.5 years). No subject had a history of neurological disease. Informed consent was obtained from all participants. This study protocol was approved by the ethical committee of the Tohoku University Graduate School of Dentistry (protocol number: 23-20 and 26–39) in accordance with the Declaration of Helsinki.

Generally, periodontal mechanoreceptors respond to only tactile stimulation. Therefore, a handmade stimulus device was used to apply the tactile stimulation (Figure 1). This device modified the stimulator previously described [26], and consisted of a resin handle and optical fibers (E32-DC200F4R; Omron Corp., Kyoto, Japan). The fibers were passed along the resin handle, and the ends positioned at the tip of the handle. The device was made of nonmagnetic material suitable for use in a magnetically shielded room. The optical fiber was attached to a photoelectric sensor (E3X-NA41F 2M; Omron Corp.) producing a red light of 680 nm. Half of the fibers were attached to the emitter and the other half were attached to the receiver. Consequently, touching the tooth with the end of the device interrupted the light signal at the receiver and was recorded as the contact trigger. Using this device, tactile stimulation was applied by tapping the left mandibular canine and first molar teeth. The tactile stimuli were constantly delivered at about 2 Hz. The stimulus intensity was about 30 gf. This stimulus intensity is sufficient to elicit the periodontal mechanoreceptors [2, 3, 5, 10, 11, 12]. No participant reported feeling any pain but all felt the tooth-tapping sensation. All stimulations were performed by the same experimenters to maintain the stimulation intensity and timing as similar as possible in all sessions. The experimenters were trained to produce similar tactile stimulations before the recording.

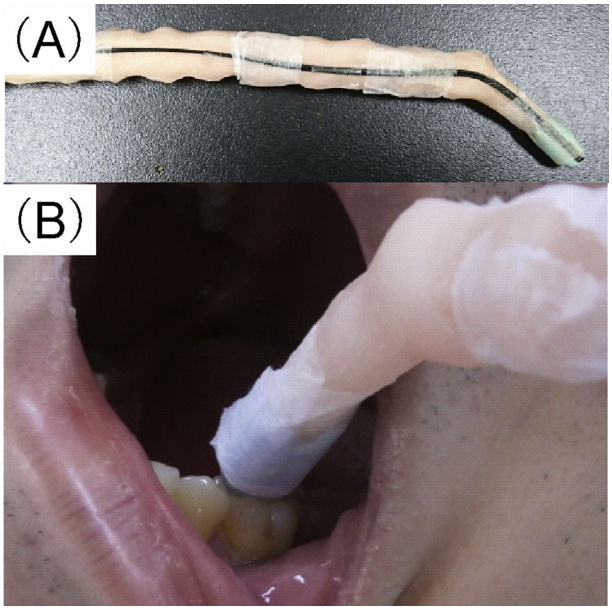

Figure 1. Tactile stimulus device. (A) Handmade stimulator (optical fibers embedded in the resin handle). (B) Stimulation of the first molar.

The SEF signals were measured using a whole-head 200-channel MEG system (PQA160C; Ricoh Co., Ltd.., Tokyo, Japan) in a magnetically shielded room. The subjects lay supine, with the head location specified by measurement of magnetic signals produced at five fiduciary markers consisting of currents passed through coils placed at known locations on the scalp. Subject face shape and coil positions were scanned using a three-dimensional digitizer (FastSCAN™ Cobra™; Polhemus Inc., Colchester, VT, USA). Three-dimensional magnetic resonance images were obtained for all subjects using a 3T MR system (Achieva; Philips Healthcare, Amsterdam, The Netherlands). The MEG signals were recorded from 50 ms before to 300 ms after the trigger point and were filtered from 0.5 to 1000 Hz, and digitized at 1000 Hz.

Bilateral SEF waveforms were recorded, and the averaged wave, the root mean square wave, was used to assess the peak latencies around 10–100 ms for further analysis.

These SEFs were modeled as an ECD calculated using analysis software (Meglaboratory; Ricoh Co., Ltd.) based on Sarvas law [27], which is a method of estimating the sources of magnetic signals in a spherical conductor. The ECD was used to estimate the location and moment of the source. The ECD was superimposed on the MR images. Only ECDs located on the central sulcus were considered. Goodness-of-fit greater than 70% was used for additional analyses.

Latency and ECD locations in 3 axes for the canine, first molar, and median nerve were compared. The results are shown as the mean ± standard error of the mean (SE). Statistical comparisons used analysis of variance or the t-test. Findings were considered significant at $p < 0.05$.

3. Results

The SEFs for the canine and first molar were detected in 35 hemispheres of 20 subjects and 34 hemispheres of 19 subjects, respectively. ECDs were estimated in the central sulcus. The SEFs for the canine were bilateral in 15 subjects, ipsilateral in 1, and contralateral in 4 to the stimulus side. The SEFs for the first molar were bilateral in 15 subjects, ipsilateral in 1, and contralateral in 3 to the stimulus side. SEFs for the median nerve were detected in 21 hemispheres of 21 subjects. Clear responses were detected in only contralateral to the stimulus side. Figures 2

and 3 show examples of waveforms and latency for the canine, first molar, and median nerve.

The latency for the canine was 62.1 ± 12.9 ms in the ipsilateral hemisphere and 65.9 ± 14.9 ms in the contralateral hemisphere. The latency for the first molar was 47.4 ± 6.6 ms in the ipsilateral hemisphere and 47.9 ± 9.1 ms in the contralateral hemisphere. The latency for the median nerve was 49.1 ± 12.4 ms in the contralateral hemisphere. The latency for the first molar was significantly shorter than that for the canine in both the contralateral and ipsilateral hemispheres ($p < 0.001$). However, latency of the canine and first molar showed no difference between the ipsilateral and contralateral hemispheres. Additionally, latency for the canine and median nerve showed no significant differences.

Figure 4 shows the isofield maps and ECD locations for the canine, first molar, and median nerve. The ECD locations for the canine and first molar had posterior orientation and anteroinferior localization, compared with locations for the SEFs of the median nerve in the contralateral hemisphere (y: $p < 0.05$, z: $p < 0.01$). However, no significant differences in the three axes were found between the canine and first molar in contralateral and ipsilateral hemispheres (Table 1). Table 2 shows the mean differences in x, y, z coordinates between the bilateral canines and first molars.

4. Discussion

The present MEG study of the somatic representation of the periodontal mechanoreceptors of the canine and first molar found bilateral somatic representation with significantly different latency, but no significant difference in location for the canine and first molar. However, the detection rate was low. Previous studies of the SEFs of oral tactile sensation have also found low detection rates [20, 22], possibly because of the difficulty in detecting SEFs for tactile stimulation due to insufficient synchronization of neural activities compared with electrical stimulation [28]. However, technical problems are also possible causes. In our study, the stimulus intensity was consistent regardless of the

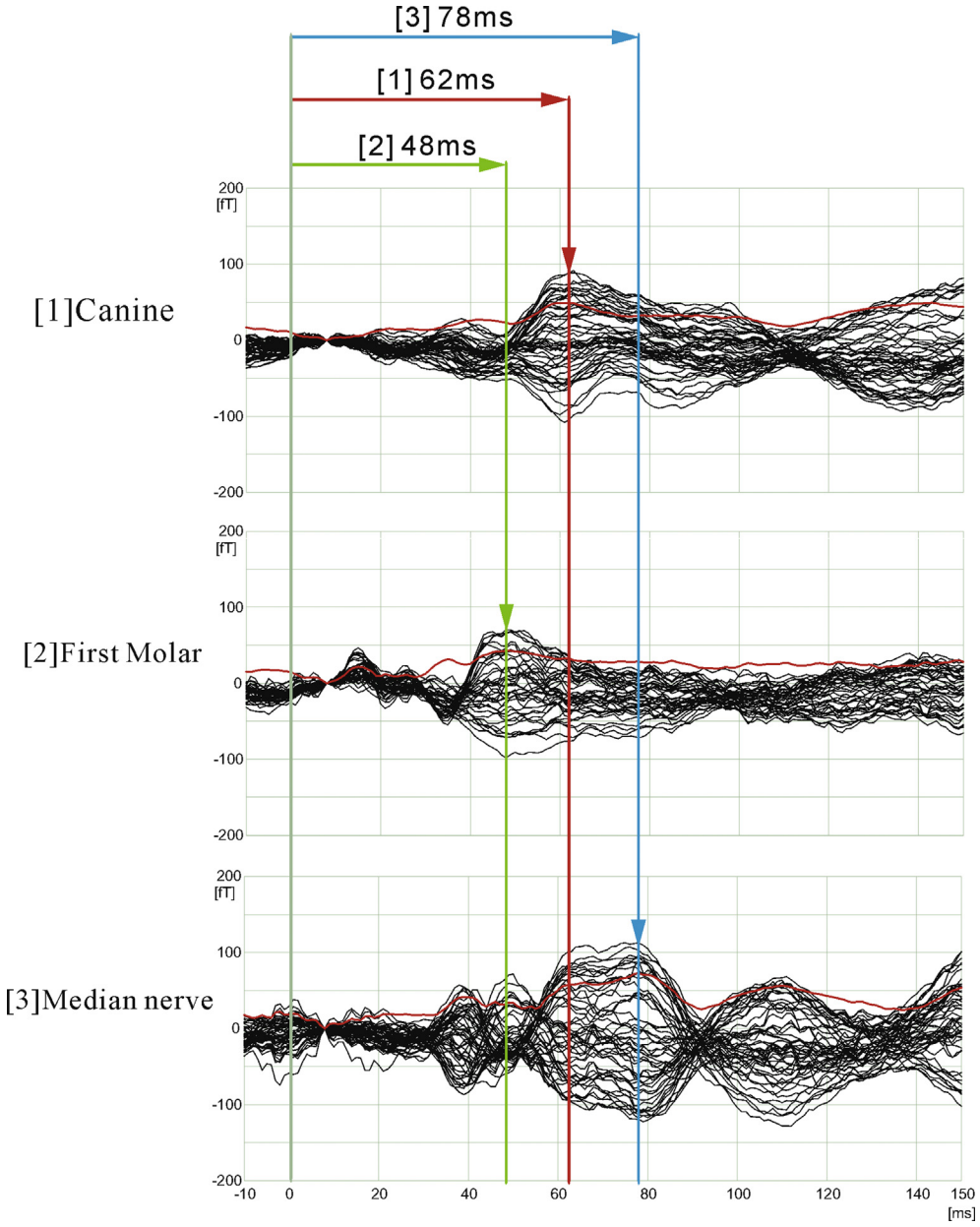

Figure 2. Contralateral waveforms and latencies for the canine, first molar, and median nerve. Waveforms extend from 10 ms before to 150 ms after stimulus onset. Red waveform shows root mean square. Red, green, and blue arrows indicate peak latencies for the canine, first molar, and median nerve, respectively.

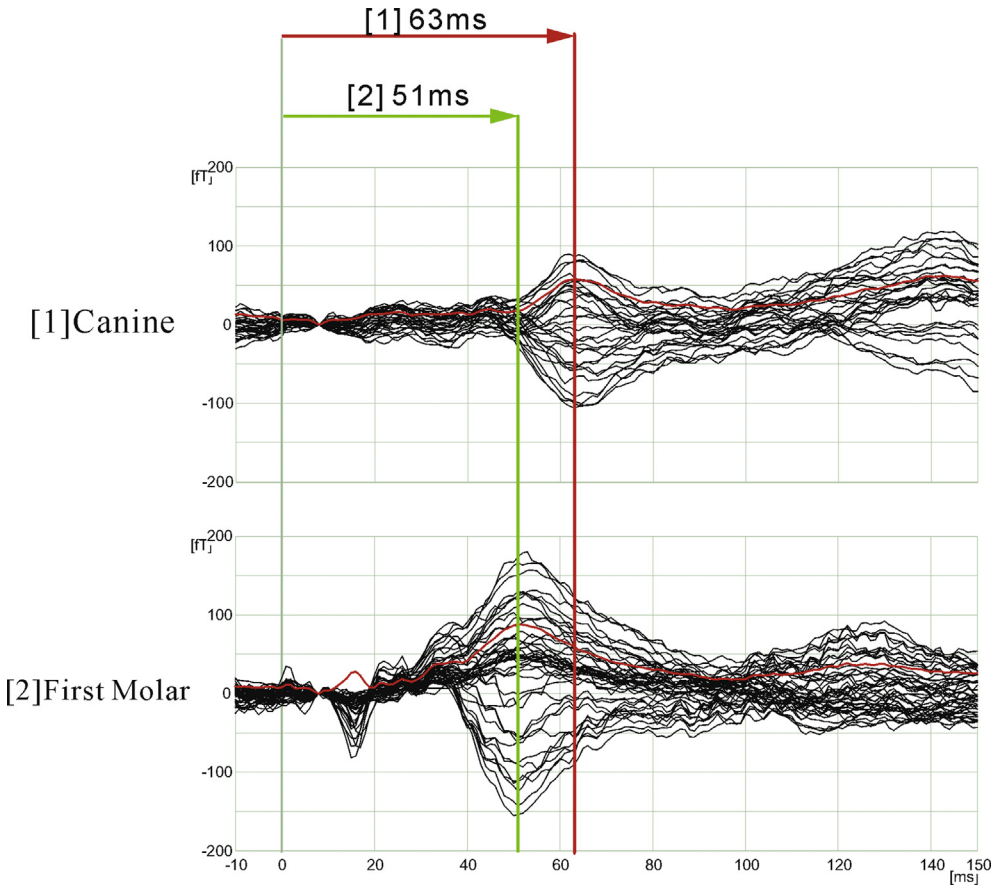

Figure 3. Ipsilateral waveforms and latencies for the canine and first molar. Each waveform extends from 10 ms before to 150 ms after stimulus onset. Red waveform shows root mean square. Red and green arrows indicate peak latencies for the canine and first molar, respectively.

threshold of each subject, so individual differences in sensitivity should also be considered. Therefore, further study will require improvements to the stimulus device.

The present study observed the most prominent peak latencies of root mean square wave for the canine, first molar, and median nerve around 40–70 ms, similar to reports of SEFs for tactile stimulation of other orofacial areas [20, 22, 26]. However, some studies reported that the peak latency was around 20 ms [22, 23, 26].

Studies of the SEFs for electrical stimulation of the lip have shown that the first peak of latency called N13m and N15m is difficult to detect [29, 30, 31]. Additionally, a study showed that early peak latency could not estimate the source location and whether the early peak latency shows the real response was unclear [22]. Generally, the early response with low amplitude can be observed by increasing the averaged number of stimulations. In this study, we cannot deny the possibility that artifacts overlapped with the actual early responses. Therefore, detection of the early peak latency around 20 ms needs more stimulation to improve the signal to noise ratio.

Latency of response of the first molar was significantly shorter than that of the canine. Some studies showed that the waveforms were different depending on the stimulation site [19, 20], possibly due to differences in the density of mechanoreceptors. In general, the density of periodontal mechanoreceptors in the front teeth is higher than that of molars. Therefore, in this study, the high density of periodontal mechanoreceptors of the canine will increase the number of reacting receptors, although the deflection rise in the waveform was larger and the latency was extended and prolonged as a result. Additionally, no difference was seen in the latency for the canine and median nerve, which was considered to be related. However, subjects had different tactile sensations in the canine and first molar, which may also suggest that differences in sensation for tooth type are due to the latency difference. Furthermore, the differences in type of periodontal mechanoreceptors may affect the latency. Generally, humans have two types of mechanoreceptors, the slow adapting unit and the rapid adapting unit [32]. Therefore, this result also suggests that the molars have the more rapid adapting units to detect the features of food for feedback to mastication control compared to the canines. Additionally, the neurons in the trigeminal ganglion are active during mastication when using the molar teeth [33, 34]. Therefore, the shorter latency of first molars may depend on the frequency of this stimulus being more suitable condition for involvement in the motor control during the masticatory function.

In this study, SEFs of the median nerve were detected only in the contralateral hemisphere, whereas SEFs of periodontal mechanoreceptors were detected mainly in the bilateral hemispheres. Additionally, latency for the canine and first molar showed no significant difference between the ipsilateral and contralateral hemisphere, and ECD moment for the canine and first molar showed no significant difference between the hemispheres. Therefore, the contralateral hemisphere was not dominant.

Monkey studies demonstrated the bilateral representation of the intraoral structures in the primary somatosensory cortex [35, 36, 37]. Ipsilateral activation was observed in the upper lip in 69%, the lower lip in 85%, and the tongue in 88% of cases by tactile stimulation [38]. Additionally, fMRI study reported the pain receptors of the teeth show bilateral activation in the primary somatosensory cortex [39]. These results agreed with our findings. Therefore, tactile stimulation of the teeth elicits bilateral activation in the primary somatosensory cortex of most cases.

Some monkey studies showed that the ventral posteromedial nucleus (VPM) of the thalamus includes ipsilateral and contralateral

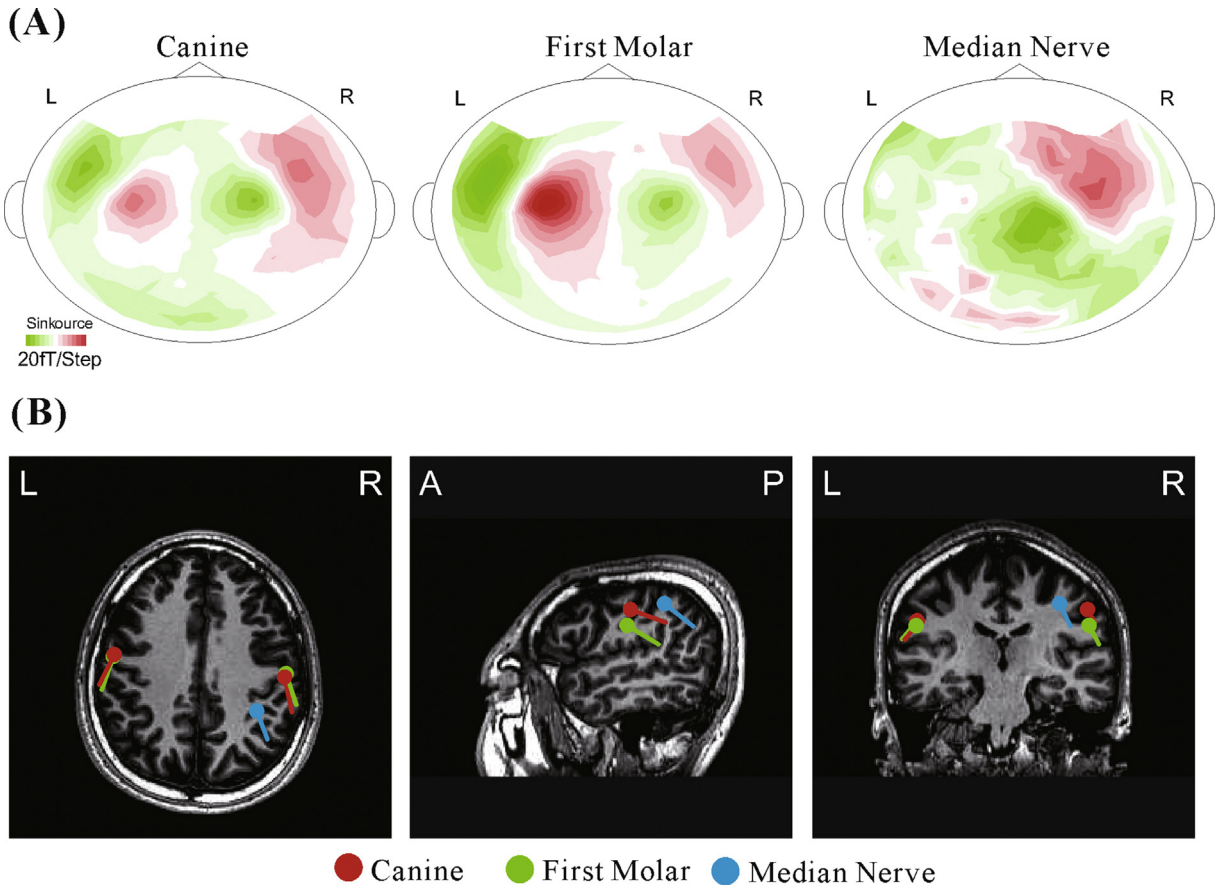

Figure 4. Isofield maps (A) and ECD locations (B). Locations of the canine and first molar are localized anterior-inferiorly relative to the median nerve in the contralateral hemisphere.

Table 1. Detected responses (N), mean ECD moments, latencies, and locations (x, y, z) in the bilateral hemispheres.

	Laterality	N	ECD moment (nAm)	Latency (ms)	Locations		
					x (mm)	y (mm)	z (mm)
Canine	Right	19	8.5 ± 5.4	65.9 ± 14.8	53.0 ± 10.2	9.5 ± 15.2	64.9 ± 8.1
	Left	16	9.3 ± 4.2	62.1 ± 12.9	-50.0 ± 10.2	7.1 ± 13.5	61.2 ± 10.7
First molar	Right	18	8.9 ± 3.1	47.8 ± 9.1***	42.2 ± 25.0	9.8 ± 13.8	61.7 ± 9.9
	Left	16	8.8 ± 4.9	47.4 ± 6.6***	-42.7 ± 26.7	8.7 ± 16.2	60.0 ± 8.5
Median nerve	Right	21	13.2 ± 6.8	51.0 ± 13.6	36.8 ± 6.7	-1.2 ± 10.8*	82.6 ± 10.7**

The locations of the canine and first molar were significantly different from that of median nerve (*$p < 0.05$, **$p < 0.01$). The latency for the first molar were significantly shorter than that of the canine (***$p < 0.001$).

representation of the trigeminal nerve [40, 41]. Other monkey studies showed the teeth have bilateral representation in the primary somatosensory cortex [42] and teeth representation in the somatosensory cortex have ipsilateral cortical connections to the VPM [43]. Nociceptive stimuli for the teeth project to the bilateral thalami in humans [44]. MEG studies of stimuli for the oral region showed bilateral representation and suggested that ipsilateral projection proceeds directly from the thalamus rather than spreads through the corpus callosum [22, 23]. fMRI study of tactile stimuli for the teeth in humans also suggested that the ipsilateral direct projection involves the uncrossed ascending pathway from the thalamus or via transcallosal projections [16, 17].

Table 2. Mean differences in x, y, z coordinates between the bilateral canines and first molars.

Laterality	N	Locations		
		x (mm)	y (mm)	z (mm)
Ipsilateral	15	8.5 ± 8.4	14.6 ± 13.9	7.7 ± 6.0
Contralateral	15	11.6 ± 12.2	15.6 ± 12.8	10.5 ± 8.3

The analysis considered only subjects with bilateral responses.

The present findings of no significant differences in latency and ECD moment between the hemispheres strongly suggests that the periodontal mechanoreceptors in humans project to the bilateral primary somatosensory cortices similar to other orofacial regions, and the ipsilateral reactions are directly projected through the uncrossed ascending pathway from the thalamus. However, some neuromagnetic studies showed unilateral activation mainly with tactile stimulation in the orofacial area [20, 22], possibly related to the difference in tactile thresholds of the right and left sides [45] or the habitual chewing side [11].

The ECDs of the canine and first molar are localized anteroinferiorly relative to that of the median nerve as proposed by the Penfield homunculus [46]. The orofacial areas are localized in anteroinferiorly compared with the fingers and median nerve [19, 21, 23]. The locations

of teeth in this study are consistent and close to other orofacial areas. However, a previous fMRI study showed no significant differences in ECD locations of the canine and first molar, and no significant difference in location between the incisor and canine [17]. Our present findings are consistent, and did not support our hypothesis of separate somatosensory representation for each tooth type.

The failure of our hypothesis could have several explanations. Single human periodontal mechanoreceptive afferents are reported to innervate several teeth [4, 47]. Therefore, the canine and first molar may be innervated by the same nerve, and consequently have the same representation in the primary somatosensory cortex. Monkey studies are shown that some oral structures have overlapping receptive fields on the primary somatosensory cortex [48, 49] In particular, neural activities caused by mechanical stimulation to several teeth converged to the same receptive fields in the primary somatosensory cortex, and sensory information of the tissue surrounding the tooth is integrated in the same receptive fields in area 2 [49] [50]. Recent neuromagnetic studies showed that ECD locations elicited by stimulation of different sites in the same oral structure were not separated in the primary somatosensory cortex [19, 23, 51]. Therefore, sensory information from the oral cavity must be integrated in the cerebral cortex to allow control of the complex oral functions [17, 23, 52]. Overlapping representations of the teeth and bilateral projections in the somatosensory cortex are suitable to control orofacial functions such as mastication and articulation. Therefore, the teeth are important in complex orofacial functions. The origin of occlusal pain in the teeth is sometimes unclear [53]. This finding suggests that single human periodontal mechanoreceptive afferents innervate several teeth. Overlapping representations of teeth are one factor in the mis-localization of the origin of pain.

5. Conclusions

This study detected SEFs with tactile stimulation of the periodontal mechanoreceptors of the canine and first molar. The ECDs of the periodontal mechanoreceptors were located in the bilateral primary somatosensory cortices with posterior orientation. Somatic locations of the periodontal mechanoreceptors of the canine and first molar agreed with the Penfield homunculus. Our findings indicate that teeth have the same sensory information pathway as other orofacial regions and are important in the control of complex oral function.

This study has several limitations. Further studies considering the sensory threshold and habitual chewing side may reveal more precise representation of the teeth in the primary somatosensory cortex. Evaluation of SEFs for the periodontal mechanoreceptors may help better understanding of the motor control of the masticatory function. Additionally, such findings may be useful for the diagnosis of periodontal pain.

Declarations

Author contribution statement

Hiroki Hihara: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Hiroyasu Kanetaka, Akitake Kanno: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Eriya Shimada, Satoko Koeda: Performed the experiments.

Ryuta Kawashima, Keiichi Sasaki: Contributed reagents, materials, analysis tools or data.

Nobukazu Nakasato: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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