



Research article

Somatosensory evoked magnetic fields caused by mechanical stimulation of the periodontal ligaments

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ABSTRACT

The periodontal ligaments are very important sensory organ for our daily life such as perception of food size or hardness, determination of jaw position, and adjustment of masticatory strength. The sensory properties of the periodontal ligament, especially those of the maxillary and mandibular molars, have not yet been fully investigated. Somatosensory evoked magnetic fields (SEFs) can be measured and evaluated for latency and intensity to determine the sensory transmission characteristics of each body parts. However, previous reports on SEFs in the oral region have only reported differences in upper and lower gingival and lip sensations. In this study, the aim was to clarify these sensory characteristics by measuring SEFs during mechanical stimulation of the periodontal ligament in the maxillary and mandibular first molars. Somatosensory evoked magnetic fields were measured in the contralateral hemispheres of 33 healthy volunteers. Mechanical stimulation of the maxillary and mandibular right first molars, and the left wrist was performed with a specific handmade tool. The first peak latency for the mandibular first molars was 41.7 ± 5.70 ms (mean \pm SD), significantly shorter than that for the maxillary first molars at 47.7 ± 7.36 ms. The peak intensity for the mandibular first molars was 13.9 ± 6.06 nAm, significantly larger than that for the maxillary first molars at 7.63 ± 3.55 nAm. The locations in the contralateral hemispheres showed no significant difference between the maxillary first molars and mandibular first molars. These locations were more anteroinferior and exterior than that of the wrist, as suggested by the brain homunculus. Neural signals from the mandibular periodontal ligaments pass faster and more intensely to the central nervous system than those from the maxillary periodontal ligaments, and may preferentially participate in adjustment of the occlusal force and the occlusal position.

1. Introduction

Somatosensory responses of the periodontal ligaments are extremely important in our daily life. The responses to mechanical stimulus provide tactile, pressure, and vibratory senses which help humans to detect the size or hardness of foods [1, 2], and recognize occlusion points [3]. In addition, the integrated senses from the masticatory muscles and temporomandibular joint allow the adjustment of the force of occlusion and mastication [4, 5]. The homunculus model of somatotopic functional organization of the primary somatosensory cortex (S1) includes the periodontal ligaments [6]. Previous studies have investigated the responses and locations

of projections in the brain to the oral senses using various experimental methods and devices, with procedures depending on the specific design. Animal experiments have involved mechanical or electrical stimulation of the teeth, tongue, lips, and other areas, and have identified the somatotopic organizations of the oral senses in S1 [7, 8, 9, 10].

Human studies have used electrical stimulation of various oral organs, and brain waves were measured by electroencephalography (EEG) to investigate the related brain activities. The initial and second peaks of the responses around 13 ms and 18 ms, called N13 and P18, were found by electrical stimulation of the tongue, and upper and lower gums [11, 12]. Somatosensory evoked potentials (SEPs) were measured with electrical

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stimulation to the upper right gums, and suggested that the intensity was larger in the contralateral than in the ipsilateral hemisphere [13]. The superior spatial resolution of functional magnetic resonance (MR) imaging has revealed the somatotopic organization of the oral senses [14, 15, 16]. Mechanical stimulation of the maxillary right and left central incisors and canines by the von Frey filaments identified response locations in S1 and secondary somatosensory cortex (S2) [17]. The cortical projections in S1 were bilateral with slight contralateral predominance for 75% of canines. Periodontal sensations from the teeth are transmitted through the trigeminal ganglion and the trigeminal mesencephalic nucleus. Periodontal sensations through the trigeminal ganglion are known to project to S1, whereas periodontal sensations through the trigeminal mesencephalic nucleus project to the main sensory nucleus [18], but not to the S1. However, functional near-infrared spectroscopy and EEG studies have failed to detect any significant difference between the maxillary and mandibular periodontal ligaments in latency and intensity [19, 20].

Magnetoencephalography (MEG) is a noninvasive brain imaging technique, with high temporal resolution but also superior spatial resolution to EEG. MEG can detect somatosensory responses and locations by recording the weak magnetic fields around human brains caused by neural activity. The oral somatosensory system has been extensively investigated [21, 22, 23, 24], but few reports have compared the oral senses, especially of the maxillary and mandibular periodontal ligaments.

MEG measurement of Somatosensory evoked magnetic fields (SEFs) to electrical stimulation of 24 points in the maxillary and mandibular oral organs found no significant difference between the maxillary and mandibular gums, or between the maxillary and mandibular lips, in latency and location, but the mandibular gum and lip tended to have shorter latencies than the maxillary gum and lip [21]. Similarly, the latency of the lower lip tended to be shorter than that of the upper lip to electrical stimulation of oral organs [25]. Therefore, the senses of the mandibular periodontal ligaments will pass neural signals to the somatosensory system faster than the maxillary periodontal ligaments. In addition, all response locations in S1 are presumably almost the same. However, no MEG study has yet measured SEFs to mechanical stimulation of the maxillary and mandibular periodontal ligaments, or identified any differences.

Studies using MEG have shown that by observing the latency and intensity of SEFs, it is possible to objectively evaluate the sensory transduction characteristics [26] of each body part and changes in sensory reception due to age and disease [24, 27, 28]. The present MEG study measured the SEFs to mechanical stimulation of the maxillary and mandibular first molar periodontal ligaments, and investigated the responses and locations of activity in S1 passed through the trigeminal ganglion. The study tried to establish whether the mandibular first molar periodontal ligaments send neural signals to the S1 faster and stronger than the maxillary first molar periodontal ligaments, and to discover any significant difference in the response location.

2. Materials and methods

2.1. Subjects

Thirty-three healthy, right-handed volunteers (10 females and 23 males, mean age 22.7 years) participated in the experiment. Handedness was evaluated using the Edinburgh Handedness Inventory. No subjects had received orthodontic treatment, had significant skeletal disharmony, or had a history of neurological disease. The study was approved by the Ethic Committee of Tohoku University Graduate School of Dentistry (protocol number: 26–39), and written informed consent was obtained from each subject.

2.2. Stimulation

Mechanical stimulation of the maxillary and mandibular right first molars, and left wrist was performed with a handmade tool based on the brush stimulator [17]. The stimulus tool consisted of a resin handle,

silicone cap, and two optic fibers (E32-DC200F4R, Omron Corp., Kyoto, Japan) (Figure 1). The fibers were attached along the resin handle, and the tip of the fibers was positioned in the silicone cap of the tip of the resin handle used to tap the occlusal surface of the teeth. The optic fibers were connected to a photoelectric switch (E3X-NA41F 2M, Omron Corp.). One of the fibers emitted red light, and the other fiber detected the reflected light. The photoelectric switch recognized the trigger point as the moment reflected light was not detected as the silicone cap contacted the tooth surface.

The maxillary and mandibular right first molars, and the left wrist were stimulated to compare the cortical responses. The stimulus intensity was around 100 g, and the interstimulus interval was 0.5–1.0 s to each tooth, depending on the speed or distance of the stimulus tool. The stimulation to the teeth was considered a constant force because all stimulating sessions were carried out by an experienced dentist. Before the measurement, the dentist performed 50 mechanical stimulation sessions in training, and the average stimulus intensity was 102.02g. No subjects complained of any tooth pain during the stimulation.

2.3. MEG recordings

MEG data were recorded using a whole-head 200-channel MEG system (PQA160C, Ricoh Co., Ltd., Tokyo, Japan) in a magnetically shielded room. The head shape of each subject was digitized using a 3D digitizer (Fast SCAN Cobra, Polhemus Inc., Colchester, VT) and co-registered with individual structural MR images acquired using a 3 T MR system (Achieva, Philips, Best, the Netherlands). The MEG signals were recorded from 50 ms prestimulus to 300 ms after the trigger point, and were band-pass filtered between 20 Hz and 500 Hz, and digitized at 1000 Hz.

2.4. Data analysis

The source location corresponding to peak latency was estimated individually using the single equivalent current dipole (ECD) model as calculated by analysis software (MEG Laboratory, Ricoh Co., Ltd.) The ECD model identified the source of the magnetic signals assuming a spherical conductor based on Sarvas law [29]. The locations of the signal sources were evaluated in the right and left hemispheres separately. The resulting data were averaged based on about 300 stimulations after removing typical noise based on visual judgment. The dipole positions were superimposed on the MR images, and the ECDs located on the central sulcus with goodness-of-fit value of 85% were extracted. The averaged wave, root mean square wave, was used to assess the peak latencies. The latencies, intensities were compared between the maxillary and mandibular right first molars by independent Student's t-tests. The latencies and intensities of the left wrist were shown in the figure as the references, and they were not statistically compared with the latencies and intensities of the maxillary and mandibular first molars. The location of the ECDs were compared between the maxillary and mandibular right first molars and the left wrist by ANOVA.

3. Results

The first responses in the contralateral hemispheres to stimulation of the maxillary and mandibular right first molars, and left wrist were detected in 10/33, 15/33, and 30/33 hemispheres, respectively. Figure 2 show the waveforms and latencies for the maxillary and mandibular right first molars, and the left wrist.

The first peak latency in the central sulcus of contralateral hemispheres occurred at 47.7 ± 7.36 ms (mean \pm SD) for the maxillary right first molar, 41.7 ± 5.70 ms for the mandibular right first molar, and 45.2 ± 12.1 ms for the left wrist (Figure 3A). The latency for the mandibular first molar was significantly shorter than that for the maxillary first molar ($p = 0.0374$). The latency for the left wrist showed no significant difference with those for the maxillary ($p = 0.566$) and mandibular first molars ($p = 0.217$).

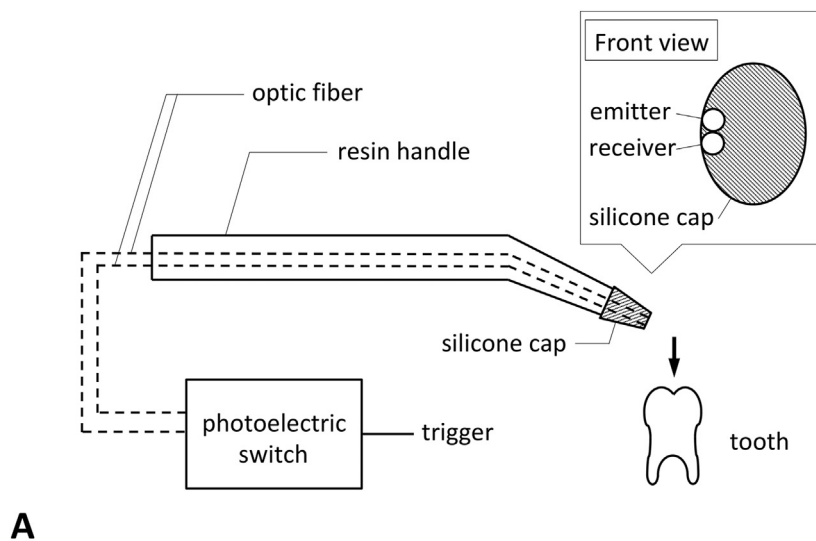


Figure 1. (A) Special handmade stimulus tool consisted of a resin handle, silicone cap, and two optic fibers. The fibers were attached along the resin handle, and the tip of the fibers was positioned in the silicone cap of the tip of the resin handle used to tap the occlusal surface of the teeth. The optic fibers were connected to a photoelectric switch. One of the fibers is the emitter, and the other fiber is the receiver. The photoelectric switch recognized the trigger point as the moment reflected light from the emitter was not detected by the receiver as the silicone cap contacted the tooth surface. (B) Maxillary first molar was mechanically stimulated by the tool.



The intensities of the first peaks in the contralateral hemispheres were 7.63 ± 3.55 nAm for the maxillary right first molar, 13.9 ± 6.06 nAm for the mandibular right first molar, and 16.5 ± 6.67 nAm for the left wrist (Figure 3B). The intensity for the mandibular first molar was significantly larger than that for the maxillary first molar ($p = 0.0099$).

Figure 4A shows the isofield maps and Figure 4B shows the ECD locations for the maxillary and mandibular right first molars in the contralateral hemispheres of the same subject (29-year-old male). The location for maxillary right first molar periodontal ligament stimulation was $x: -50.9 \pm 9.56$ mm, $y: 13.5 \pm 8.07$ mm, $z: 61.9 \pm 7.07$ mm, and that for mandibular right first molar periodontal ligament stimulation was $x: -48.5 \pm 8.32$ mm, $y: 12.2 \pm 9.52$ mm, $z: 63.8 \pm 6.27$ mm. In the left wrist stimulation, the signal was $x: 35.2 \pm 8.57$ mm, $y: 0.133 \pm 8.86$ mm, $z: 86.7 \pm 8.54$ mm. The x-axis values of the maxillary and mandibular right first molar were taken as absolute values for comparison, and the locations showed no significant difference between the maxillary right first molar and mandibular right first molar ($x: p = 0.525$, $y: p = 0.724$, $z: p = 0.509$) (Figure 5). The locations for the left wrist showed significant differences with those of the maxillary right first molars and mandibular right first molars along all axes (maxillary vs. wrist, $x: p < 0.0001$, $y: p = 0.0002$, $z: p < 0.0001$; mandibular vs. wrist, $x: p < 0.0001$, $y: p = 0.0002$, $z: p < 0.0001$).

4. Discussion

The present study is the first to investigate SEFs to mechanical stimulation of the maxillary and mandibular first molars. The findings showed that the periodontal ligaments of the mandibular first molar sent neural signals to the contralateral S1 faster than those of the maxillary first molar, but the locations in S1 showed no significant difference between the maxillary and mandibular first molars.

4.1. Validity of the experimental procedure

Previous studies showed the peak latency was 43–56 ms by mechanical stimulation to the fingers and wrist [22, 30, 31]. In the present study, mechanical stimulation of the middle nerves in the left wrist evoked a peak around 45 ms. Compared with the previous studies, the present results show that the responses in S1 were caused by the tactile stimulation.

The tactile detection threshold of the first molar is 7.5 ± 3.1 g [32], and human periodontal ligament sensory receptors show a markedly curved relationship between firing rate and force amplitude, with the greatest sensitivity to changes in tooth load occurring below 1 N for incisors and below 4 N for molars [33]. For this reason, Habre-Hallage et al. used fMRI to investigate the response of the cerebral cortex during

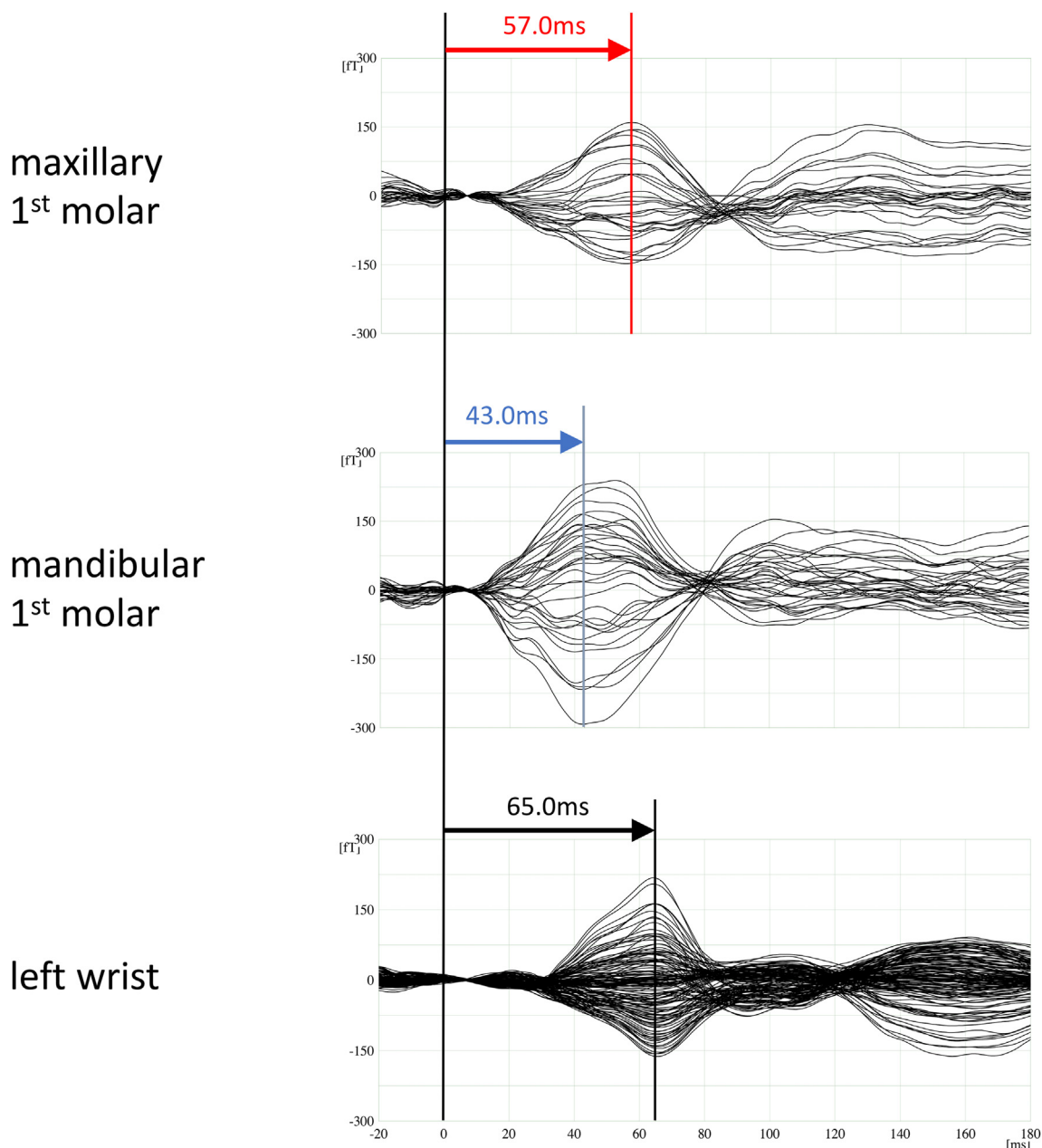


Figure 2. Waveforms for the maxillary and mandibular right first molars, and the left wrist in the contralateral hemisphere of a subject (29-year-old male). Arrows indicate the first peak latency.

periodontal ligament mechanical stimulation. They performed periodontal ligament mechanical stimulation at 100 g and 180 g to the anterior teeth, and they detected responses in the primary and secondary somatosensory cortices [17]. When stimulating teeth, if the stimulus intensity is too small even beyond the threshold, SEFs may not be able to detect sufficient responses. In this study, around 100 g was exerted based on these reports. The mechanical stimulation force of around 100 g caused no pain, but evoked neural signals from the A β fibers. The A β nerve fibers pass signals from the mechanoreceptors in the periodontal ligaments. In contrast, the A δ and C nerve fibers pass signals from the nociceptors. The diameter of the A β nerve fiber is greater than those of the A δ and C nerve fibers, and the nerve conduction velocity of the A β is 3–4 times faster than that of A δ and C. Since painful orofacial stimulation through A δ and C fibers have latencies of around 100 ms [34, 35], the early component within 100 ms of the SEFs was targeted to increase the sensitivity of measurement of the signals from the A β fibers. In addition, the first peak latency was considered to reflect the time from the

stimulation point to the response in the central sulcus, allowing comparison of the responses of the periodontal ligaments of the maxillary and mandibular first molars.

4.2. Importance of the contralateral hemispheres in the primary SEFs and selection of the first molars

The present study focused on the responses in the contralateral hemisphere to the stimulation. Basically, the right hemisphere corresponds to sensation of the left side of the body, and the left hemisphere to the sensation of the right side of the body. Electrical stimulation of the maxillary right lips and gums was used to measure SEFs [13]. The intensity of the waveform showed contralateral predominance. Electrical stimulation of the pulp of the maxillary right premolar was used to investigate SEFs [23]. The early component was detected only in the contralateral hemispheres. Mechanical stimulation of the maxillary right and left central incisors and canines by the von Frey filaments was used to

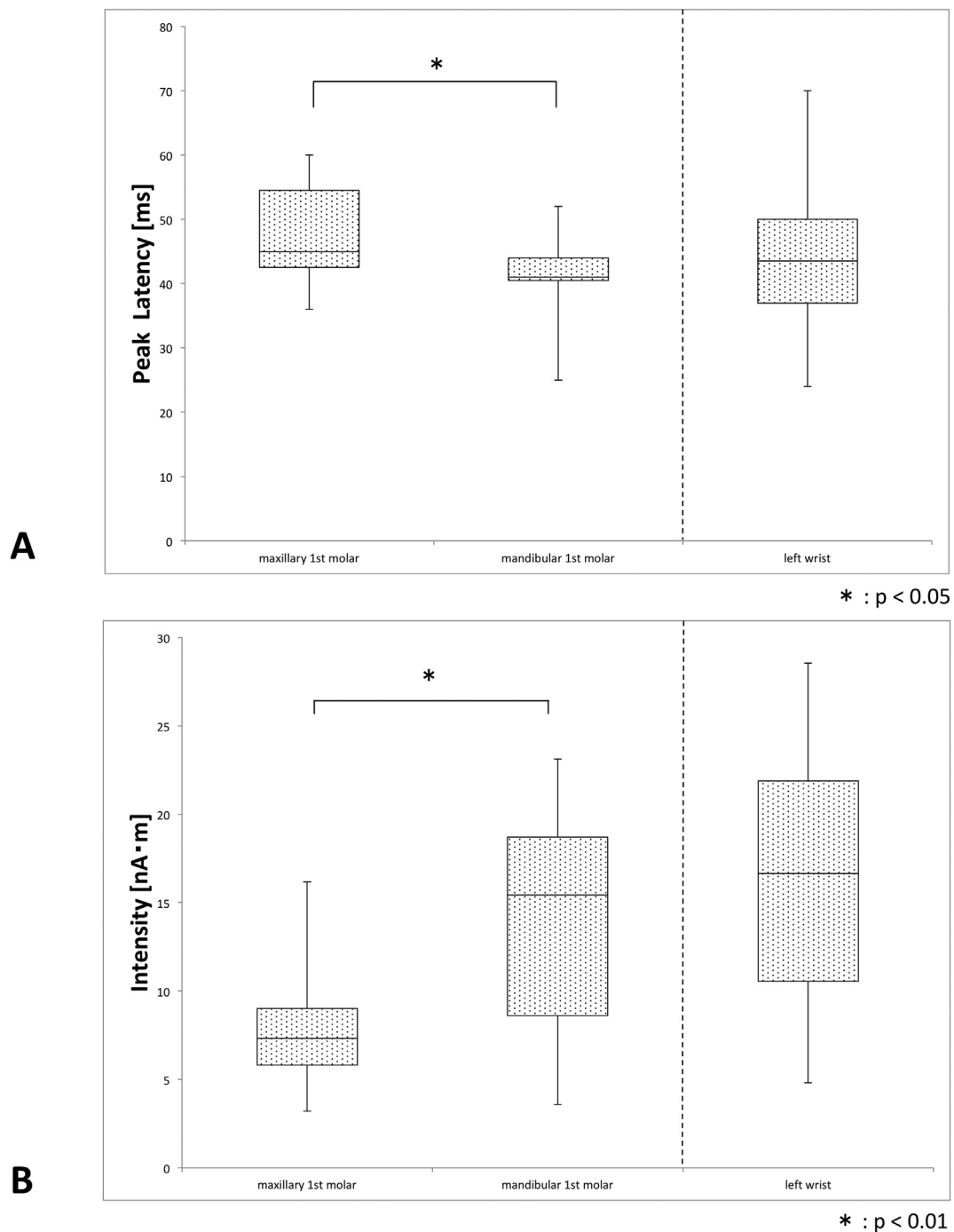


Figure 3. (A) First peak latencies for the maxillary and mandibular right first molars, and the left wrist in the contralateral hemisphere. Asterisks indicate significant differences at $p < 0.05$. (B) Intensities of the first peaks for the maxillary and mandibular right first molars, and the left wrist in the contralateral hemisphere. Asterisks indicate significant differences at $p < 0.01$.

measure the locations of the responses in the somatosensory cortex by functional MR imaging [17]. The bilateral responses for all stimulated teeth were located in S1 and S2, and the responses showed no significant differences between the right and left hemispheres for the central incisors, whereas contralateral predominance was significant for 3 of 4 stimulated canines only in S1. Therefore, slight contralateral predominance for the teeth may be located at a certain distance from the midline in S1. Consequently, measurement of the SEFs in the contralateral hemisphere in S1 was performed in the present study.

Brain activities for vibratory stimulation to each tooth were compared by functional near-infrared spectroscopy, which detects changes in

cerebral blood flow in the somatosensory cortex [20]. Brain activation was significantly stronger for stimulation of the first molars than for other teeth. The present study was intended to compare the brain activities for stimulation of the maxillary and mandibular teeth, so the first molar with the strongest brain activations was chosen as stimulation site.

4.3. Differences in the responses of the maxillary and mandibular periodontal ligaments

Studies stimulating teeth and gums to measure SEPs suggested the latency tended to be slightly shorter in the maxillary structures [12, 19],

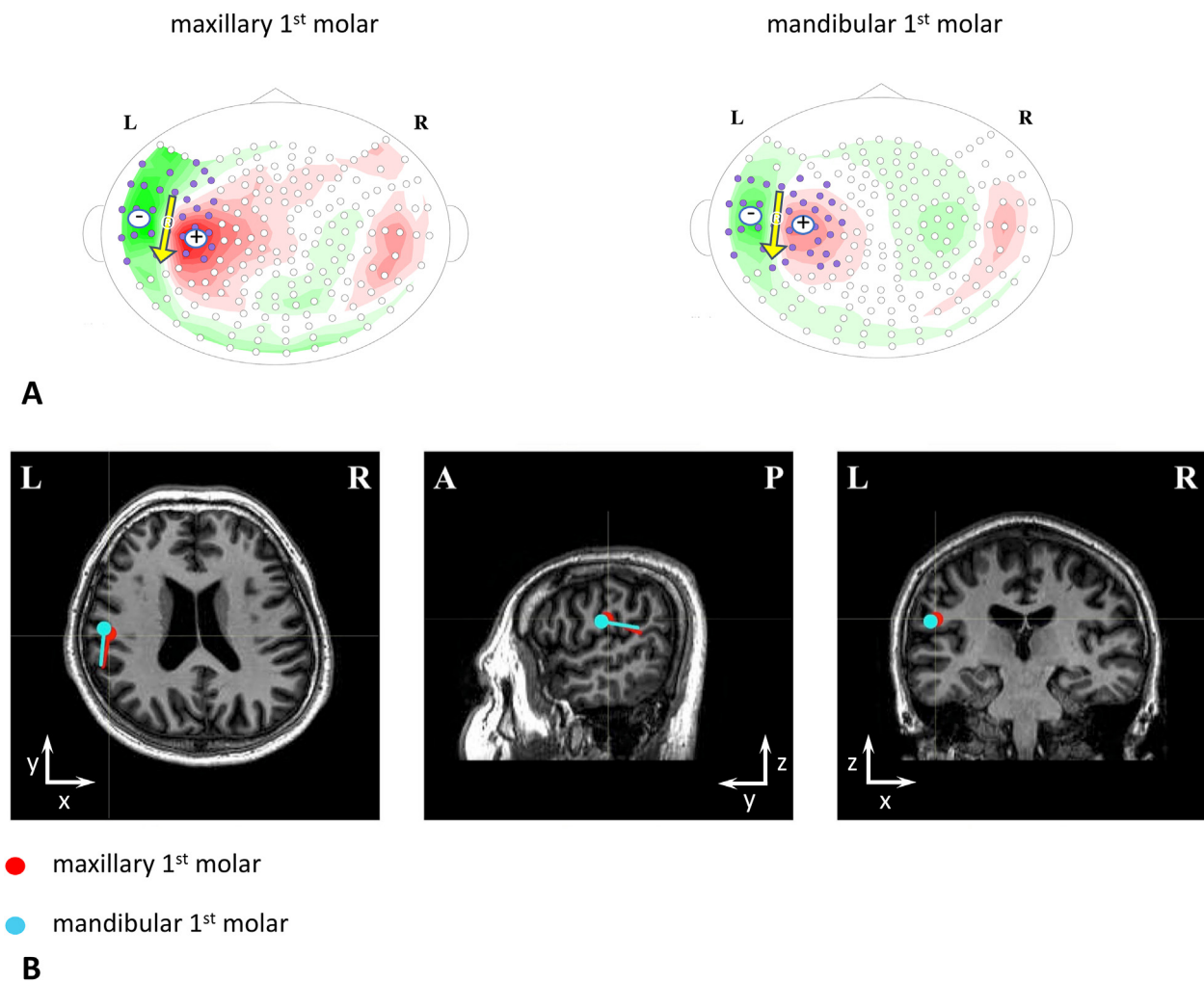


Figure 4. (A) Isofield maps and (B) ECD locations for the maxillary and mandibular right first molars in the contralateral hemispheres of the same subject (29-year-old male). The ECD (circle) and the direction of the neural signal (attached bar) in the maxillary (red dipole) and mandibular first molars (blue dipole).

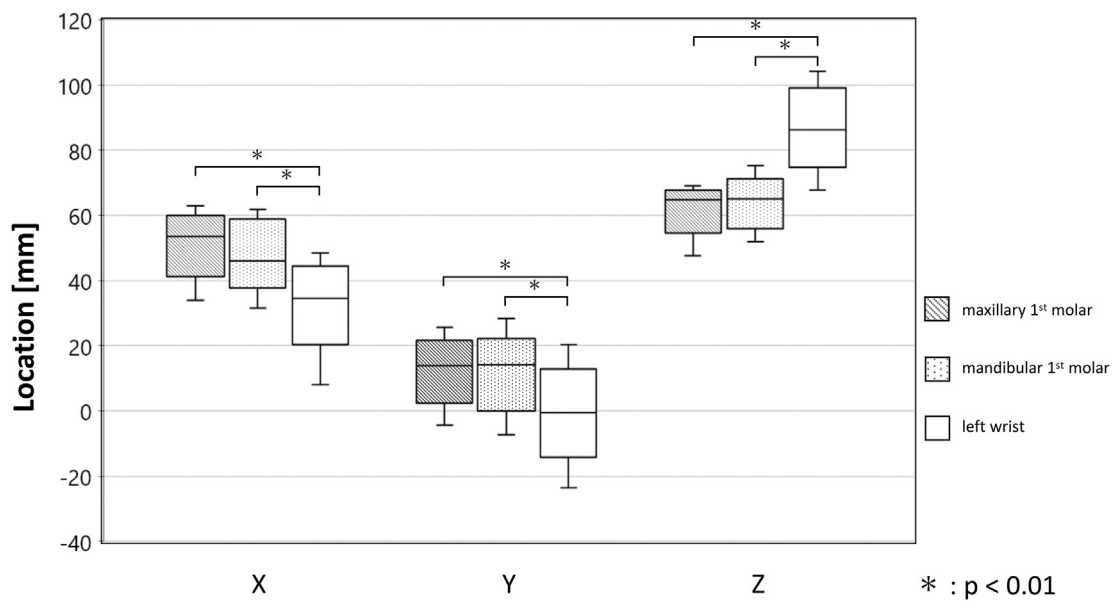


Figure 5. Locations (x, y, z) in the contralateral hemispheres. The x axis values of the maxillary and mandibular right first molars are absolute values. The diagonal line, dots, and white boxes indicate the maxillary first molar, mandibular first molar, and left wrist, respectively. Asterisks indicate significant differences at p < 0.01.

but it showed the opposite trend in SEFs [21]. The present study showed that the latency for the mandibular was significantly shorter than that for the maxillary periodontal ligaments. Both EEG and MEG provide high time resolution. MEG is much better than EEG for detecting signals in the tangential direction to the head shape. In addition, EEG measures the associated wave only in the whole brain, whereas MEG can detect the waves in the separate hemispheres. Consequently, the present study could observe the difference in latency because only the responses in the contralateral hemisphere were measured.

Latency differences in the trigeminal SEFs could be explained by the peripheral conduction time, the central conduction time, and the central processing time within the cortex [21]. In this study, the difference in latency may be due to the difference in peripheral receptors. The periodontal ligaments are innervated by many sensory nerves, and there are two types of receptors for these sensory nerves: rapid adapting receptors, which increase in threshold over time as the stimulus is received, and slow adapting receptors, which continue to respond while the stimulus is received. In cats, the latencies during stimulation of fast adapting receptors and slow adapting receptors were 10.7 ms and 7.3 ms, respectively, and the latency during stimulation of slow adapting receptors was reported to be shorter than rapid adapting receptors [36]. In this study, the latency of mandibular first molar stimulation was shorter than that of maxillary first stimulation, suggesting that the density of slow adapting receptors in the periodontal ligaments of mandibular molars may be large, and that these receptors continue to transmit stimuli to the center, contributing to the control of jaw position and occlusal force. However, no study has examined the density of nerve endings receptors in human maxillary and mandibular molars, and further research is needed to prove this.

Few studies have investigated the differences in the brain responses of the maxillary and mandibular periodontal ligaments. Study of quantitative vibratory stimulation did not detect any significant difference in the response intensity between the right and left somatosensory cortices to stimulation of the maxillary and mandibular first molars [20]. In contrast, the present study showed a significant difference in the intensity between the maxillary and mandibular periodontal ligaments. The MEG intensity was larger for the lower than the upper lip to vibratory stimulation [37]. The lower lip was suggested to be richer than the upper lip in masticatory and phonatory functions. In addition the sensitivities were presumably higher in the mandibular in the maxillary periodontal ligaments as the mandibular teeth normally contact with the tongue. The sensation of the periodontal ligaments is important for control of tongue movement [38, 39]. The present study found the latencies were shorter and the intensities were larger for the mandibular than the maxillary periodontal ligaments, presumably because the mandibular periodontal ligaments recognize tongue movement at all times and might be more involved in control of tongue movements. Sakamoto et al. summarized several reports of SEPs and SEFs measurements during tongue stimulation [40]. According to them, the first observed latency varied 10–55 ms. However, considering that most of the reports indicate that the first peak latency was observed within 20 ms, the latency of the tongue is probably shorter than that of the periodontal ligaments. The difference in latency may be caused by whether the sensory receptors on the tongue surface transmit stimuli directly or whether the periodontal ligament sensory receptors indirectly transmit stimuli transmitted through the teeth to the brain.

No differences were found in the response locations between the maxillary and mandibular first molars. However, the response locations of the maxillary and mandibular first molars both showed significant differences in x (absolute value), y, and z axes compared with the response location of the left wrist. These locations were more anterior-inferior and exterior than that of the wrist, as suggested by the brain homunculus [6]. In addition, electrical stimulation of the wrist and the pulp of the maxillary first premolar showed significant differences of the location in the x, y, and z axes in the S1 [23]. The locations were anterior-inferior and exterior to that for the wrist. The findings of the present

study agree with previous conclusions. Presumably complex jaw movements can be controlled despite the close proximity of the response locations of the maxillary and mandibular first molars.

4.4. Importance of the maxillary and mandibular periodontal ligaments to the oral functions

Investigation of the main occlusion area by biting a small piece of dental putty identified three main groups: normal occlusion, mandibular prognathism, and mandibular prognathism corrected by orthodontic surgery [41], and was reported that the mandibular first molar is more important in the main occlusion area than the maxillary first molar, and even the anteroposterior jaw relationship is different. The reports using Electromyography (EMG) showed the mandibular periodontal ligament was more important than the maxillary periodontal ligament for adjusting jaw position during exertion of relatively weak occlusal force [42], and the unit EMG activities were smaller in the muscle of mastication under anesthesia of the mandibular periodontal ligament than under no anesthesia and anesthesia of the maxillary periodontal ligaments [43].

In the present study, the first peak latency for the response of the mandibular periodontal ligament was significantly shorter than for the maxillary periodontal ligament. Therefore, the mandibular periodontal ligament sends neural signals faster to the central nervous system than the maxillary periodontal ligament in the early stage of occlusion, and preferentially participates in adjustment of the occlusal force and the decision making of the occlusal position.

Declarations

Author contribution statement

Eriya Shimada: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Hiroyasu Kanetaka: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Hiroki Hihara: Performed the experiments.

Akitake Kanno: Performed the experiments; Analyzed and interpreted the data.

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

Nobukazu Nakasato: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Kaoru Igarashi: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

The data that has been used is confidential.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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