Hokkaido J. Dent. Sci., 38 (*Special issue*) : 68-73, 2017.

Clinical application of MEG for the evaluation of sensory disturbances of the lip and tongue in patients with mandibular nerve injury

Hitoshi Maezawa

Oral Physiology, Department of Oral Functional Science, Faculty of Dental Medicine and Graduate School of Dental Medicine, Hokkaido University

ABSTRACT : This paper reviews the clinical applications of MEG in patients with sensory disturbances of the lip and tongue due to unilateral injury of the mandibular nerve. Multiple non-invasive approaches are available for the evaluation of human brain function. Some of these approaches are electroencephalography (EEG), magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), and positron emission tomography (PET). MEG is particularly advantageous due to its high spatiotemporal resolution. Mandibular nerve injury during orofacial surgery may result in sensory deficits of the lower lip and tongue, which often lead to speech disorders, eating difficulties, and significant reductions in patients quality of life. Conventional methods for evaluating abnormalities in lip and tongue sensation in clinical settings include the von Frey and two-point discrimination tests. However, the reproducibility and reliability of such tests remains low due to the subjective nature of the information provided by the patient. In this paper we propose that MEG can be used to effectively and objectively detect sensory abnormalities of the lower lip and tongue.

Key Words : magnetoencephalography, lingual nerve, inferior alveolar nerve, somatosensory evoked fields, trigeminal nerve

Introduction

Currently, multiple non-invasive modalities are available for the mapping of human brain function, including electroencephalography (EEG), magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), and near-infrared spectroscopy (NIRS). EEG and MEG can be used to estimate neural activity based on scalp potentials or magnetic fields (primary effects), while fMRI, PET, SPECT, and NIRS can be used to detect hemodynamic and metabolic changes associated with neural activity (secondary effects)[1]. EEG and MEG are advantageous due to their remarkably high temporal resolution below the level of one millisecond. However, MEG is superior to EEG in terms of spatial resolution, which is limited in the latter due to the low current conductivity of the skull. MEG is now widely utilized for the non-invasive investigation of human brain functions, such as sensorimotor and cognitive functions[2, 3]. In clinical settings, MEG is most frequently used to assess pathological neural activity in patients with epilepsy[4]. In addition, previous studies have reported that MEG can be used to effectively assess the degree of somatosensory processing dysfunction in patients with cerebrovascular diseases[5, 6], cortical reflex myoclonus[7-9], and polymicrogyria[10] via the analysis of somatosensory evoked fields (SEFs) following peripheral nerve stimulation in the limbs. Some studies have also reported that SEFs associated with oral stimulation can be used to evaluate sensory abnormalities in orofacial regions such as the lip[11] and tongue[12, 13] associated with damage to the mandibular nerve.

The mandibular nerve is the largest of the three branches of the trigeminal nerve. Somatosensory

Address of Correspondence
Hitoshi Maezawa, DDS, PhD.
Oral Physiology, Department of Oral Functional Science, Faculty of Dental Medicine and Graduate School of Dental Medicine, Hokkaido University, Kita 13 Nishi 7, Kita-ku, Sapporo, Hokkaido 060-8586, Japan
TEL : +81-11-706-4229 ; FAX : +81-11-706-4229 ; E-mail : maezawa@den.hokudai.ac.jp

sensation of the lower lip and anterior portion of the tongue are associated with specific branches of the mandibular nerve : the inferior alveolar nerve (IAN) and lingual nerve (LN), respectively. Sensory disturbances of the lower lip and tongue may be caused by injury to the mandibular nerve during orofacial surgeries such as third molar extraction, dental implantation, root canal procedures, mandibular cyst removal, and local anesthetic injection. Previous reports have documented that the incidence of IAN injury ranges from 2 to 17% during third molar extraction[14-18], while that of LN injury ranges from 0.06 to 10%[19]. Although sensory deficits of the lip and tongue due to mandibular nerve injury are comparatively rare, such deficits may result in speech disorders and eating difficulties, significantly reducing the patient's quality of life. However, clinicians often use subjective assessment methods, such as the von Frey test and two-point discrimination test, when evaluating sensory disturbances of the lip and tongue. Because they depend on the patient's subjective interpretation of sensory information, these commonly used tests exhibit low reproducibility and reliability. Thus, objective assessment methods are required for proper evaluation in clinical settings. Previously, my research group reported that sensory abnormalities of the lip[11] and tongue[12, 13] can be effectively and objectively evaluated using a whole-head MEG system (Fig. 1a). In the present report, I review the clinical applications of MEG in patients with sensory disturbances of the lip and tongue caused by damage to the mandibular nerve.

1. Somatosensory evoked fields associated with stimulation of the lip and tongue

SEFs are small magnetic fields evoked by repetitive external stimulation. The evoked fields occur at the same latency to the timing of stimulation. Thus, when averaging to the time-locked onset of stimulation, background magnetic activity can be averaged to zero, and the small evoked fields that occur in conjunction with stimulus onset can differentiated from background activity. The latency, amplitude, and polarity of SEF peaks have been used to identify the primary somatosensory cortex (S1) of the target peripheral regions. Nakamura *et al.*[20] reproduced the functional somatosensory homunculus for multiple regions of the human body (such as the fingers, arm, trunk, leg, foot, tongue, and lips) using SEFs associated with tactile stimulation. Subsequent studies further demonstrated the somatotopic organization of the orofacial region using SEFs for the lips, tongue, and gingiva associated with both electrical[21] and mechanical[22] stimulation.

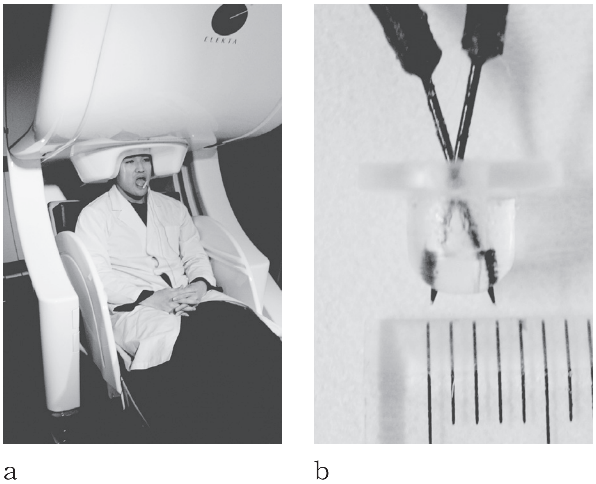

Fig. 1 Measurement of somatosensory evoked fields (SEFs) following lip and tongue stimulation using pin electrodes.
a : Measurement of SEFs using a whole-head magnetoencephalography system. **b** : A pair of pin electrodes used for electrical stimulation. The interelectrode distance was 3 mm. Images modified with permission from Maezawa *et al*[24].

When recording SEFs following stimulation of the orofacial regions, artifacts associated with stimulation and/or muscle activity represent a major concern, due to the short distance between the areas of stimulation (orofacial region) and recording (head)[23]. As the early portion of the SEF (*i.e.*, the period immediately following electrical stimulation) is easily contaminated by such artifacts, it is sometimes difficult to differentiate cortical responses from stimulus-induced artifacts. To resolve this issue, Maezawa *et al.*[11, 24] recorded SEFs following low-intensity electrical stimulation of the lip and tongue stimulation using pin electrodes (0.4 mm in diameter) (Fig. 1b), successfully reducing the influence of stimulus-induced artifacts. The magnitude of SEFs quickly returned to baseline levels before the first component was observed, approximately 25 ms (P25m) following lip[11] and tongue[24] stimulation, indicating that the use of pin electrodes allows for easy and reliable detection of early SEF components following orofacial stimulation. In addition, the use of pin electrodes possesses the following two advantages. First, pin electrodes allow for safe, low-intensity electrical stimulation of the orofacial regions, reducing the risk of damage associated with electric shocks. Second, the use of pin electrodes allows for precise stimulation of a small area, which is often difficult using ball electrodes or tactile stimulation devices with larger contact areas. This capacity for the stimulation of relatively small areas is particularly advantageous for patients with highly localized damage to orofacial regions.

When it remains difficult to distinguish early SEF components from artifacts related to electromyography (EMG) activity induced by electrical stimulation using other types of electrodes (*e.g.*, ball electrodes), simultaneous EMG recordings from other orofacial muscles may be useful[25]. In addition, mechanical stimulation in the form of compressed nitrogen[26] or via a piezo-driven tactile stimulation device[22] can also be used to avoid the influence of electrical artifacts.

2. Clinical applications of SEFs associated with lip and tongue stimulation

2.-1 Sensory disturbances of the lip

In our previous study, we objectively evaluated sensory disturbances of the lower lip in patients with unilateral IAN injury, based on SEFs associated with electrical stimulation of the lip using pin electrodes[11]. The first component of lip SEFs was stably detected at approximately 25 ms (P25m) (Fig. 2), and at least one of the following three components (P45m, P60m, or P80m) was observed over the contralateral hemisphere for either side of the lip in all 10 healthy volunteers. In contrast, the P25m component was absent following stimulation of the affected side in all six patients with unilateral sensory disturbances of the lip (Fig. 2), although traceable responses were observed in five of the six patients. The stable detection of a P25m component in healthy volunteers indicates that unilateral sensory disturbance can only be assessed via stimulation of the affected side. Since this method does not require a control side, it may also be useful in patients who have undergone bilateral oral surgery involving the region innervated by the IAN (*e.g.*, sagittal split ramus osteotomy).

In addition, an understanding of IAN anatomy is necessary when recording SEFs associated with lip stimulation. When stimulation is applied near the midline of the lip electrical stimulation may activate the IAN branch of the non-target side, as this branch may cross over the midline to the target side. Indeed, we observed the P25m component following stimulation of the unaffected side in two of six patients in our previous study, while it was observed as a notch or shoulder

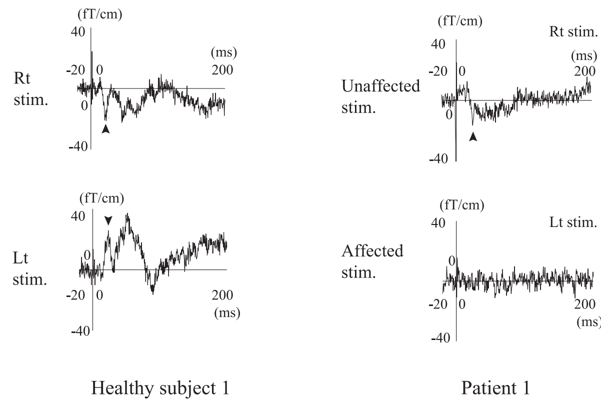

Fig. 2 Waveforms of lip somatosensory evoked fields (SEFs) in a representative healthy volunteer and a patient with sensory disturbance of the left lower lip.

Waveforms are shown in the maximum amplitude channel over the contralateral hemisphere for the right and left sides in the healthy volunteer, and for the unaffected and affected sides in the patient (vertical scale : 40 fT/cm in both). The P25m components are indicated by the arrowheads. Note that P25m components were detected following stimulation of either side in healthy volunteers and of the unaffected side in the patient, while stimulation of the affected side did not produce the P25m component. Rt stim., right-side stimulation ; Lt stim., left-side stimulation; Unaffected stim., unaffected-side stimulation ; Affected stim., affected-side stimulation. Images modified with permission from Maezawa *et al*[11].

embedded in the following components in the remaining four patients. This different waveform configuration of the P25m component in healthy volunteers may have been associated with the area in which stimulation was applied to the lip: When stimulation was applied 2 cm lateral to the midline of the lip, patients were asked to self-report whether electrical stimulation had occurred only on the target side. Nevertheless, since the midline region of the lip is innervated by the bilateral branches of the IAN, stimulation on one side of the lip may have recruited trans-median excitation of the nerve branch on the other side in some participants. Further studies are required to clarify the influence of stimulus location when applied near the midline of the lip.

2.-2 Sensory disturbances of the tongue

In our previous study, we identified three or four components of tongue SEFs (P25m, P40m, P60m, and P80m) over the contralateral hemisphere following pin-electrode stimulation in all 10 healthy volunteers[24]. However, in contrast to the consistent detection of the P25m component among participants following lip stimulation, none of these four components (P25m, P40m, P60m, and P80m) was stably observed across participants following tongue stimulation. These findings suggest that each component of the tongue SEF cannot be used as an objective parameter for evaluating sensory disturbances of the tongue. We then analyzed the activated root-mean-square (aRMS) of spatial and temporal summation, which represents the mean amplitude of SEFs from the 18-channel RMS over the contralateral hemisphere between 10 and 150 ms[24]. Moreover, as intra-individuals similarities in SEF waveforms were detected between the right and left sides of the tongue in each healthy volunteer, we utilized the unaffected-side of the tongue as a control to evaluate sensory disturbances of the tongue associated with unilateral LN injury[12, 24]. The laterality index of the aRMS, expressed as [(left - right) / (left + right)], was out of the pre-defined normal range in 12 of 13 patients with sensory disturbances of tongue, and within the normal range in all 10 healthy volunteers. The test sensitivity and specificity of the procedure utilizing the laterality index of aRMS were 92.3% and 100%, respectively, suggesting that tongue SEFs can be used to objectively evaluate unilateral sensory disturbances of the tongue (Fig. 3)[12]. However, this method of analysis is limited in that it cannot be applied in patients who have undergone bilateral oral surgery or in those with bilateral sensory disturbances of the tongue due to the loss of the control side (unaffected side).

We recently reported two cases in which tongue SEFs were useful for the objective evaluation of sensory recovery during patient follow-up[13]. In both patients, sensory deficits of the tongue were caused by unilateral LN injury during lower third molar extraction. Both patients underwent oral surgery to repair the injured LN, and all tongue sensory evaluations were performed both prior to and following surgery. Sensation of the tongue was initially highly lateralized between the affected and unaffected sides of the tongue in both patients, but had been restored to approximately normal by the time of post-surgery evaluation. SEFs were recorded following separate stimulation of the affected and unaffected sides of the tongue, and cortical activity was evaluated over the contralateral hemisphere using the laterality index of the aRMS. In both patients, tongue stimulation of the unaffected side evoked clear, reproducible differences between preoperative and postoperative SEFs. Preoperative stimulation failed to evoke SEFs on the affected side, whereas postoperative stimulation evoked clear SEFs. In both patients, the laterality index of the aRMS was out of the pre-determined normal range before

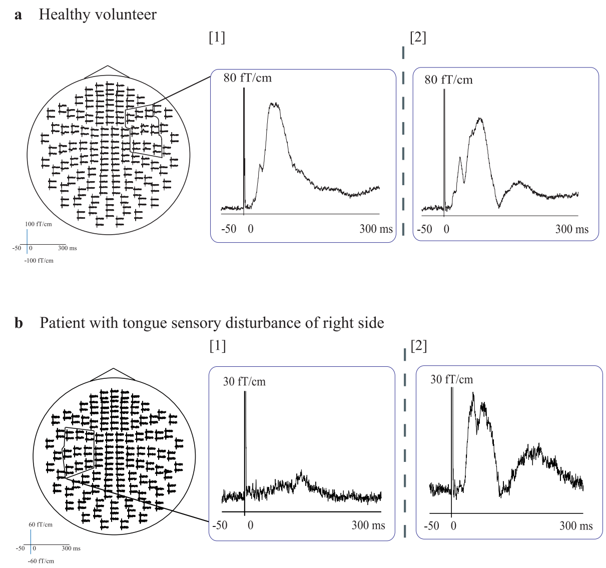

Fig. 3 Waveforms of tongue somatosensory evoked fields (SEFs) in a representative healthy volunteer (**a**) and a patient with sensory disturbance of the right tongue (**b**).
a : The RMS waveforms were calculated from 18 channels around the channel containing the local maximum amplitude over the contralateral hemisphere following left tongue stimulation in a healthy volunteer (a[1]). The vertical scale was 80 fT/cm for RMS waveforms associated with left- (a[1]) and right-side stimulation (a[2]). Note the high correlation between the shape and amplitude of these waveforms between the left and right side following stimulation in a health volunteer.
b : The RMS waveforms were calculated from the 18 channels over the contralateral hemisphere following affected-side (right side) stimulation in a representative patient (b[1]). The vertical scale was 30 fT/cm in for RMS waveforms following both affected- (b[1]) and unaffected-side stimulation (left side) (b[2]). Note that the magnitude of the RMS waveform for the affected side was significantly lower than that for the unaffected side. Images modified with permission from Maezawa *et al*[12, 24].

sensory recovery, but was within the normal range after sensory recovery. Such findings indicate that tongue SEFs may have clinical use as an objective parameter for the evaluation of tongue sensory recovery. Similarly, Yamashita *et al*[27]. recruited three patients with tongue carcinoma who had recovered flap sensation following flap reconstruction surgery. The authors reported a peak SEF latency between 20 and 40 ms following tactile stimulation of the tongue edge on either the reconstructed or the unaffected side. However, since the number of patients included in these studies was low[27], further studies are required to clarify the usefulness of tongue SEFs for evaluating the recovery of tongue sensation in various clinical settings.

Conclusions

SEFs associated with stimulation of the lip and tongue may represent effective baseline parameters for evaluating sensory abnormalities of these regions following mandibular nerve injury. Quantitative assessment using such SEF parameters is advantageous since it provides objective evidence of lip and tongue impairments at a given measurement time.

Conflict of interest

The author has no potential conflicts of interest to disclose.

Author contributions

HM wrote the manuscript and approved the final version.

Funding

This work was supported by Grants-in-Aid for Scientific Research (C)16K11621 (HM) from the Japan Society for the Promotion of Science.

References

1) Shibasaki H : Human brain mapping: hemodynamic response and electrophysiology. Clin Neurophysiol 119(4) : 731-743, 2008.
2) Hari R, Salmelin R : Magnetoencephalography : From SQUIDs to neuroscience. Neuroimage 20th anniversary special edition. Neuroimage 61(2): 386-396, 2012.
3) Baillet S : Magnetoencephalography for brain electrophysiology and imaging. Nat Neurosci 20(3) : 327-339, 2017.
4) Nakasato N, Levesque MF, Barth DS, Baumgartner C, Rogers RL, Sutherling WW : Comparisons of MEG, EEG, and ECoG source localization in neocortical partial epilepsy in humans. Electroencephalogr Clin Neurophysiol 91 : 171-178, 1994.
5) Maclin EL, Rose DF, Knight JE, Orrison WW, Davis LE : Somatosensory evoked magnetic fields in patients with stroke. Electroencephalogr Clin Neurophysiol 91(6) : 468-475, 1994.
6) Wikström H, Roine RO, Salonen O, Lund KB, Salli E, Ilmoniemi RJ, Aronen HJ, Huttunen J : Somatosensory evoked magnetic fields from the primary somatosensory cortex (SI) in acute stroke. Clin Neurophysiol 110(5) : 916-923, 1999.
7) Uesaka Y, Ugawa Y, Yumoto M, Sakuta M, Kanazawa I : Giant somatosensory evoked magnetic field in patients with myoclonus epilepsy. Electroencephalogr Clin Neurophysiol 87(5) : 300-305, 1993.
8) Karhu J, Hari R, Paetau R, Kajola M, Mervaala E : Cortical reactivity in progressive myoclonus epilepsy. Electroencephalogr Clin Neurophysiol 90(2) : 93-102, 1994.
9) Mima T, Nagamine T, Ikeda A, Yazawa S, Kimura J, Shibasaki H : Pathogenesis of cortical myoclonus studied by magnetoencephalography. Ann Neurol 43(5) : 598-607, 1998.
10) Ishitobi M, Nakasato N, Yoshimoto T, Iinuma K : Abnormal primary somatosensory function in unilateral polymicrogyria : an MEG study. Brain Dev 27(1) : 22-29, 2005.
11) Maezawa H, Matsuhashi M, Yoshida K, Mima T, Nagamine T, Fukuyama H : Evaluation of lip sensory disturbance using somatosensory evoked magnetic fields. Clin Neurophysiol 125(2) : 363-369, 2014.
12) Maezawa H, Yoshida K, Matsuhashi M, Yokoyama Y, Mima T, Bessho K, Fukuyama H : Evaluation of tongue sensory disturbance by somatosensory evoked magnetic fields following tongue stimulation. Neurosci Res 71 : 244-250, 2011.
13) Maezawa H, Tojyo I, Yoshida K, Fujita S : Recovery of impaired somatosensory evoked fields after improvement of tongue sensory deficits with neurosurgical reconstruction. J Oral Maxillofac Surg 74 : 1473-1482, 2016.
14) Renton T, Hankins M, Sproate C, McGurk M : A randomised controlled clinical trial to compare the incidence of injury to the inferior alveolar nerve as a result of coronectomy and removal of mandibular third molars. Br J Oral Maxillofac Surg 43 : 7-12, 2005.
15) Hatano Y, Kurita K, Kuroiwa Y, Yuasa H, Ariji E : Clinical evaluations of coronectomy (intentional partial odontectomy) for mandibular third molars using dental computed tomography: a case-control study. J Oral Maxillofac Surg 67 : 1806-1814, 2009.
16) Leung YY, Cheung LK : Safety of coronectomy vs. excision of wisdom teeth : a randomized controlled

trial. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 108 : 821-827, 2009.

17) Cilasun U, Yildirim T, Guzeldemir E, Pektas ZO : Coronectomy in patients with high risk of inferior alveolar nerve injury diagnosed by computed tomography. J Oral Maxillofac Surg 69 : 1557-1561, 2011.

18) Long H, Zhou Y, Liao L, Pyakurel U, Wang Y, Lai W : Coronectomy vs. total removal for third molar extraction : a systematic review. J Dent Res 91 : 659-665, 2004.

19) Kim SY, Hu KS, Chung IH, Lee EW, Kim HJ : Topographic anatomy of the lingual nerve and variations in communication pattern of the mandibular nerve branches. Surg Radiol Anat 26(2) : 128-135, 2004.

20) Nakamura A, Yamada T, Goto A, Kato T, Ito K, Abe Y, Kachi T, Kakigi R : Somatosensory homunculus as drawn by MEG. Neuroimage 7 : 377-386, 1998.

21) Nakahara H, Nakasato N, Kanno A, Murayama S, Hatanaka K, Itoh H, Yoshimoto T : Somatosensory-evoked fields for gingiva, lip, and tongue. J Dent Res 83 : 307-311, 2004.

22) Tamura Y, Shibukawa Y, Shintani M, Kaneko Y, Ichinohe T : Oral structure representation in human somatosensory cortex. Neuroimage 15 : 128-135, 2008.

23) Maezawa H : Cortical mechanisms of tongue sensorimotor functions in humans: a review of the magnetoencephalography approach. Front Hum Neurosci 2017 doi : 10.3389/fnhum. 2017. 00134

24) Maezawa H, Yoshida K, Nagamine T, Matsubayashi J, Enatsu R, Bessho K, Fukuyama H : Somatosensory evoked magnetic fields following electric tongue stimulation using pin electrodes. Neurosci Res 62 : 131-139, 2008.

25) Sakamoto K, Nakata H, Kakigi R : Somatosensory-evoked magnetic fields following stimulation of the tongue in humans. Clin Neurophysiol 119 : 1664-1673, 2008.

26) Yoshida K, Maezawa H, Nagamine T, Fukuyama H, Murakami K, Iizuka T : Somatosensory evoked magnetic fields to air-puff stimulation on the soft palate. Neurosci Res 55(2) : 116-122, 2006.

27) Yamashita H, Kumamoto Y, Nakashima T, Yamamoto T, Inokuchi A, Komiyama S : Magnetic sensory cortical responses evoked by tactile stimulations of the human face, oral cavity and flap reconstructions of the tongue. Eur Arch Otorhinolaryngol 256 : 42-46, 1999.