Evaluation of lip sensory disturbance using somatosensory evoked magnetic fields

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Highlights

· We evaluated unilateral sensory disturbance of the lip by the unilateral lip-stimulated somatosensory evoked fields

· Either side of lip stimulation induced response at 25 ms in all healthy volunteers, which was not detected by affected-side stimulation in patients

· Response at 25 ms can be an objective and effective parameter to indicate lip sensory abnormality

Abstract

Objective: To evaluate lip sensory dysfunction in patients with inferior alveolar nerve injury by lip-stimulated somatosensory evoked fields (SEFs).

Methods: SEFs were recorded following electrical lip stimulation in 6 patients with unilateral lip sensory disturbance and 10 healthy volunteers. Lip stimulation was applied non-invasively to each side of the lip with the same intensity using pin electrodes.

Results: All healthy volunteers showed the earliest response clearly and consistently at around 25 ms (P25m) and at least one of the following components, P45m, P60m, or P80m, over the contralateral hemisphere. The ranges of the peak latencies were 23–33, 42–50, 56–67, and 72–98 ms for right-side stimulation and 23–34, 46–49, 52–68, and 71–90 ms for left-side stimulation. Affected-side stimulation did not evoke P25m component in any patients, but invoked traceable responses in 5 patients whose latencies were 57, 89, 65, 53, and 54 ms. Unaffected-side stimulation induced P25m in 2 patients at 27 and 25 ms, but not in the other 4 patients.

Conclusion: The P25m component of lip SEFs can be an effective parameter to indicate lip sensory abnormality.

Significance: Lip sensory dysfunction can be objectively evaluated using magnetoencephalography.

1. Introduction

Iatrogenic inferior alveolar nerve (IAN) injury causes complication of the patients due to its resultant sensory impairment of the lower lip, chin, and lower teeth (Kobayashi et al., 2006; Lee et al., 2011). For example, previous reports have documented that the incident rate of IAN injury by third molar extraction varied from 2 to 17% (Renton et al., 2005; Hatano et al., 2009; Leung and Cheung, 2009; Cilasun et al., 2011; Long et al., 2012). However, precise evaluation and management of lip sensory abnormality is difficult because there is no quantitative testing battery. Commonly-used sensibility tests, e.g., two-point discrimination (TPD), have low reproducibility and reliability because they depend on the patient's subjective reporting of sensory information. Thus, a means of quantitative objective measurement is needed.

Our previous studies demonstrated that the evoked cortical response for tongue stimulation measured by magnetoencephalography (MEG) can serve as an objective method to detect sensory disturbance of the tongue caused by unilateral lingual nerve damage (Maezawa et al., 2008, 2011). In those studies, we calculated the laterality of the somatosensory evoked magnetic fields (SEFs) for affected-side and unaffected-side (control-side) stimulation of the tongue to estimate the asymmetry of the cortical activation between stimulus sides. However, this method has limited application for patients with bilateral deficits because it requires a control-side and cannot be applied to disturbances caused by surgeries such as sagittal split ramus osteotomy (SSRO), which carry major risks of IAN damage (Westermark et al., 1998; Panula et al., 2001). To evaluate sensory abnormality of the lip using MEG, we need an objective indicator of lip SEFs that does not require a control-side.

The aim of the study was to investigate the unilateral lip SEFs in patients with unilateral IAN injury, which can be used for evaluating the lip sensory dysfunction.

2. Materials and methods

2.1. Subjects

We recruited 6 right-handed patients with sensory disturbance of the lower lip after minor oral surgery underwent at privately owned dental clinic (4 men and 2 women aged 32–56 years; mean 47.6 years) (Table 1). All of the patients met 3 requirements: (1) The sensory defect was caused by unilateral IAN injury; (2) Rating of the subjective sensation of the affected area was lower than half of that of the unaffected area; (3) TPD of the affected area exceeded 5 mm. For comparison, 10 right-handed volunteers (6 men and 4 women aged 24–62 years; mean 39.1 years) without a history of neurological illness were recruited. There was no significant difference in age between the healthy volunteers group and the patients group by Mann-Whitney U-test ($p = 0.147$). Written informed consent was obtained from all participants, which followed the study protocol approved by the Ethics Committee, Kyoto University Graduate School of Medicine.

2.2. Sensibility tests of the lip in patients

TPD and tactile sensation of the affected- and unaffected-sides were evaluated in a quiet room by the same observer (HM) similarly to our previous study (Maezawa et al., 2011). Subjects were requested to close their eyes, and sensibility tests were started.

TPD was evaluated by 5 grades: ≤ 5 mm and >5, 10, 15, and 20 mm using the Disk-Criminator (Kono Seisakusyo, Chiba, Japan) with 4 stepwise spaces between 5 to

20 mm. Subjects were instructed to indicate with their fingers whether they felt one or two-points during the application of the Disk-Criminator.

Tactile sensation was also classified into 5 grades from S1 to S5, indicating most severe to mildest impairment, using a perception tester (Kono Seisakusyo, Chiba, Japan). The perception tester is composed of four discrete monofilaments having different diameters to produce 4 steps of stimulus magnitude. The monofilament was applied to the same point as electrical stimulation (2 cm lateral to the midline of the lower lip crust) with sufficient force until it bended, and held for 2 s. Subjects were required to gesture “yes” each time when they sense the application of the monofilaments. The force expressed by S1, S2, S3, and S4 corresponded to 2.83, 3.61, 4.31, and 6.65 using filament marking number by Semmes-Weinstein monofilaments, respectively (Semmes et al., 1960; Weinstein, 1962).

2.3. Lip stimulation

The right- and left-sides of the lower lip (2 cm lateral to the midline) were stimulated separately using an electrical stimulator (SEN7203, Nihon Kohden, Tokyo, Japan) through a pair of pin electrodes non-invasively as described previously (Maezawa et al., 2008, 2011). Biphasic current square pulses (0.5 ms for 1 phase) were used to reduce stimulus artifact effectively. Inter-stimulus interval was 1.00 s. A stimulus intensity at 3 times the sensory threshold for the unaffected area was used for both sides in the patients. The intensity for the healthy volunteers was thrice the sensory threshold for each side. In total, 600 responses were averaged in each session. The unaffected-side was stimulated first in the patients. The order of stimulus side was counterbalanced for the healthy volunteers.

2.4. MEG recordings

SEFs were recorded with a whole-head neuromagnetometer (Vectorview; Elekta Neuromag, Helsinki, Finland). This device had 102 trios that are composed of a magnetometer and a pair of planar gradiometers. A pair of two orthogonally-oriented planar gradiometer detects the two orthogonal derivatives of the magnetic fields along either latitude or longitude on the location of the sensor specified by the device system. Data from 204 planar gradiometers were collected for analysis, since they can detect the largest signal just above the corresponding generator source (Hämäläinen et al., 1993). The recording passband was 0.1 to 990 Hz and the sampling rate was 2997 Hz. The analysis window for averaging extended from 100 ms before to 500 ms after each trigger signal, and epochs with signal variations greater than 3000 fT/cm were excluded automatically from averaging. Two sessions separated by a rest period were performed for each stimulus side of the lip. Waveforms were averaged only when their reproducibility was confirmed. Group-averaged data of two sessions were used for later analysis. The baseline activity of SEFs was calculated from −20 to 0 ms before stimulus onset.

Four head position indicator coils were placed on the scalp and their locations with respect to the anatomical fiducial points (nasion, bilateral preauricular points) were determined with a 3-dimensional digitizer (Fastrak; Polhemus, USA). Location of the head with respect to the sensors was determined before each MEG measurement condition. Consequently, it was possible to align the MEG and magnetic resonance image (MRI) coordinate systems.

2.5. Data analysis

2.5.1. Criterion for response detection

A response was defined when the signal exceeded 2 standard deviations (SD) (Nagamine et al., 1996; Yoshida et al., 2006) of the baseline activity for at least 5 ms in components earlier than 40 ms and for at least 10 ms in those later than 40 ms. To assess responses derived from the primary somatosensory cortex, components whose peak latency ranged between 10 and 100 ms were used for further analysis. The peak latency of the response was measured from the channel showing the maximal signal. Isocontour maps were constructed at the selected time points using the minimum-norm estimate after the signals were digitally low-pass filtered at 100 Hz.

2.5.2. Source modeling

The sources of the magnetic fields were modeled as equivalent current dipoles (ECDs). To identify the source of ECDs, a spherical head model whose center best fit the local curvature of the individual's brain surface was adopted based on MRI. We accepted only ECDs attaining 85% goodness-of-fit. Patient 2 was excluded from the estimation of ECDs because MRI information was unavailable.

2.5.3. Statistical analysis

To assess the activated cortical response of P25m (details of the component will be illustrated in the results section), we selected the maximal signal channel over the contralateral hemisphere and calculated the mean of its absolute amplitude (ABS) during the 5 ms time period centering at the peak latency between 20 and 35 ms. We introduced the term "mean ABS (mABS)" for this value. In the cases when no

prominent peak could be detected, mABS was calculated during the 5 ms period centering at the time point of maximum amplitude between 20 and 35 ms. Laterality between the stimulus sides was analyzed with Wilcoxon signed-rank test for sensory threshold, latency, magnitude, dipole moment, and mABS. A significant level was set at $p<0.05$.

3. Results

3.1. Sensibility tests in patients

The TPD grades for the affected-side were >5 mm in 2 patients and >10 mm in 4 patients (Table 2). Tactile deficit was graded as S2 in 2 patients and S3 in 4 patients.

For the unaffected-side, TPD was ≤5 mm and tactile sensation was S5 in all patients.

3.2. Sensory threshold and stimulus intensity

The sensory threshold of the right- (0.06–0.23 mA) and left- (0.05–0.20 mA) sides in the healthy volunteers was not significantly different ($P = 0.263$). In the patients, the sensory threshold of the affected area (0.55–2.8 mA) was significantly higher than that of the unaffected area (0.07–0.25 mA) ($P = 0.028$) (Table 2). Therefore, the intensity used for stimulation in healthy volunteers was 0.18–0.69 mA for the right-side and 0.15–0.60 mA for the left-side, and the intensity adopted for patients was 0.21–0.75 mA for both sides.

3.3. Waveform configuration

Clear responses were detected over the bilateral temporoparietal areas in all healthy volunteers. A representative subject (Subject 2) showed 2 main deflections peaking at

25 and 67 ms over the left hemisphere following right-side stimulation (Fig. 1A[1]). We designated these 2 responses as P25m and P60m according to the nomenclature system employed in previous studies of lip SEFs by electrical stimulation (Hoshiyama et al., 1996; Nagamatsu et al., 2001; Nakahara et al., 2004) and mechanical stimulation (McDonald et al., 1996; Nakamura et al., 1998; Yamashita et al., 1999; Disbrow et al., 2003; Nguyen et al., 2004; Nevalainen et al., 2006; Tamura et al., 2008). In addition, as in the case of subject 4, we detected 2 components other than P25m and P60m at around 45 ms and 80 ms over the contralateral hemisphere, i.e., at 47 and 73 ms over the right hemisphere for left-side stimulation, which we named P45m and P80m (Fig. 1A[2]). While P25m was identified only over the contralateral hemisphere, P45m, P60m, and P80m were all detected over bilateral hemispheres.

3.4. Contralateral responses in healthy volunteers

P25m was detected over the contralateral hemisphere in all healthy volunteers following stimulation of either side (Fig. 2). The range of peak latencies of P25m was 23–33 ms and 23–34 ms for the right-side stimulation and left-side stimulation, respectively. The range of magnitude of P25m was 11.6–27.4 fT/cm after right-side stimulation and 10.3–24.3 fT/cm after left-side stimulation.

P45m, P60m, and P80m were observed in 5, 6, and 5 subjects for the right-side stimulation, and in 6, 5, and 6 subjects for the left-side stimulation. The range of latencies of P45m, P60m, and P80m was 42–50, 56–67, and 72–98 ms, respectively, for the right-side stimulation and 46–49, 52–68, and 71–90 ms for the left-side stimulation. The response magnitudes of P45m, P60m, and P80m were 10.5–38.1, 8.5–31.6, and

11.5–43.7 fT/cm for the right-side stimulation and 7.1–61.5, 23.9–50.8, and 13.8–48.8 fT/cm for the left-side stimulation.

Isofield contour maps of each component showed a dipolar pattern (Fig. 1B). The directions of estimated ECDs were similarly posteriorly-oriented in all the components (Fig. 1B). Estimated ECDs were located around the lower part of the central sulcus in each subject's MRI (Fig. 1C). The strength of the P25m ECDs was 2.1–3.2 nAm and 1.4–4.8 nAm after right- and left-sides stimulation, respectively. The strength of the P45m, P60m, and P80m ECDs were 2.9–8.4, 2.5–6.3, and 2.2–8.4 nAm for right-side stimulation, and 4.4–10.8, 4.0–11.5, and 2.5–12.9 nAm for left-side stimulation. No significant difference was noted in latency, magnitude, or strength of the ECDs between sides in the P25m component ($P = 0.417$, 0.767, and 0.260). The analysis for side difference was not performed for P45m, P60m, and P80m because of the small sample size.

3.5. Contralateral responses in patients

P25m was detected in 2 patients (Patients 1 and 2) at 27 and 25 ms after unaffected-side stimulation, respectively (Fig. 3, Table 2). In the remaining 4 patients (Patients 3–6), P25m component was not identified since response around 25 ms did not appear as an independent component but looked like a notch or a shoulder (Fig. 3, Table 2). The magnitudes of the P25m components were 25.8 and 17.5 fT/cm in patients 1 and 2, respectively. The strength of the ECDs was 3.3 and 2.4 nAm in patients 1 and 2, respectively. P45m, P60m, and P80m were observed in 3, 3, and 3 patients, and their latencies were 41–46, 57–64, and 78–90 ms, respectively. The magnitudes of each

component were 27.4–37.1, 14.5–27.7, and 12.9–31.6 fT/cm. The ECD strengths for P45m, P60m, and P80m were 4.6–10.6, 4.5–5.4, and 1.6–6.4 nAm, respectively.

P25m was not detected following the affected-side stimulation in any patients (Fig. 3, Table 2). Small responses were observed for affected-side in 5 patients (Patient 1 and 3–6) whose first peaks were at 57, 89, 65, 53, and 54 ms, respectively. The magnitudes of these responses were 10.4–22.4 fT/cm. The strength of the ECDs was 4.2, 3.8, and 3.2 nAm in patients 1, 5, and 6, respectively. The remaining 2 components observed in patients 3 and 4 did not meet the necessary criteria for dipole analysis. Statistical analysis was not applicable to P25m, P45m, P60m, and P80m because of the small sample size.

3.6. mABS in healthy volunteers and patients

The mABS for the right- and left-sides in healthy volunteers ranged from 8.2 to 23.2 fT/cm and from 9.8 to 20.4 fT/cm, respectively (Fig. 4). No significant difference was recognized for the mABS between the sides in healthy volunteers ($P = 0.683$). The mABS for the affected-side in patients was 2.3 to 4.6 fT/cm, which could be recognized as the noise level since no responses were detected. This range was definitely smaller than that for the unaffected-side of 10.1 to 19.5 fT/cm (Table 2, Fig. 4).

4. Discussion

We evaluated lip sensory disturbance in patients with IAN injury objectively by cortical activation following lip stimulation using a MEG system. The P25m component of lip SEFs was detected over the contralateral hemisphere following unilateral

stimulation in all healthy volunteers, but it was not observed in every patient after affected-side stimulation.

P25m, the first component recognized, was detected consistently and only over the contralateral hemisphere in all of the healthy volunteers. This can be regarded as the component corresponding to the P20m response after electrical lip stimulation using a pair of ball electrodes in the previous SEFs study (Hoshiyama et al., 1996), because the latency and the dipole orientation of these components were similar to each other, and both of the responses were the first prominent components observed only over the contralateral hemisphere.

Nagamatsu et al. (2001) delivered electrical stimulation at 9 times the sensory threshold through a clip electrode and demonstrated that the initial component of the lip SEFs had an anteriorly directed ECD with a peak latency of 15 ms (N15m). However, we did not detect this component here. This might be because of the different type of electrical stimulation used in our study. We used pin electrodes because they can safely and accurately stimulate a small region of the lip with low stimulus intensity. In our unpublished data comparing 2 types of electrical stimulation in 5 healthy volunteers, the sensory threshold of the lower lip using clip electrodes was 5.4 times greater than that using pin electrodes (Unique Medical, Tokyo, Japan; clip 0.344 mA, pin 0.064 mA). Moreover, the 9 times sensory threshold intensity employed in the previous study was greater than the 3 times sensory threshold used here, so the reduction of the initial component may have been a result of the wide gap in absolute intensities of electrical stimulation. The P23m component following N15m over the contralateral hemisphere in the previous report corresponds to our P25m because of its similar latency and the posteriorly oriented direction of the dipole.

P25m was not the initial component, but it can still be a useful and reliable baseline indicator of lip sensory function because it was observed consistently in all of the healthy volunteers based on the criterion for the response detection. The main problems associated with SEPs and SEFs for trigeminal nerve are the contamination of stimulus artifacts and muscle activities due to the short distance between stimulus and recording area (Altenmüller et al., 1990; Karhu et al., 1991; Nagamatsu et al., 2000). Since the early time rage of trigeminal SEFs was easily contaminated by these artifacts, it is sometimes difficult to differentiate cortical responses from artifacts. In our methods, by low stimulus intensity using pin electrodes, the magnitude returned to baseline level in a short time before P25m component started (Fig 2, 3). Thus, recording lip SEFs using pin electrodes has an advantage to detect the early component of P25m reliably and easily.

The constant detection of a P25m component for unilateral stimulation indicates that unilateral sensory disturbance can be judged solely by affected-side stimulation. Since this method would not require a control-side, it can also be useful for the patients with bilateral oral surgery applied for the region innervated by IAN, and so has an advantage of wide clinical application.

A P25m component was detected for the unaffected-side in 2 patients (Patients 1 and 2) (Fig. 2). However, it was not identified in the rest of 4 patients (Patients 3–6) since it appeared as a notch or a shoulder embedded in the following components. This alternative waveform configuration might be related to the point of stimulation of the lip. We applied the stimulation 2 cm laterally from the midline, as in the previous study (Hoshiyama et al., 1996), and self-reporting by the subjects confirmed that electrical stimulation was induced only for one side of the lip. Nevertheless, since the lip around

the midline is innervated by bilateral fibers, stimulation one side of the lip may have recruited trans-median excitation from the other side forming responses of containing contribution from both sides in some subjects. Therefore, this stimulation site of "2 cm lateral from the midline" in unaffected-side might have missed the excitation of the other side (affected-side) resulting suppressed response over the cortex contralateral to the stimulus-side. Further studies are needed to clarify this issue by concentrating on the effect of the stimulus location around the midline.

In conclusion, the P25m component of lip SEFs by MEG measurement can serve as an effective baseline parameter of sensory function of the lip. Lip sensory disturbances associated with oral surgery can be detected objectively using MEG.

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Table 1

Profiles of the patients with unilateral lip sensory disturbance.

Pt	Sex	Age (year)	Affected side	Period (month)	Oral surgery
1	M	45	R	6	Mandibular cyst removal
2	F	32	L	1.5	Impacted tooth extraction
3	M	46	L	36	Mandibular cyst removal
4	M	51	R	2	Mandibular cyst removal
5	M	56	L	2	Mandibular cyst removal
6	F	56	R	2	Implant operation

Pt, Patient Number; M, Male; F, Female; L, Left; R, Right.

Table 2

Sensory function of the lip detected by sensibility tests and electrophysiological findings.

Pt	Sensibility tests		Sensory threshold (mA)		Intensity * (mA)		mABS (fT/cm)		P25m	
	TPD (mm)	TS	U	A			U	A	U	A
1	15	S2	0.25	2.5	0.75		19.5	4.6	○	×
2	20	S2	0.07	2.8	0.21		10.1	2.3	○	×
3	20	S3	0.09	0.55	0.27		16.1	3.6	×	×
4	20	S2	0.20	0.75	0.60		11.3	2.6	×	×
5	15	S3	0.15	0.85	0.45		17.1	3.2	×	×
6	20	S3	0.20	1.7	0.60		16.3	2.9	×	×
		Mean	0.155	1.53	0.465					
Healthy volunteers			R	L	R	L	R	L		
		Mean	0.125	0.114	0.375	0.342	13.80	14.72		

* Thrice the sensory threshold of the unaffected-side in the patients. Pt, Patient number; TPD, Two-point discrimination; TS, Tactile sensation; U, Unaffected side; A, Affected side; R, Right; L, Left; Intensity, Stimulus intensity; ○, Detected; ×, Non-detected.

Figure legends

Figure 1. (A) SEF waveforms of a single channel over the contralateral hemisphere in healthy volunteers (Subjects 2 and 4). Each tracing started 20 ms before to 200 ms after the stimulus onset. [1] Two components (P25m and P60m) were detected over the left hemisphere following right-side stimulation at the peak latency of 25 ms and 67 ms in subject 2. [2] Three components (P25m, P45m, and P80m) were observed over the right hemisphere for left-side stimulation at 24 ms, 47 ms, and 73 ms in subject 4. While P25m was detected consistently in all of the healthy volunteers, the other components, P45m, P60m, and P80m, were not observed stably. Since the polarity of the signal's derivative along either latitude or longitude axis was determined by the device system, downward or upward deflection of the waveform was subject to the relationship between the directions of source and sensor. **(B)** Isocontour maps were obtained from 2 components (P25m and P60m) over the left hemisphere following right-side stimulation in subject 2, and acquired from other 2 components (P45m and P80m) over the right hemisphere for left-side stimulation in subject 4. The exact timing is shown in each map. The contour steps are 5 fT (P25m) and 8 fT (P60m) in subject 2, and 5 fT (P45m and P80m) in subject 4, respectively. The red and blue lines indicate outgoing and incoming magnetic fluxes, respectively. The green arrows show the location and direction of estimated ECDs projected on the skull surface to produce the SEF distribution. Arrowheads indicate the negative pole of the ECDs. The directions of all ECDs are similarly posteriorly-oriented among them. **(C)** ECDs of each component were superimposed on the slices of the MR images of subject 2 (P25m and P60m) and subject 4 (P45m and P80m). They were located in the same area around the lower part of the central sulcus. Subject, Healthy subject number.

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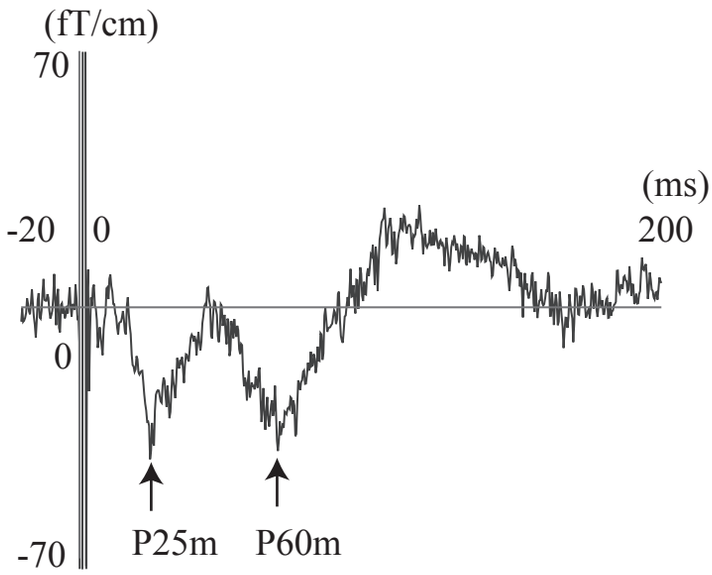
Figure 2. Waveforms of the maximum amplitude channel over the contralateral hemisphere for right- and left-sides stimulation in all of the healthy volunteers. The vertical scale was 70 fT/cm in subjects 1~3, and 40 fT/cm in subjects 4~10. P25m components are indicated by the arrowheads. Note that P25m components were constantly detected for stimulation of either side in all of the healthy volunteers. Rt stim., Right-side stimulation; Lt stim., Left-side stimulation; Subject, Healthy subject number.

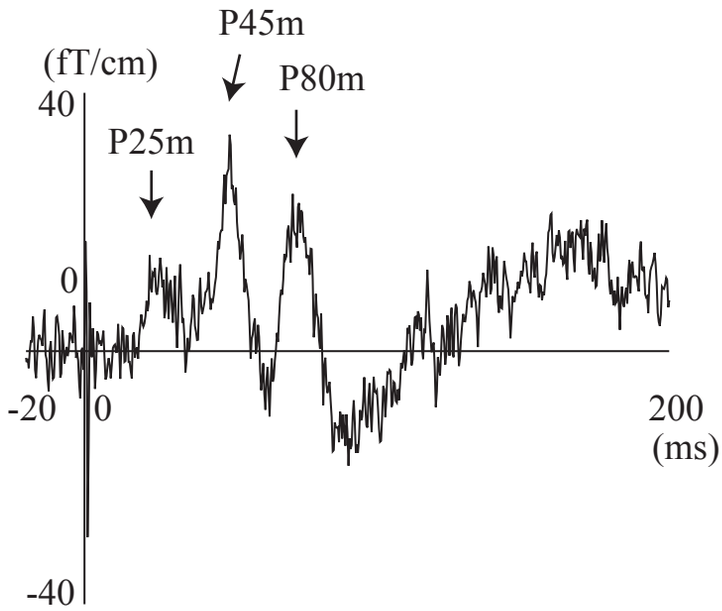
Figure 3. Waveforms of the maximum amplitude channel over the contralateral hemisphere for unaffected- and affected-sides stimulation in the patients. The vertical scale was 40 fT/cm. P25m components for the unaffected-side are indicated by the arrowheads. The responses for the affected-side stimulation are shown by the circles. Note that the affected-side stimulation did not induce the P25m component in any patients. Unaffected stim., Unaffected-side stimulation; Affected stim., Affected-side stimulation; Rt stim., Right-side stimulation; Lt stim., Left-side stimulation; Patient, Patient number.

Figure 4. The mABS in all healthy volunteers and patients. **(A)** The mABS between the right-side and the left-side in healthy volunteers. No significant difference of the mABS was recognized between sides. **(B)** The mABS between the affected-side and the unaffected-side in patients. The mABS in the affected-side was clearly smaller than that in the unaffected-side. Rt stim., Right-side stimulation; Lt stim., Left-side stimulation; Unaffected stim., Unaffected-side stimulation; Affected stim., Affected-side stimulation; Healthy, Healthy subject number; Patient, Patient number.

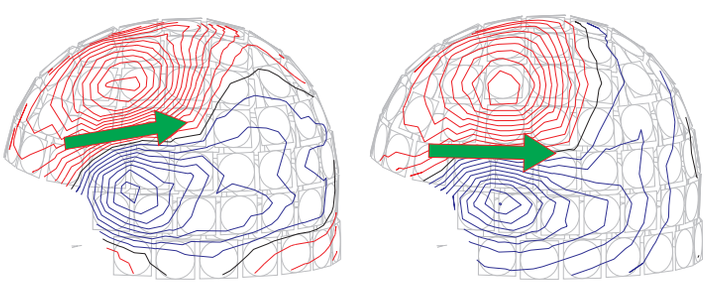
(A) [1] Subject 2



[2] Subject 4

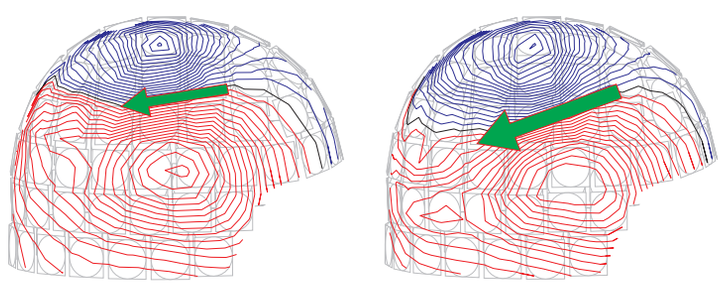


(B) Left hemispheres in subject 2



25 ms (P25m) 67 ms (P60m)

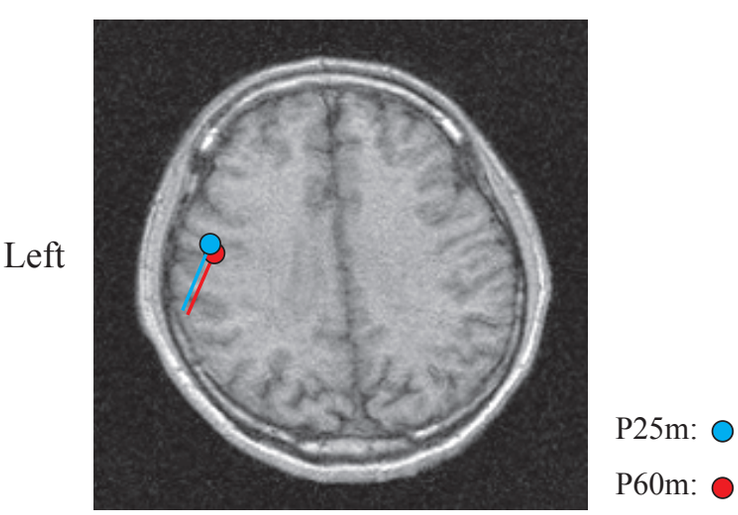
Right hemispheres in subject 4



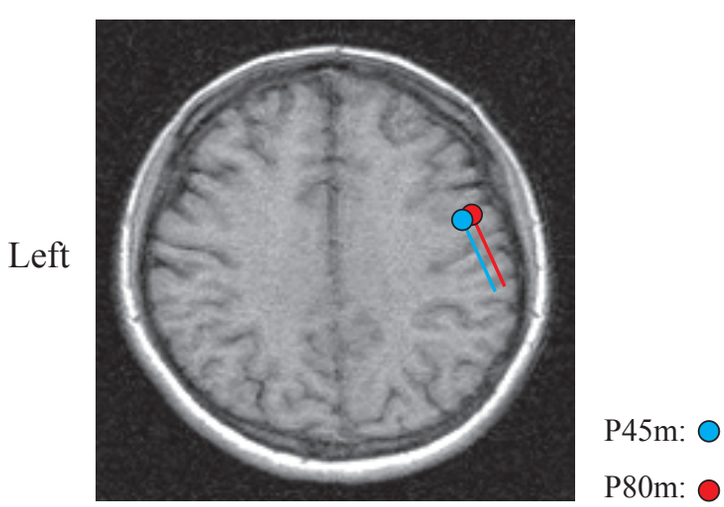
47 ms (P45m) 73 ms (P80m)

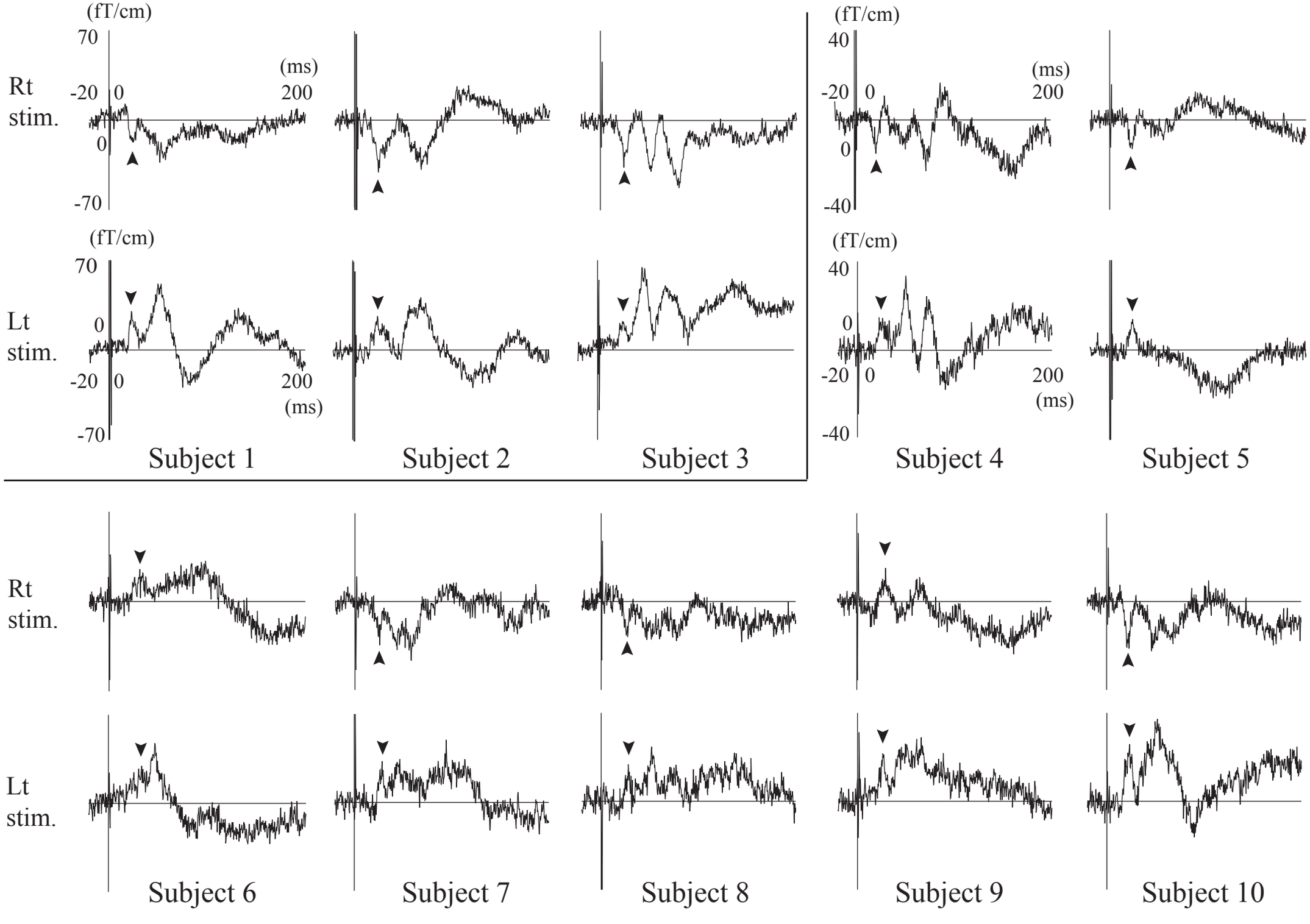
(C)

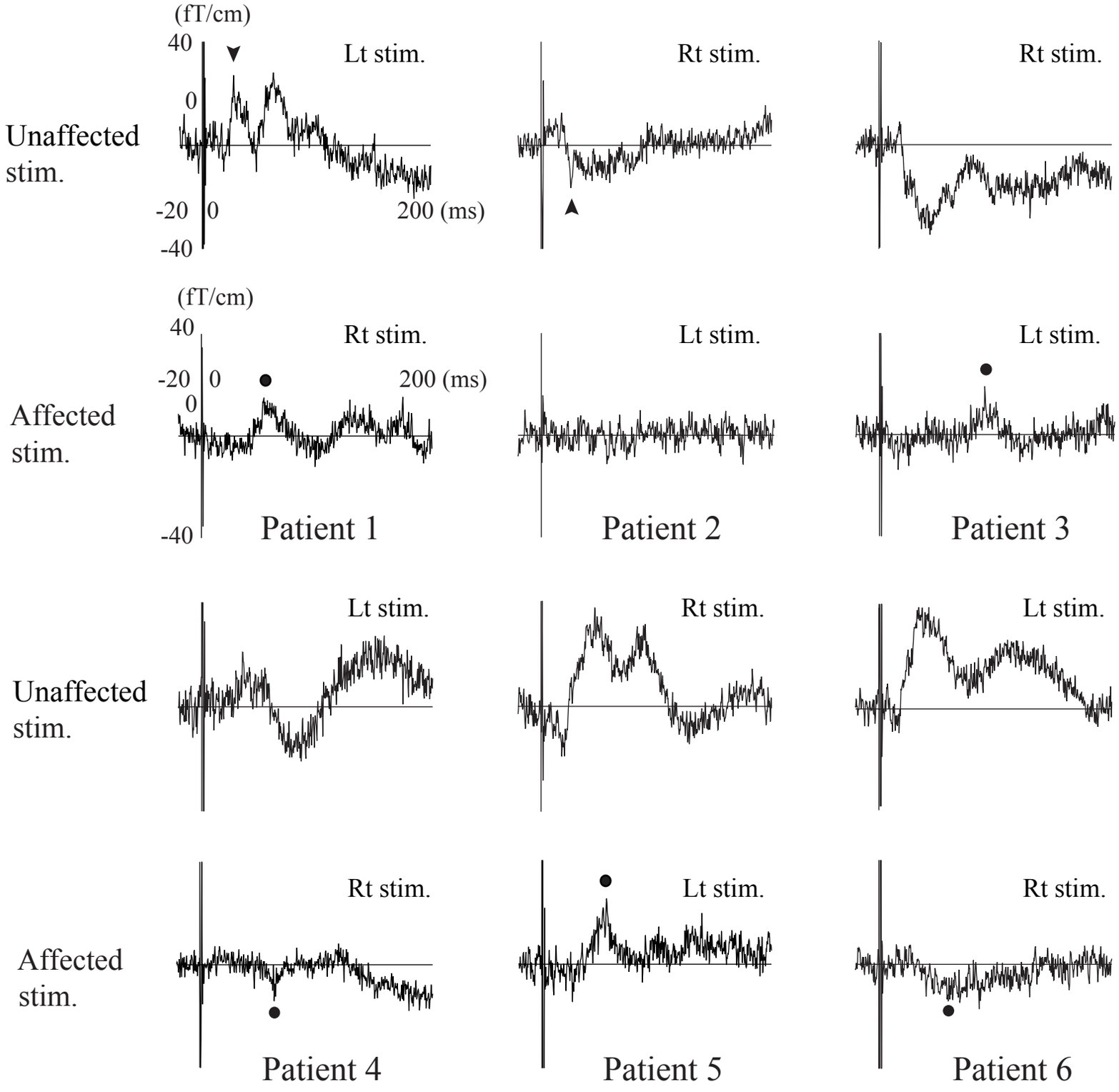
Subject 2

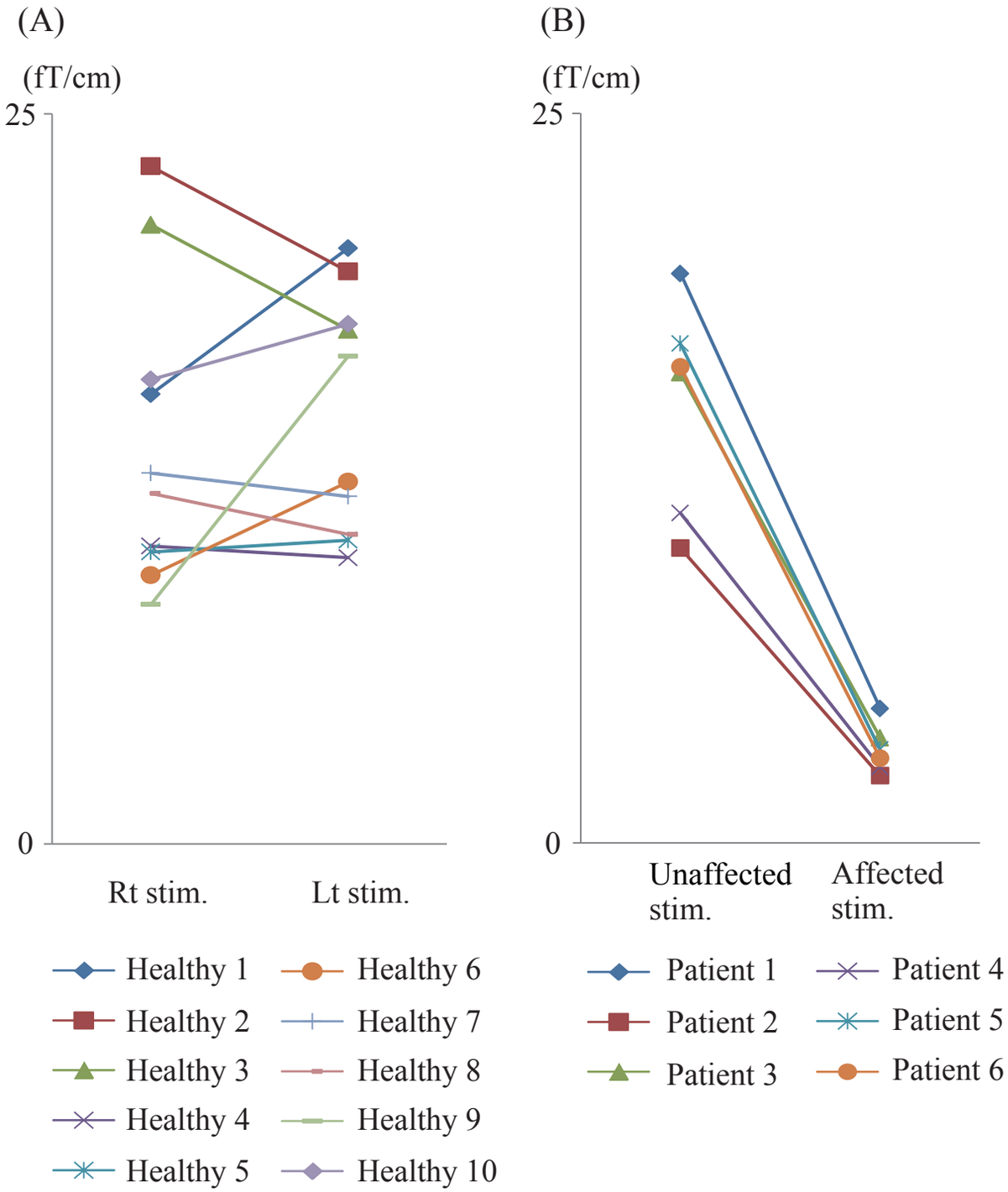


Subject 4




(fT/cm)
70
-70
-20
0
200
(ms)
Rt stim.
Lt stim.
(fT/cm)
40
-40
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
Subject 6
Subject 7
Subject 8
Subject 9
Subject 10


(fT/cm)
40
0
-20
0
200 (ms)
-40
Lt stim.
Rt stim.
Rt stim.
Unaffected stim.
(fT/cm)
40
-20
0
200 (ms)
0
-40
Rt stim.
Lt stim.
Lt stim.
Affected stim.
Patient 1
Patient 2
Patient 3
Lt stim.
Rt stim.
Lt stim.
Unaffected stim.
Rt stim.
Lt stim.
Rt stim.
Affected stim.
Patient 4
Patient 5
Patient 6


(A)
(fT/cm)
25
0
Rt stim.
Lt stim.
Healthy 1
Healthy 2
Healthy 3
Healthy 4
Healthy 5
Healthy 6
Healthy 7
Healthy 8
Healthy 9
Healthy 10
(B)
(fT/cm)
25
0
Unaffected stim.
Affected stim.
Patient 1
Patient 2
Patient 3
Patient 4
Patient 5
Patient 6